

MARK G. PAPICH

Saunders Handbook of
**VETERINARY
DRUGS** **THIRD EDITION**

Small and Large Animal



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Conversion Information

Weights and Measures

Prefixes for Fractions

deci = 10^{-1}

centi = 10^{-2}

milli = 10^{-3}

micro = 10^{-6}

nano = 10^{-9}

pico = 10^{-12}

Temperature Measures

$^{\circ}\text{C} = 5/9 \times (^{\circ}\text{F} - 32)$

$^{\circ}\text{F} = 9/5 \times (^{\circ}\text{C}) + 32$

Percentage Equivalents

0.1% solution contains: 1 mg per mL

1% solution contains: 10 mg per mL

10% solution contains: 100 mg per mL

Milliequivalent Conversions:

1 mEq Na = 23 mg Na = 58.5 mg NaCl

1 g Na = 2.54 g NaCl = 43 mEq Na

1 g NaCl = 0.39 g Na = 17 mEq Na

1 mEq K = 39 mg K = 74.5 mg KCl

1 g K = 1.91 g KCl = 26 mEq K

1 g KCl = 0.52 g K = 13 mEq K

1 mEq Ca = 20 mg Ca

1 g Ca = 50 mEq Ca

1 mEq Mg = 0.12 g $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$

1 g Mg = 10.2 g $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ =
82 mEq Mg

10 mmol P_i = 0.31 g P_i = 0.95 g PO_4

1 g P_i = 3.06 g PO_4 = 32 mmol P_i

Metric Conversions

Volume Measurements:

Teaspoonful = 5 mL

Tablespoonful = 15 mL

Fluid ounce = 30 mL

Pint = 473 mL

Quart = 946 mL

Linear Measurements:

1 mm = 0.04 in

1 in = 25.4 mm = 2.54 cm

1 m = 39.4 in

1 in = 0.025 m

Weight Measurements:

1 mg = 0.017 grain

1 grain = 65 mg

1 g = 0.035 oz

1 oz = 28.3 g

1 kg = 2.2 lb

1 lb = 0.45 kg

Weights and Equivalents: Metric System

Weight:

kilogram = kg = 1000 grams

gram = g = 1 gram

milligram = mg = 0.001 gram

microgram = mcg = 0.001 milligram

Volume:

liter = L = 1 L

milliliter = mL = 0.001 L

Avoirdupois Weight:

1 ounce (oz) = 437.5 grains

1 pound (lb) = 16 ounces = 7000 grains

Metric and Apothecary Equivalents

Exact Weight Equivalents:

Metric	Apothecary
1 mg	1/64.8 grain
64.8 mg	1 grain
324 mg	5 grains
1 g	15.432 grains
31.103 g	1 ounce (480 grains)

Exact Volume Equivalents:

Metric	Apothecary
1.00 mL	16.23 minims
3.69 mL	1 fluidram (60 minims)
29.57 mL	1 fluid ounce (480 minims)
473.16 mL	1 pint (7,680 minims)
946.33 mL	1 quart (15,360 minims)

Conversion of Body Weight

Kilograms to Pounds and to Body Surface Area in Square Meters

Body Weight in Kilograms	Body Weight in Pounds	Body Surface Area in Square Meters	Body Weight in Kilograms	Body Weight in Pounds	Body Surface Area in Square Meters
1	2.2	0.1	36	79.37	1.11
2	4.41	0.16	37	81.57	1.13
3	6.61	0.21	38	83.77	1.15
4	8.82	0.26	39	85.98	1.17
5	11.02	0.3	40	88.18	1.19
6	13.23	0.33	41	90.39	1.21
7	15.43	0.37	42	92.59	1.22
8	17.64	0.41	43	94.8	1.24
9	19.84	0.44	44	97	1.26
10	22.05	0.47	45	99.21	1.28
11	24.25	0.5	46	101.41	1.3
12	26.46	0.53	47	103.62	1.32
13	28.66	0.56	48	105.82	1.34
14	30.86	0.59	49	108.03	1.36
15	33.07	0.62	50	110.23	1.38
16	35.27	0.64	51	112.43	1.39
17	37.48	0.67	52	114.64	1.41
18	39.68	0.7	53	116.84	1.43
19	41.89	0.72	54	119.05	1.45
20	44.09	0.75	55	121.25	1.47
21	46.3	0.77	56	123.46	1.48
22	48.5	0.8	57	125.66	1.5
23	50.71	0.82	58	127.87	1.52
24	52.91	0.84	59	130.07	1.54
25	55.12	0.87	60	132.28	1.55
26	57.32	0.89	61	134.48	1.57
27	59.52	0.91	62	136.69	1.59
28	61.73	0.93	63	138.89	1.61
29	63.93	0.96	64	141.09	1.62
30	66.14	0.98	65	143.3	1.64
31	68.34	1	66	145.5	1.66
32	70.55	1.02	67	147.71	1.67
33	72.75	1.04	68	149.91	1.69
34	74.96	1.06	69	152.12	1.71
35	77.16	1.08	70	154.32	1.72

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- **Clear, concise instructions** that guide clients step-by-step through drug administration.

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Saunders Handbook of

VETERINARY DRUGS

Small and Large Animal

THIRD EDITION

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ELSEVIER
SAUNDERS

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With respect to any drug or pharmaceutical products identified, readers are advised to check the most current information provided (i) on procedures featured or (ii) by the manufacturer of each product to be administered, to verify the recommended dose or formula, the method and duration of administration, and contraindications. It is the responsibility of practitioners, relying on their own experience and knowledge of their patients, to make diagnoses, to determine dosages and the best treatment for each individual patient, and to take all appropriate safety precautions.

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*This is dedicated to the working professionals
who are at the forefront of veterinary practice,
administering medications every day to their patients.
Animal owners entrust these veterinarians with the care
of their animals, and it is my hope that this book
will facilitate safe and effective use of medicines
in their patients.*

Mark G. Papich

DISCLAIMER

Doses listed are species specific, unless otherwise listed. There is no assurance for safety and efficacy in other animal species not listed. Many of the doses listed are extralabel or are human drugs used in an off-label or extralabel manner. Federal regulations allow use of extralabel veterinary drugs and human drugs in non-food-producing animals when there is a valid veterinarian-client-patient relationship. However, there are restrictions for using these drugs in food-producing animals under the Animal Medicinal Drug Use Clarification Act (AMDUCA) of 1994. These drugs are prohibited from use in food-producing animals unless certain requirements are met, which include extended withdrawal times for meat and milk. These requirements can be found at www.avma.org/reference/amduca/amduca1.asp.

Doses listed are based on best available evidence at the time of the drug handbook preparation; however, the author cannot ensure efficacy of drugs used according to recommendations in this book. Other patient factors, or actions of the drug not known at the time of the book preparation, may affect efficacy. Adverse effects of which the author was not aware at the time of the handbook's preparation may be possible from drugs listed in this handbook.

Veterinarians using this handbook are encouraged to check current literature, product label, federal Freedom of Information (FOI), and the manufacturer's disclosure for information regarding efficacy and any known adverse effects or contraindications not identified at the time of preparation of this handbook.

Mark G. Papich

Preface

The third edition of this handbook was developed using a similar style, layout, and format as the second edition. Additions, changes in individual drug monographs, and expanded sections were provided with input and helpful suggestions from veterinarians and students and because new information has become available. New drugs that have been approved by the U.S. Food and Drug Administration (FDA), or for which there is new information about its use in the literature, have been added. The drugs listed represent the most important medications used in companion animals and livestock. Practically every drug monograph has been updated, and more than 35 new drugs have been added. In this edition, as in the one that preceded it, I included the most recently approved drugs for animals in addition to human medications for which veterinary uses have been identified. Information has been updated on clinical uses and regulatory requirements. The information on drug stability, storage, and compounding has been expanded. An increased effort has been made to include evidence-based information on the drug's efficacy and clinical use in the "Indications and Clinical Uses" and "Instructions for Use" sections. To make it easier to locate important information for each medication, the sections are divided into categories for drug interactions, precautions, pharmacology, and clinical use. Tables for quick reference can be found in the Appendix. These appendix tables include antibiotics of choice, drug interactions, regulatory information, phone numbers and Internet sites for drug information, and a section on drug dose calculations.

The book is designed for busy practitioners and students who need to use their time efficiently and locate accurate and reliable drug information quickly. The format is consistent from drug to drug, and veterinarians and their staff will quickly become familiar with the layout of each drug monograph in order to rapidly locate concise and accurate information about each drug.

In preparing this handbook, my priorities were accuracy and reliability. As in each of the first two editions, the indications for use and drug dosing information were prepared from a review of the literature or derived from reviews presented by clinical experts. In some cases, dosages originated from clinical studies; in other cases, they represent a consensus of clinical experience. Manufacturers' recommendations are considered in the dosing recommendations, but other suggestions (off-label indications and uses) also may be listed where the use and dosage have gone beyond those listed on the product's label. Where dosage recommendations have varied among sources, I have applied my clinical judgment and more than 25 years of experience in veterinary clinical pharmacology to derive a scientifically valid dose. In some cases, it may have been necessary to derive a dose based on extrapolations from human medicine, but this was limited to drugs for which the therapeutic index of the drug is high. To derive withdrawal times for food animals, the highest priority has been given to the withdrawal time approved by the FDA. When there was not an FDA-approved withdrawal time, suggestions made by the Food Animal Residue Avoidance Databank (FARAD; www.farad.org) were used. If neither of these was available, I listed a conservative estimate for a suggested withdrawal time based on the drug's pharmacokinetics and likelihood that it may cause harmful residues.

Each drug is listed primarily by its official name (USAN) that is recognized by the United States Pharmacopeia (USP; www.usp.org). Following each drug name is the brand or trade name and synonyms by which the drug also may be known. Not all of the generic names are necessarily listed. Drugs are listed alphabetically according to

their official name. Tables are presented in the front section of the book that cross-reference each drug's USAN to other names by which the drug is known. The cross-reference table lists drugs according to their functional classification and drug use. It may not include all of the known uses for a drug but represents the most common clinical use.

As clinical experience increases and our knowledge of the pharmacology of these drugs expands, new information may become available for the medications listed in this book. I welcome feedback relating to adverse effects observed, clinical experience, and omissions or errors identified. For these and other input and suggestions, I can be reached at mark_papich@ncsu.edu. Adverse drug events also should be reported to the drug sponsor directly or the FDA using this website: www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/.

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Mark G. Papich
Raleigh, North Carolina

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Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name
Acidifying agent	Ammonium chloride
Adrenal suppressant	Racemethionine
Adrenergic agonist	Trilostane
	Ephedrine hydrochloride
	Epinephrine
	Fenoldopam mesylate
	Phenylpropanolamine hydrochloride
	Pseudoephedrine hydrochloride
Adrenolytic agent	Mitotane
Alkalinizing agent	Potassium citrate
	Sodium bicarbonate
Alpha-2 antagonist	Atipamezole hydrochloride
	Yohimbine
Analgesic	Acetaminophen
	Amantadine
	Gabapentin
	Pregabalin
	Tramadol
Analgesic, nonsteroidal anti-inflammatory drug	Aspirin
	Carprofen
	Deracoxib
	Etodolac
	Firocoxib
	Flunixin meglumine
	Ibuprofen
	Indomethacin
	Ketoprofen
	Ketorolac tromethamine
	Meclofenamate sodium; Meclofenamic acid
	Meloxicam
	Naproxen
	Phenylbutazone
	Piroxicam
	Tepoxalin
Analgesic, opioid	Acetaminophen + codeine
	Buprenorphine hydrochloride
	Butorphanol tartrate
	Fentanyl citrate
	Fentanyl transdermal
	Hydrocodone
	Hydromorphone
	Loperamide hydrochloride
	Meperidine
	Methadone hydrochloride
	Morphine sulfate
	Oxymorphone hydrochloride
	Pentazocine
	Remifentanil
	Sufentanil citrate
Analgesic, opioid, antitussive	Butorphanol
	Codeine
	Hydrocodone

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name
Anesthetic	Alfuxalone Ketamine hydrochloride Propofol
Anesthetic, alpha-2 agonist	Tiletamine + zolazepam Detomidine hydrochloride Dexmedetomidine Medetomidine hydrochloride Romifidine hydrochloride
Anesthetic, barbiturate	Xylazine hydrochloride Methohexital sodium Pentobarbital sodium
Anesthetic, inhalant	Thiopental sodium Enflurane Halothane Isoflurane Methoxyflurane Sevoflurane
Antacid	Aluminum hydroxide and aluminum carbonate
Antiarrhythmic	Amiodarone Carvedilol Disopyramide Lidocaine Mexiletine Procainamide hydrochloride Quinidine Quinidine gluconate Quinidine polygalacturonate Quinidine sulfate Tocanide hydrochloride
Antiarrhythmic, calcium channel blocker	Diltiazem hydrochloride Verapamil hydrochloride
Antiarthritic agent	Chondroitin sulfate Glucosamine + chondroitin sulfate
Antibacterial	Polysulfated glycosaminoglycan Chloramphenicol Clofazimine Dapsone Florfenicol Fosfomycin Isoniazid Linezolid Methenamine Nitrofurantoin Polymyxin B Pyrimethamine Rifampin
Antibacterial, aminoglycoside	Amikacin Gentamicin sulfate Kanamycin sulfate Neomycin Tobramycin sulfate
Antibacterial, antidiarrheal	Sulfasalazine

Continued

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name
Antibacterial, antiparasitic	Metronidazole
Antibacterial, beta-lactam	Ronidazole
	Amoxicillin
	Amoxicillin + clavulanate potassium
	Ampicillin
	Ampicillin + sulbactam
	Carbenicillin
	Cefaclor
	Cefadroxil
	Cefazolin sodium
	Cefdinir
	Cefepime
	Cefixime
	Cefotaxime sodium
	Cefotetan disodium
	Cefovecin
	Cefoxitin sodium
	Cefpodoxime proxetil
	Cefquinome
	Ceftazidime
	Ceftiofur crystalline free acid
	Ceftiofur hydrochloride
	Ceftiofur sodium
	Cephalexin
	Cloxacillin sodium
	Dicloxacillin sodium
	Doripenem
	Ertapenem
	Imipenem + cilastatin
	Meropenem
	Oxacillin sodium
	Penicillin G
	Piperacillin sodium
	Ticarcillin + clavulanate potassium
Ticarcillin disodium	
Antibacterial, fluoroquinolone	Ciprofloxacin hydrochloride
	Danofloxacin mesylate
	Difloxacin hydrochloride
	Enrofloxacin
	Marbofloxacin
	Moxifloxacin
	Norfloxacin
	Orbifloxacin
Antibacterial, glycopeptide	Pradofloxacin
	Vancomycin
Antibacterial, lincosamide	Clindamycin hydrochloride
	Clindamycin palmitate
	Clindamycin phosphate
	Lincomycin hydrochloride
	Lincomycin hydrochloride monohydrate

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name
Antibacterial, macrolide	Azithromycin
	Clarithromycin
	Erythromycin
	Tilmicosin phosphate
	Tulathromycin
Antibacterial, potentiated sulfonamide	Tylosin
	Ormetoprim + sulfadimethoxine
	Trimethoprim + sulfadiazine
	Trimethoprim + sulfamethoxazole
Antibacterial, sulfonamide	Sulfachlorpyridazine
	Sulfadiazine
	Sulfadimethoxine
	Sulfamethazine
	Sulfamethoxazole
	Sulfaquinoxaline
Antibacterial, tetracycline	Chlortetracycline
	Doxycycline
	Minocycline hydrochloride
	Oxytetracycline
	Tetracycline
	Spectinomycin
Antibiotic, aminocyclitol Anticancer agent	Asparaginase (L-asparaginase)
	Bleomycin sulfate
	Busulfan
	Carboplatin
	Chlorambucil
	Cisplatin
	Cyclophosphamide
	Cytarabine
	Dacarbazine
	Doxorubicin hydrochloride
	Fluorouracil
	Hydroxyurea
	Lomustine
	Melphalan
	Mercaptopurine
	Methotrexate
	Mitoxantrone hydrochloride
	Plicamycin
	Streptozocin
	Thioguanine
Thiotepa	
Toceranib	
Anticholinergic	Vinblastine sulfate
	Vincristine sulfate
	Aminopentamide
	Atropine sulfate
	Glycopyrrolate
	Hyoscyamine
	Oxybutynin chloride

Continued

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name
Anticholinesterase agent	Neostigmine Physostigmine
Anticoagulant	Pyridostigmine bromide Dalteparin Dipyridamole Enoxaparin Heparin sodium Warfarin sodium
Anticonvulsant	Bromide Clonazepam Clorazepate dipotassium Felbamate Levetiracetam Lorazepam Midazolam hydrochloride Oxazepam Phenobarbital Phenobarbital sodium Phenytoin Phenytoin sodium Primidone Valproate sodium Valproic acid Zonisamide
Anticonvulsant, analgesic	Gabapentin Pregabalin
Anticonvulsant, tranquilizer	Diazepam
Antidiarrheal	Bismuth subsalicylate Diphenoxylate Kaolin + pectin Mesalamine Olsalazine sodium Paregoric
Antidote	Propantheline bromide Charcoal, activated Deferoxamine mesylate Dimercaprol Edetate calcium disodium Flumazenil Fomepizole Leucovorin calcium Methylene blue 0.1% Penicillamine Pralidoxime chloride Succimer Trientine hydrochloride

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name	
Antiemetic	Aprepitant	
	Dolasetron mesylate	
	Dronabinol	
	Granisetron hydrochloride	
	Maropitant	
	Meclizine	
	Mirtazapine	
	Ondansetron hydrochloride	
	Trimethobenzamide	
	Prochlorperazine edisylate	
Antiemetic, antidiarrheal	Prochlorperazine maleate (with isopropamide iodide)	
	Chlorpromazine	
Antiemetic, phenothiazine	Prochlorperazine edisylate	
	Prochlorperazine maleate	
	Trifluoperazine hydrochloride	
	Triflupromazine hydrochloride	
	Trimeprazine tartrate	
Antiemetic, phenothiazine, antihistamine	Promethazine hydrochloride	
	Propiopromazine hydrochloride	
Antiemetic, prokinetic agent	Metoclopramide hydrochloride	
Antiestrogen	Tamoxifen citrate	
Antifungal	Amphotericin B	
	Enilconazole	
	Fluconazole	
	Flucytosine	
	Griseofulvin	
	Itraconazole	
	Ketoconazole	
	Posaconazole	
	Terbinafine hydrochloride	
	Voriconazole	
	Antifungal, expectorant	Potassium iodide
		Cetirizine hydrochloride
	Antihistamine	Chlorpheniramine maleate
Clemastine fumarate		
Cyproheptadine hydrochloride		
Dimenhydrinate		
Diphenhydramine hydrochloride		
Hydroxyzine		
Tiludronate disodium		
Tripelennamine citrate		
Antihypercalcemic agent		Alendronate
		Etidronate disodium
	Pamidronate disodium	
Antihyperglycemic agent	Zoledronate	
	Gemfibrozil	
	Glipizide	
	Glyburide	
	Metformin	
Anti-inflammatory	Allopurinol	
	Colchicine	
	Dimethyl sulfoxide (DMSO)	
	Niacinamide	
	Pentoxifylline	

Continued

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name
Anti-inflammatory, corticosteroid	Betamethasone
	Budesonide
	Desoxycorticosterone pivalate
	Dexamethasone
	Dexamethasone sodium phosphate
	Flumethasone
	Hydrocortisone
	Isoflupredone acetate
	Methylprednisolone
	Prednisolone
	Prednisolone acetate
	Prednisolone sodium succinate
	Prednisone
	Triamcinolone acetonide
	Triamcinolone diacetate
	Triamcinolone hexacetonide
	Edrophonium chloride
Antimyasthenic	Dirloptapide
Antiobesity	Mitratapide
Antiparasitic	Albendazole
	Amitraz
	Amprolium
	Bunamidine hydrochloride
	Dichlorvos
	Diethylcarbamazine citrate
	Dithiazanine iodide
	Doramectin
	Epsiprantel
	Febantel
	Fenbendazole
	Furazolidone
	Ivermectin
	Ivermectin + praziquantel
	Levamisole hydrochloride
	Lufenuron
	Lufenuron + milbemycin oxime
	Mebendazole
	Melarsomine
	Metaflumizone
	Milbemycin oxime
	Moxidectin
	Nitenpyram
	Oxfendazole
	Oxibendazole
	Paromomycin sulfate
	Piperazine
	Praziquantel
	Pyrantel pamoate
	Pyrantel tartrate
	Quinacrine hydrochloride
	Selamectin
Spinosad	
Thenium closylate	

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name
Antiplatelet agent Antiprotozoal	Thiabendazole
	Thiacetarsamide sodium
	Clopidogrel
	Atovaquone
	Diclazuril
	Imidocarb hydrochloride
	Metronidazole
	Nitazoxanide
	Ponazuril
	Pyrimethamine + sulfadiazine
	Ronidazole
	Tinidazole
	Toltrazuril
Antispasmodic	N-butylscopolammonium bromide (Butylscopolamine bromide)
Antithyroid agent	Carbimazole
	Iopanoic acid
Antitussive, analgesic	Iodate
	Methimazole
	Propylthiouracil
	Butorphanol
	Dextromethorphan
	Hydrocodone bitartrate
Antiulcer agent	Misoprostol
	Sucralfate
Antiulcer agent, H ₂ -blocker	Cimetidine hydrochloride
	Famotidine
	Nizatidine
Antiulcer agent, proton-pump inhibitor	Ranitidine hydrochloride
	Omeprazole
	Pantoprazole
Antiviral	Acyclovir
	Famciclovir
	Lysine (L-Lysine)
	Zidovudine
	Amantadine
Antiviral analgesic	Buspirone hydrochloride
	Trazodone
Behavior-modifying drug	Fluoxetine hydrochloride
	Paroxetine
Behavior-modifying drug, SSRI	Amitriptyline hydrochloride
Behavior-modifying drug, Tricyclic	Clomipramine hydrochloride
	Doxepin
	Imipramine hydrochloride
Beta-agonist	Isoproterenol hydrochloride
	Atenolol
Beta-blocker	Bisoprolol
	Esmolol hydrochloride
	Metoprolol tartrate
	Propranolol hydrochloride
	Sotalol hydrochloride

Continued

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name
Bronchodilator	Aminophylline Oxtriphylline Theophylline
Bronchodilator, beta-agonist	Albuterol sulfate Clenbuterol Metaproterenol sulfate Terbutaline sulfate Zilpaterol
Calcium supplement	Calcitriol Calcium carbonate Calcium chloride Calcium citrate Calcium gluconate and calcium borogluconate Calcium lactate
Cardiac inotropic agent	Digitoxin Digoxin Dobutamine hydrochloride Pimobendan
Cholinergic	Bethanechol chloride
Corticosteroid, hormone	Fludrocortisone acetate
Dermatologic agent	Isotretinoin
Diuretic	Acetazolamide Chlorothiazide Dichlorphenamide Furosemide Hydrochlorothiazide Mannitol Methazolamide Spironolactone Triamterene
Diuretic, laxative	Glycerin
Dopamine agonist	Bromocriptine mesylate Levodopa Pergolide Pergolide mesylate Selegiline hydrochloride
Emetic	Apomorphine hydrochloride Ipecac
Expectorant; muscle relaxant	Guaifenesin
Fluid replacement	Dextran Dextrose solution Hetastarch Lactated Ringer's solution Pentastarch Ringer's solution Sodium chloride 0.9% Sodium chloride 7.2%
Hepatic protectant	S-adenosylmethionine (S-AdoMet) Silymarin

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name
Hormone	Altrenogest
	Colony-stimulating factors
	Corticotropin
	Cosyntropin
	Danazol
	Desmopressin acetate
	Diethylstilbestrol
	Epoetin alpha (erythropoietin)
	Estradiol cypionate
	Estriol
	Gonadorelin hydrochloride, gonadorelin diacetate tetrahydrate
	Gonadotropin, chorionic
	Growth hormone
	Insulin
	Levothyroxine sodium
	Liothyronine sodium
	Medroxyprogesterone acetate
	Megestrol acetate
	Mibolerone
	Testosterone
	Urofollitropin
	Vasopressin
	Hormone, anabolic agent
Methyltestosterone	
Nandrolone decanoate	
Oxymetholone	
Stanozolol	
Hormone, antagonist	Finasteride
	Oxytocin
Hormone, labor induction	Thyroid-releasing hormone
Hormone, thyroid	Thyrotropin
	Interferon
Immunostimulant	Lithium carbonate
Immunosuppressive agent	Auranofin
	Aurothioglucoase
	Azathioprine
	Cyclophosphamide
	Cyclosporine
	Gold sodium thiomalate
	Mycophenolate
	Tacrolimus
Iodine supplement	Iodide
	Potassium iodide
	Sodium iodide (20%)
Laxative	Bisacodyl
	Cascara sagrada
	Castor oil
	Docusate
	Lactulose
	Magnesium citrate
	Magnesium hydroxide
	Mineral oil

Continued

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name
	Polyethylene glycol electrolyte solution
	Psyllium
	Senna
	Ursodeoxycholic acid
	Ursodiol
Laxative, antiarrhythmic	Magnesium sulfate
Local anesthetic	Bupivacaine hydrochloride
	Mepivacaine
Local anesthetic, antiarrhythmic	Lidocaine hydrochloride
Mucolytic, antidote	Acetylcysteine
Muscle relaxant	Atracurium besylate
	Dantrolene sodium
	Methocarbamol
	Pancuronium bromide
Nutritional supplement	Ferrous sulfate
	Iron dextran
	MCT oil
	Taurine
	Zinc
Opioid antagonist	Naloxone hydrochloride
	Naltrexone
Pancreatic enzyme	Pancrelipase
Phosphate supplement, urine acidifier	Potassium phosphate
Potassium supplement	Potassium chloride
	Potassium gluconate
Prokinetic agent	Cisapride
	Domperidone
	Methylnaltrexone
	Metronidazole
	Tegaserod
Prostaglandin	Cloprostenol
	Dinoprost tromethamine
	Prostaglandin F-2 alpha
Respiratory stimulant	Doxapram hydrochloride
Tranquilizer, benzodiazepine	Alprazolam
Tranquilizer, phenothiazine	Acepromazine maleate
Vasodilator	Hydralazine hydrochloride
	Irbesartan
	Isosorbide dinitrate
	Isosorbide mononitrate
	Isoxsuprine
	Nitroglycerin
	Nitroprusside (sodium nitroprusside)
	Phenoxybenzamine hydrochloride
	Phentolamine mesylate
	Prazosin
	Sildenafil
Vasodilator, ACE-inhibitor	Benazepril hydrochloride
	Captopril
	Enalapril maleate
	Lisinopril
	Ramipril
	Trandolapril

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name
Vasodilator, calcium channel blocker	Amlodipine besylate Losartan
Vasopressor	Nifedipine Arginine vasopressin Methoxamine
Vitamin	Phenylephrine hydrochloride Ascorbic acid Cyanocobalamin Dihydrotachysterol Ergocalciferol Phytonadione Riboflavin Thiamine hydrochloride Vitamin A Vitamin E Vitamin K

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
2-PAM	Pralidoxime chloride
4-Methylpyrazole	Fomepizole
5-Fluorouracil	Fluorouracil
A180	Danofloxacin mesylate
Abbecillin	Penicillin G
ABCD	Amphotericin B
ABELCET	Amphotericin B
Accutane	Isotretinoin
ACE	Acepromazine maleate
Aceproject	Acepromazine maleate
Aceprotabs	Acepromazine maleate
Acetadote	Acetylcysteine
Acetylpromazine	Acepromazine maleate
Acetylsalicylic acid	Aspirin
Achromycin V	Tetracycline
ActaChar	Charcoal activated
ACTH	Cosyntropin
Acthar	Corticotropin
Actigall	Ursodeoxycholic acid
Actigall	Ursodiol
Activated charcoal	Charcoal activated
Adalat	Nifedipine
Adenosylmethionine (SAME)	S-adenosylmethionine (SAME)
Adequan Canine	Polysulfated glycosaminoglycan
Adequan IA	Polysulfated glycosaminoglycan
Adequan IM	Polysulfated glycosaminoglycan
Adrenaline	Epinephrine
Adriamycin	Doxorubicin hydrochloride
Adrucil	Fluorouracil
Adspec	Clenbuterol
Advil	Ibuprofen
Aggrenex	Dipyridamole
Albon	Sulfadimethoxine
Aldactone	Spirolactone
Aleve	Naproxen
Alfaxan	Alfaxalone
Alimemazine	Trimeprazine (Temaril-P)
Alinia	Nitazoxanide
Alkeran	Melphalan
Allopur	Allopurinol
Alpha-tocopherol	Vitamin E
Alupent	Metaproterenol sulfate
AmBisome	Amphotericin B
Amiglyde-V	Amikacin
Amikin	Amikacin
Amino acid solution	Travasol
Aminophylline	Theophylline
Aminosalicylic acid	Mesalamine
Ammonium chloride	Ammonium chloride
Amoxicillin trihydrate	Amoxicillin
Amoxi-Drops	Amoxicillin
Amixo-Inject	Amoxicillin
Amoxil	Amoxicillin
Amoxi-Tabs	Amoxicillin

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Amp-Equine	Ampicillin
Amphogel	Aluminum hydroxide
Amphotec	Amphotericin B
Amprol	Amprolium
Amtech iron dextran	Iron dextran
AmVet	Calcium borogluconate
AmVet	Calcium gluconate
Anadrol	Oxymetholone
Anafen	Ketoprofen
Anafranil	Clomipramine hydrochloride
Anaplasmosis block	Chlortetracycline
Ancef	Cefazolin sodium
Ancobon	Flucytosine
Andro-Cyp	Testosterone
Android	Methyltestosterone
Andronate	Testosterone
Anipryl	Selegiline hydrochloride
Anthelcide EQ	Oxibendazole
Antidiuretic Hormone (ADH)	Vasopressin; arginine vasopressin
Antilirium	Physostigmine
Antirobe	Clindamycin palmitate
Antisedan	Atipamezole hydrochloride
Antivert	Meclizine
Antizole	Fomepizole
Antizol-Vet	Fomepizole
Anzemet	Dolasetron mesylate
APL	Gonadotropin chorionic
Apomorphine	Apomorphine hydrochloride
Apresoline	Hydralazine hydrochloride
Aquacillin	Penicillin G
AquaMEPHYTON	Phytonadione
AquaMEPHYTON	Vitamin K
Aquasol E	Vitamin E
Aquasol-A	Vitamin A
Ara-C	Cytarabine
Aredia	Pamidronate disodium
Arginine Vasopressin	Vasopressin
Aristocort	Triamcinolone
Arm & Hammer pure baking soda	Sodium bicarbonate
Arquel	Meclofenamic acid
ASA	Aspirin
Asacol	Mesalamine
Ascriptin	Aspirin
Atabrine	Quinacrine hydrochloride
Atarax	Hydroxyzine
Atgard	Dichlorvos
Ativan	Lorazepam
Atopica	Cyclosporine
Atravet	Acepromazine maleate
Atropine	Atropine sulfate
Augmentin	Amoxicillin + clavulanate potassium
Aureomycin soluble calf tablets	Chlortetracycline
Aureomycin soluble powder	Chlortetracycline

Continued

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Aureomycin tablets	Chlortetracycline
Avapro	Irbesartan
Avelox	Moxifloxacin
AVP	Arginine vasopressin; vasopressin
Axid	Nizatidine
Azium	Dexamethasone
Azulfidine	Sulfasalazine
Bactrim	Trimethoprim + sulfamethoxazole
Bactrovet	Sulfadimethoxine
Baking soda	Sodium bicarbonate
BAL in oil	Dimercaprol
Banamine	Flunixin meglumine
Basalgel	Aluminum carbonate
Baycox	Toltrazuril
Baytril	Enrofloxacin
Benadryl	Diphenhydramine hydrochloride
Benylin	Dextromethorphan
Benza-Pen	Penicillin G
Benzelmin	Oxfendazole
Betapace	Sotalol hydrochloride
Bewon	Thiamine hydrochloride
Biaxin	Clarithromycin
Biomox	Amoxicillin
Biomycin	Oxytetracycline
Biosol	Neomycin
Blenoxane	Bleomycin sulfate
Bonine	Meclizine
Brethine	Terbutaline sulfate
Brevibloc	Esmolol hydrochloride
Brevital	Methohexital sodium
Bricanyl	Terbutaline sulfate
British anti-lewisite	Dimercaprol
Bufferin	Aspirin
Buprenex	Buprenorphine hydrochloride
Buscopan	Butylscopolamine bromide
BuSpar	Bupirone hydrochloride
Butazolidin	Phenylbutazone
Bute	Phenylbutazone
Butylscopolamine bromide	N-butylscopolammonium bromide
Calan	Verapamil hydrochloride
Calciferol	Ergocalciferol
Calcijex	Calcitriol
Calci-mix	Calcium carbonate
Calcium	Calcium chloride; calcium lactate
Calcium disodium	Edetate calcium disodium
ethylenediaminetetra-acetate	
Calcium disodium versenate	Edetate calcium disodium
Calcium ipodate	Ipodate
Calf scour bolus	Chlortetracycline
Cal-Nate	Calcium borogluconate; calcium gluconate
Canopar	Thenium closylate
Caparsolate	Thiacetarsamide sodium
Capoten	Captopril
Capstar	Nitenpyram

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Carafate	Sucralfate
Carbocaine-V	Mepivacaine
Cardioquin	Quinidine
Cardizem	Diltiazem hydrochloride
Cardoxin	Digoxin
Caricide	Diethylcarbamazine citrate
Carmilax	Magnesium hydroxide
Castor	Castor oil
CCNU	Lomustine
Ceclor	Cefaclor
CeeNU	Lomustine
Cefa-Drops	Cefadroxil
Cefa-Tabs	Cefadroxil
Cefotan	Cefotetan disodium
Celestone	Betamethasone
CellCept	Mycophenolate
Centrine	Aminopentamide
Cephaguard	Cefquinome
Ceptaz	Ceftazidime
Cerenia	Maropitant
Cestex	Epsiprantel
Charcodote	Charcoal activated
Chemet	Succimer
Cheque-drops	Mibolerone
Chloromycetin	Chloramphenicol
Chlor-Trimeton	Chlorpheniramine maleate
Choledyl-SA	Oxtriphylline
Chondroitin sulfate	Glucosamine + chondroitin sulfate
Chronulac	Lactulose
Ciclosporin	Cyclosporine
Cin-Quin	Quinidine
Cipro	Ciprofloxacin hydrochloride
Citracal	Calcium citrate
Citrocarbonate	Sodium bicarbonate
Citroma	Magnesium citrate
Citro-Mag	Magnesium citrate
Citro Nesia	Magnesium citrate
Claforan	Cefotaxime sodium
Clavamox	Amoxicillin + clavulanate potassium
Cleocin	Clindamycin palmitate
ClinaFarm-EC	Enilconazole
Clincox	Diclazuril
Clindrops	Clindamycin palmitate
Clinsol	Clindamycin palmitate
Clintabs	Clindamycin palmitate
Clomicalm	Clomipramine hydrochloride
Cloxapen	Cloxacillin sodium
Cobactan	Cefquinome
Colace	Docusate
Co-Lav	Polyethylene glycol electrolyte solution
ColBENEMID	Colchicine
Colyte	Polyethylene glycol electrolyte solution
Comfortis	Spinolad

Continued

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Compazine	Prochlorperazine edisylate
Contac	Clemastine fumarate
Convenia	Cefovecin
Cordarone	Amiodarone
Coreg	Carvedilol
Corid	Amprolium
Corloпам	Fenoldopam mesylate
Corrective mixture	Paregoric
Cortef	Hydrocortisone
Cortrosyn	Cosyntropin
Cosequin	Glucosamine + chondroitin sulfate
Cosequin	Chondroitin sulfate
Cotazym	Pancrelipase
Coumadin	Warfarin sodium
Cozaar	Losartan potassium
Creon	Pancrelipase
Crysticillin	Penicillin G
Crystodigin	Digitoxin
CSA	Cyclosporine
CTX	Cyclophosphamide
Cuprimine	Penicillamine
Cyanocobalamin	Cobalamin
Cyclosporin A	Cyclosporine
Cytrin	Medroxyprogesterone acetate
Cydectin	Moxidectin
Cystorelin	Gonadorelin diacetate tetrahydrate
Cytomel	Liothyronine sodium
Cytosar	Cytarabine
Cytosine arabinoside	Cytarabine
Cytotec	Misoprostol
Cytoxan	Cyclophosphamide
D5W	Dextrose solution
Danocrine	Danazol
Dantrium	Dantrolene sodium
Daranide	Dichlorphenamide
Daraprim	Pyrimethamine
Darbazine	Prochlorperazine edisylate
Darbazine	Prochlorperazine maleate
DDAVP	Desmopressin acetate
DDVP	Dichlorvos
Decadron	Dexamethasone
Deca-Durabolin	Nandrolone decanoate
Dectomax	Doramectin
Delta-Cortef	Prednisolone
Deltasone	Prednisone
Demerol	Meperidine
Denosyl	S-adenosylmethionine (S-AMe)
Depakene	Valproate sodium
Depakote	Valproate sodium
Depen	Penicillamine
Depo-Estradiol	Estradiol cypionate
Depo-Medrol	Methylprednisolone acetate
Depo-Provera	Medroxyprogesterone acetate
Depo-Testosterone	Testosterone

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Deprenyl	Selegiline hydrochloride
Deramaxx	Deracoxib
DES	Diethylstilbestrol
Desferal	Deferoxamine mesylate
Desyrel	Trazodone
Dexaject	Dexamethasone
Dexaject SP	Dexamethasone
Dexasone	Dexamethasone
Dexatrim	Phenylpropanolamine hydrochloride
Dexavet	Dexamethasone
Dex-A-Vet	Dexamethasone
Dexdomitor	Dexmedetomidine
Dextran 70	Dextran
DHT	Dihydrotachysterol
Diabeta	Glyburide
Diaminodiphenylsulfone	Dapsone
Diamox	Acetazolamide
Dibenzyline	Phenoxybenzamine hydrochloride
Dichlorvos	Dichlorvos
Dicural	Difloxacin hydrochloride
Didronel	Etidronate disodium
Diflucan	Fluconazole
Dilacor	Diltiazem hydrochloride
Dilantin	Phenytoin
Dilaudid	Hydromorphone
Dinoprost	Dinoprost tromethamine
Dinoprost	Prostaglandin F2 alpha
Dipentum	Olsalazine sodium
Diprivan	Propofol
Di-Trim	Trimethoprim + sulfadiazine
Ditropan	Oxybutynin chloride
Diuril	Chlorothiazide
Divalproex	Valproate sodium
Dizan	Dithiazanine iodide
DMSO	Dimethyl sulfoxide (DMSO)
Dobutrex	Dobutamine hydrochloride
DOCA pivalate	Desoxycorticosterone pivalate
DOCP	Desoxycorticosterone pivalate
Dolophine	Methadone hydrochloride
Domitor	Medetomidine hydrochloride
Domoso	Dimethyl sulfoxide (DMSO)
Dopram	Doxapram hydrochloride
Doribax	Doripenem
Dormosedan	Detomidine hydrochloride
Doxan	Docusate
Doxidan	Docusate
Doxy Caps	Doxycycline
Dramamine	Dimenhydrinate
Draxxin	Tulathromycin
Drisdol	Ergocalciferol
Droncit	Praziquantel
Drontal	Praziquantel
Droxia	Hydroxyurea

Continued

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
DSS	Docusate
DTIC	Dacarbazine
Dulcolax	Bisacodyl
Duracillin	Penicillin G
Duragesic	Fentanyl, transdermal
Duramycin	Tetracycline
Duraquin	Quinidine
Duricef	Cefadroxil
Dynapen	Dicloxacillin sodium
Dyrenium	Triamterene
ECP	Estradiol cypionate
EDDI	Iodide; potassium iodide
EDTA	Edetate calcium disodium
Elavil	Amitriptyline hydrochloride
Eldepryl	Selegiline hydrochloride
Elspar	Asparaginase
Emend	Aprepitant
Enacard	Enalapril maleate
Enisyl-F	Lysine (L-Lysine)
Enterocort	Budesonide
Ephedrine	Ephedrine hydrochloride
Epival	Valproate sodium
EPO	Epoetin alpha (erythropoietin)
Epogen	Epoetin alpha (erythropoietin)
Epsom salts	Magnesium sulfate
Equidone	Domperidone
Equigard	Dichlorvos
Equimax	Ivermectin + praziquantel
Equimectrin	Ivermectin
Equipoise	Boldenone undecylenate
Equisyn-T4 (equine powder)	Levothyroxine sodium
Equizole	Thiabendazole
Eqvalan liquid	Ivermectin
Ergamisol	Levamisole hydrochloride
Erythro-100	Erythromycin
Erythropoietin	Epoetin alpha (erythropoietin)
Eskacillin	Penicillin G
Estrumate	Cloprostenol
EstroPlan	Cloprostenol
Ethrane	Enflurane
EtoGesic	Etodolac
Excede	Ceftiofur crystalline free acid
Excenel	Ceftiofur hydrochloride
Factrel	Gonadorelin diacetate tetrahydrate
Famvir	Famciclovir
Felbatol	Felbamate
Feldene	Piroxicam
Felimazole	Methimazole
Fenesin	Guaifenesin
Fermycin	Chlortetracycline
Ferospace	Ferrous sulfate
Ferrodex	Iron dextran
Fertagyl	Gonadorelin diacetate tetrahydrate
Fertelin	Gonadorelin diacetate tetrahydrate

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Fertinex	Urofollitropin
Filaribits	Diethylcarbamazine citrate
Filgrastim	Colony stimulating factor
FK506	Tacrolimus
Flagyl	Metronidazole
Flavor Tabs	Lufenuron + milbemycin oxime
Florinef	Fludrocortisone acetate
Flovent	Fluticasone propionate
Flucort	Flumethasone
Fluopromazine	Trifluopromazine hydrochloride
Fluothane	Halothane
Folex	Methotrexate
Fortaz	Ceftazidime
Fortekor	Benazepril hydrochloride
Fosamax	Alendronate
Fragmin	Dalteparin
FSH	Urofollitropin
Fulvicin P/G	Griseofulvin
Fulvicin U/F	Griseofulvin
Fungizone	Amphotericin B
Furadantin	Nitrofurantoin
Furalan	Nitrofurantoin
Furatoin	Nitrofurantoin
Furoxone	Furazolidone
Gabapetin	Gabapentin
Gallimycin	Erythromycin
Gantanol	Sulfamethoxazole
Garacin	Gentamicin
Garasol	Gentamicin
GastroGard	Omeprazole
Gengraf	Cyclosporine
Gentocin	Gentamicin sulfate
Gentran-70	Dextran
Geocillin	Carbenicillin indanyl sodium
Geocolate	Guaifenesin
Geopen	Carbenicillin
Glibenclamide	Glyburide
Glucophage	Metformin
Glucotrol	Glipizide
Glycerol	Glycerin
Glycoflex	Glucosamine + chondroitin sulfate
Glycotuss	Guaifenesin
Glyceryl guaiacolate	Guaifenesin
Glynase	Glyburide
Glytuss	Guaifenesin
GnRh	Gonadorelin diacetate tetrahydrate
Golytely	Polyethylene glycol electrolyte solution
Gonadorelin	Gonadorelin hydrochloride
Gravol	Dimenhydrinate
Grifulvin	Griseofulvin
Grisactin	Griseofulvin
GrisPEG	Griseofulvin
Guailaxin	Guaifenesin

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List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Guaiphenesin	Guaifenesin
Gyrocaps	Theophylline
Heartguard	Ivermectin
HemaJect	Iron dextran
Hepalean	Heparin sodium
HES	Hetastarch
Hespan	Hetastarch
Hetastarch	Hetastarch
Hiprex	Methenamine
HSS	Sodium chloride 7.2%
Humabid LA	Guaifenesin
Humatin	Paromomycin sulfate
Humatrope	Growth hormone
Humulin (human insulin)	Insulin
Hycodan	Hydrocodone bitartrate
Hydrea	Hydroxyurea
HydroDiuril	Hydrochlorothiazide
Hydrostat	Hydromorphone
Hyoscine N-butylbromide	Butylscopol-ammonium bromide
Hypertonic saline	Sodium chloride 7.2%
Hytakerol	Dihydrotachysterol
Hytuss	Guaifenesin
Imaverol	Enilconazole
Imizol	Imidocarb hydrochloride
Immiticide	Melarsomine
Imodium	Loperamide hydrochloride
Imuran	Azathioprine
Inderal	Propranolol hydrochloride
Indocin	Indomethacin
Interceptor	Milbemycin oxime
Intropin	Dopamine hydrochloride
Invanz	Ertapenem
Iodide	Potassium iodide; EDDI
Iodopen	Sodium iodide (20%)
Ipodate	Iopanoic acid
Isonicotinic acid hydrazide	Isoniazid
Isoprenaline hydrochloride	Isoproterenol hydrochloride
Isoptin	Verapamil hydrochloride
Isorbid	Isosorbide dinitrate
Isordil	Isosorbide dinitrate
Isuprel	Isoproterenol hydrochloride
Itrafungol	Itraconazole
Ivercare	Ivermectin
Ivercide	Ivermectin
IverEase	Ivermectin
Ivermax	Ivermectin
Ivomec	Ivermectin
Kalcinate	Calcium borogluconate; calcium gluconate
Kantrim	Kanamycin sulfate
Kaon	Potassium gluconate
KaoPectate	Kaolin + pectin
Keflex	Cephalexin
Kefzol	Cefazolin sodium
Keppra	Levetiracetam

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Ketalar	Ketamine hydrochloride
Ketavet	Ketamine hydrochloride
Ketofen	Ketoprofen
Klonopin	Clonazepam
K-Phos	Potassium phosphate
Kytril	Granisetron hydrochloride
Lamisil	Terbinafine hydrochloride
Lamprene	Clofazimine
Lanoxin	Digoxin
Lanvis	Thioguanine
Largactil	Chlorpromazine
Larodopa	Levodopa
Lasix	Furosemide
L-asparaginase	Asparaginase
L-deprenyl	Selegiline hydrochloride
L-dopa	Levodopa
Lente insulin	Insulin
Leukeran	Chlorambucil
Leukine	Colony-stimulating factors
Levasole	Levamisole hydrochloride
Levo-Powder	Levothyroxine sodium
Levsin	Hyoscyamine
LHRH	Gonadorelin diacetate tetrahydrate
Lincocin	Lincomycin hydrochloride monohydrate
Lincomix	Lincomycin hydrochloride monohydrate
Lincomycin	Lincomycin hydrochloride
Lincomycin	Lincomycin hydrochloride monohydrate
Liquaemin	Heparin sodium
Liquamycin-LA 200	Oxytetracycline
Liqui-cal	Calcium carbonate
Liqui-Char	Charcoal activated
Lithotabs	Lithium carbonate
LMWH	Dalteparin; enoxaparin
Lodine	Etodolac
Lomotil	Diphenoxylate
Lopid	Gemfibrozil
Lopressor	Metoprolol tartrate
Lopurin	Allopurinol
Losac	Omeprazole
Lotensin	Benazepril hydrochloride
Lovenox	Enoxaparin
LRS	Lactated ringer's solution
Luminal	Phenobarbital
Lutalyse	Dinoprost tromethamine
Lutalyse	Prostaglandin F ₂ alpha
Lyrica	Pregabalin
Lysodren	Mitotane
Maalox	Calcium carbonate
Macrodantin	Nitrofurantoin
Magnalax	Magnesium hydroxide
Malogen	Testosterone propionate ester
Mandelamine	Methenamine mandelate
Marbocyl	Marbofloxacin

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List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Marcaine	Bupivacaine hydrochloride
Marin	Silymarin
Marinol	Dronabinol
Marquis	Ponazuril
Matrix	Altrenogest
Mavik	Trandolapril
Maxipime	Cefepime
Maxolon	Metoclopramide hydrochloride
Meclofen	Meclofenamic acid
Meclofenamate sodium	Meclofenamic acid
Meclofenamic acid	Meclofenamate sodium
Meclozine	Meclizine
Medium chain triglycerides	MCT oil
Medrol	Methylprednisolone
Mefoxin	Cefoxitin sodium
Megace	Megestrol acetate
Mephyton	Phytonadione; vitamin K
Mepron	Atovaquone
Merrem	Meropenem
Mesalazine	Mesalamine
Mesasal	Mesalamine
Mestinon	Pyridostigmine bromide
Metacam	Meloxicam
Metamucil	Psyllium
Metaprel	Metaproterenol sulfate
Methanamine hippurate	Methenamine
Methio-Form	Racemethionine
Methodose	Methadone hydrochloride
Methylpyrazole	Fomepizole
Meticorten	Prednisone
Metofane	Methoxyflurane
Metrodin	Urofollitropin
Metronidazole benzoate	Metronidazole
Metronidazole hydrochloride	Metronidazole
Mexate	Methotrexate
Mexitil	Mexiletine
Micotil	Tilmicosin phosphate
Micronase	Glyburide
Milk of Magnesia	Magnesium hydroxide
Milk Thistle	Silymarin
Mineral oil	Mineral oil
Minipress	Prazosin
Minocin	Minocycline hydrochloride
Mitaban	Amitraz
Mithracin	Plicamycin
Mithramycin	Pilcamycin
Mobic	Meloxicam
Modrenal	Trilostane
Monodox	Doxycycline
Monoket	Isosorbide mononitrate
Monurol	Fosfomycin
Motilium	Domperidone
Motrin	Ibuprofen
MS Contin	Morphine sulfate

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
MTX	Methotrexate
Mucinex	Guaifenesin
Mucomyst	Acetylcysteine
Mylepsin	Primidone
Myleran	Busulfan
Myochrysin	Gold sodium thiomalate
Mysoline	Primidone
Naprosyn	Naproxen
Narcan	Naloxone hydrochloride
Nature's Remedy	Cascara sagrada
Navigator	Nitazoxanide
Naxcel	Ceftiofur sodium
Naxen	Naproxen
N-butylscopolammonium bromide	Butylscopolamine bromide
Nebcin	Tobramycin sulfate
Nemacide	Diethylcarbamazine citrate
Nembutal	Pentobarbital sodium
Nemex	Pyrantel
Neomercazole	Carbimazole
Neoral	Cyclosporine
Neosar	Cyclophosphamide
Neostigmine bromide	Neostigmine
Neostigmine methylsulfate	Neostigmine
Neo-synephrine	Phenylephrine hydrochloride
Neptazane	Methazolamide
Neupogen	Colony-stimulating factors
Neurontin	Gabapentin
Neurosyn	Primidone
Neutra-Phos-K	Potassium phosphate
New Methylene Blue	Methylene Blue
Nicotinamide	Niacinamide
Niravam	Alprazolam
Nitro-bid	Nitroglycerin
Nitrol	Nitroglycerin
Nitropress	Nitroprusside (sodium nitroprusside)
Nitrostat	Nitroglycerin
Nizoral	Ketoconazole
Nolvadex	Tamoxifen citrate
Normal saline	Sodium chloride 0.9%
Noroxin	Norfloxacin
Norpace	Disopyramide
Norvasc	Amlodipine besylate
Novantrone	Mitoxantrone hydrochloride
Noxafil	Posaconazole
NPH insulin	Insulin
Nuflor	Florfenicol
Numorphan	Oxymorphone hydrochloride
Nuprin	Ibuprofen
Nutropin	Growth hormone
Omega	Interferon
Omnicef	Cefdinir
Omnipen	Ampicillin
Omnizole	Thiabendazole

Continued

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Oncovin	Vincristine sulfate
op-DDD	Mitotane
Optimmune	Cyclosporine
Oramorph SR	Morphine sulfate
Oragrafin	Ipodate
Orbax	Orbifloxacin
Orbenin	Cloxacillin sodium
Orciprenaline sulphate	Metaproterenol sulfate
Orudis-KT	Ketoprofen
Osmitrol	Mannitol
Ovaban	Megestrol acetate
OvaCyst	Gonadorelin diacetate tetrahydrate
Oxpentifylline	Pentoxifylline
Oxy 500, or Oxy 1000	Oxytetracycline
Oxybiotic	Oxytetracycline
Oxyglobin	Hemoglobin glutamer
Oxy-Tet	Oxytetracycline
Palladia	Toceranib
PAM	Pralidoxime chloride
Panacur	Fenbendazole
Pancoate	Pancrelipase
Pancrease	Pancrelipase
Pancrezyme	Pancrelipase
Panectyl	Trimeprazine tartrate
Panmycin	Tetracycline
Paraplatin	Carboplatin
Parencillin	Penicillin G
Parlodel	Bromocriptine mesylate
Pavulon	Pancuronium bromide
Paxil	Paroxetine
PBZ	Phenylbutazone
Pedameth	Racemethionine
PEG	Polyethylene glycol electrolyte solution
Pelamine	Tripeleminamine citrate
Pentahydrate	Spectinomycin
Pentasa	Mesalamine
Pentaspan	Pentastarch
Pentothal	Thiopental sodium
Pen-Vee	Penicillin V
Pepcid	Famotidine
Pepto Bismol	Bismuth subsalicylate
Percorten-V	Desoxycorticosterone pivalate
Pergolide mesylate	Pergolide
Periactin	Cyproheptadine hydrochloride
Permax	Pergolide
Persantine	Dipyridamole
Pfizerpen	Penicillin G
PGF ₂ alpha	Prostaglandin F ₂ alpha; dinoprost tromethamine
Phenergan	Promethazine hydrochloride
Phenetron	Chlorpheniramine maleate
Phenobarbital sodium	Phenobarbital
Phenobarbitone	Phenobarbital
Phenytoin sodium	Phenytoin

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Phylloquinone	Phytonadione; vitamin K
Phytomenadione	Phytonadione; vitamin K
Pipa-Tabs	Piperazine
Pipracil	Piperacillin sodium
Pitocin	Oxytocin
Pitressin	Vasopressin
Platinol	Cisplatin
Plavix	Clopidogrel
Polycillin	Ampicillin
PolyFlex (ampicillin trihydrate)	Ampicillin
Polymox	Amoxicillin
Potassium	Potassium chloride
Potassium bromide	Bromide
PPA	Phenylpropanolamine hydrochloride
Predef 2X	Isoflupredone acetate
Prednisolone acetate	Prednisolone
PrednisTab	Prednisolone
Pregnyl	Gonadotropin chorionic
Prepulsid	Cisapride
Previcox	Firocoxib
Priex	Pyrantel
Prilosec	Omeprazole
Primaxin	Imipenem + cilastatin
Primor	Ormetoprim + sulfadimethoxine
Principen	Ampicillin
Prinivil	Lisinopril
Privermectin	Ivermectin
Pro-Banthine	Propantheline bromide
Procardia	Nifedipine
Prochlorperazine maleate	Prochlorperazine edisylate
Profasi	Gonadotropin chorionic
Program	Lufenuron
ProHeart	Moxidectin
Proin-ppa	Phenylpropanolamine hydrochloride
ProMACE	Acepromazine maleate
ProMeris	Metaflumizone
Pronestyl	Procainamide hydrochloride
Propagest	Phenylpropanolamine hydrochloride
Propalin	Phenylpropanolamine hydrochloride
Propoflo	Propofol
Propulsid	Cisapride
Propyl-Thyracil	Propylthiouracil
Proscar	Finasteride
Prospec	Clenbuterol
Prostaglandin F ₂ alpha	Dinoprost tromethamine
ProstaMate	Dinoprost tromethamine
Pro-staphlin	Oxacillin sodium
Prostigmin	Neostigmine
Prostin F ₂ alpha	Dinoprost tromethamine
Protamine zinc insulin	Insulin
Protonix	Pantoprazole
Protopam chloride	Pralidoxime chloride
Protopic	Tacrolimus

Continued

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Protopin	Growth hormone
Proventil	Albuterol sulfate
Provera	Medroxyprogesterone acetate
Prozac	Fluoxetine hydrochloride
PTU	Propylthiouracil
Pulmotil tilmicosin premix	Tilmicosin phosphate
Purinethol	Mercaptopurine
Pyopen	Carbenicillin
Pyran	Pyrantel
Pyr-A-Pam	Pyrantel
PZI	Insulin
PZI Vet	Insulin
Quadrinal	Potassium iodide
Quest	Moxidectin
Quinaglute	Quinidine
Quinora	Quinidine
Rapinivet	Propofol
ReBalance	Pyrimethamine + sulfadiazine
Reconcile	Fluoxetine
Regitine	Phentolamine mesylate
Reglan	Metoclopramide hydrochloride
Regonol	Pyridostigmine bromide
Regu-Mate	Altrenogest
Relistor	Methylnaltrexone
Remeron	Mirtazapine
Resipram	Dopram
Retinol	Vitamin A
Retrovir	Zidovudine
Revolution	Selamectin
Rheumatrex	Methotrexate
r-HuEPO	Epoetin alpha (erythropoietin)
Rythmodan	Disopyramide
Ridaura	Auranofin
Rifadin	Rifampin
Rifampicin	Rifampin
Rimadyl	Carprofen
Ringers	Ringer's solution
Rintal	Febantel
Ripercol	Levamisole hydrochloride
Robamox-V	Amoxicillin
Robaxin-V	Methocarbamol
Robinul-V	Glycopyrrolate
Robitussin	Dextromethorphan
Rocaltrol	Calcitriol
Rogitine	Phentolamine mesylate
Romazicon	Flumazenil
Rompun	Xylazine hydrochloride
SafeGuard	Fenbendazole
SafeHeart	Milbemycin oxime
Salazopyrin	Sulfasalazine
Salbutamol	Albuterol sulfate
Saline solution	Sodium chloride 0.9%
SAMe	S-adenosylmethionine (SAMe)
Sandimmune	Cyclosporine

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Sargramostim	Colony stimulating factor
Scolaban	Bunamidine hydrochloride
Sedivet	Romifidine hydrochloride
Senokot	Senna
Sentinel	Milbemycin oxime
Sentinel tablets	Lufenuron + milbemycin oxime
Septra	Trimethoprim + sulfamethoxazole
Serax	Oxazepam
Silybin	Silymarin
Simplicef	Cefpodoxime proxetil
Sinequan	Doxepin
Skelid	Tiludronate disodium
Slentrol	Dirlotapide
Slo-bid	Theophylline
Soda Mint	Sodium bicarbonate
Sodium ascorbate	Ascorbic acid
Sodium bromide	Bromide
Solganal	Aurothioglucose
Soloxine	Levothyroxine sodium
Solu-Cortef	Hydrocortisone sodium succinate
Solu-Delta-Cortef	Prednisolone sodium succinate
Solu-Medrol	Methylprednisolone sodium succinate
Somatrem	Growth hormone
Somatropin	Growth hormone
Sorbitrate	Isosorbide mononitrate
Spectam	Clenbuterol
Spectogard	Clenbuterol
Sporanox	Itraconazole
Stelazine	Trifluoperazine hydrochloride
Stiglyl	Neostigmine
Streptozotocin	Streptozocin
Strongid	Pyrantel
Sublimaze	Fentanyl citrate
Sudafed	Pseudoephedrine hydrochloride
Sufenta	Sufentanil citrate
Sulcrate	Sucralfate
Sulfa-Nox	Sulfaquinoxaline
Sulmet	Sulfamethazine
Suprax	Cefixime
Surfak	Docusate
Symmetrel	Amantadine
Synanthic	Oxfendazole
Synthroid	Levothyroxine sodium
Syntocinon	Oxytocin
Syprine	Trientine hydrochloride
Syrup of Ipecac	Ipecac
T4	Levothyroxine sodium
Tagamet	Cimetidine hydrochloride
Talwin-V	Pentazocine
Tapazole	Methimazole
Task	Dichlorvos
Tavist	Clemastine fumarate
Tazicef	Ceftazidime

Continued

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Tazidime	Ceftazidime
TBZ	Thiabendazole
Tegopen	Cloxacillin sodium
Telezol	Tiletamine + zolazepam
Telmin	Mebendazole
Telmintic	Mebendazole
Temaril	Trimeprazine tartrate
Temaril-P (with prednisolone)	Trimeprazine tartrate
Tenormin	Atenolol
Tensilon	Edrophonium chloride
Terramycin	Oxytetracycline
Testex	Testosterone propionate ester
Testosterone cypionate ester	Testosterone
Tetracosactide	Cosyntropin
Tetracosactrin	Cosyntropin
Theo-Dur	Theophylline
Theophylline	Aminophylline
Thiamazole	Methimazole
Thibenzole	Thiabendazole
Thioplex	Thiotepa
Thorazine	Chlorpromazine
Thyrel	Thyroid releasing hormone
Thyrogen	Thyrotropin
Thyroid hormone (T ₃)	Liothyronine sodium
Thyroid hormone (T ₄)	Levothyroxine; L-thyroxine
Thyrolar	Levothyroxine + Liothyronine
Thyro-L	Levothyroxine sodium
ThyroMed	Levothyroxine sodium
Thyro-Tabs	Levothyroxine sodium
Thytropar	Thyrotropin
Ticar	Ticarcillin disodium
Ticillin	Ticarcillin + clavulanate potassium
Tigan	Trimethobenzamide
Tildren	Tiludronate disodium
Timentin	Ticarcillin + clavulanate potassium
Tindamax	Tinidazole
Titralac	Calcium carbonate
Tocopherol	Vitamin E
Tofranil	Imipramine hydrochloride
Tonocard	Tocainide hydrochloride
Toradol	Ketorolac tromethamine
Torbugesic	Butorphanol tartrate
Torbutrol	Butorphanol tartrate
Torpex equine inhaler	Albuterol sulfate
Totacillin	Ampicillin
Toxiban	Charcoal activated
Tracurium	Atracurium besylate
Tramisol	Levamisole hydrochloride
Tranvet	Propiopromazine hydrochloride
Tranxene	Clorazepate dipotassium
Travasol	Amino acid solution
Trental	Pentoxifylline
Trexan	Naltrexone
Trexonil	Naloxone hydrochloride

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
TRH	Thyroid releasing hormone
Triamtabs	Triamcinolone
Tribrissen	Trimethoprim + sulfadiazine
Trimox	Amoxicillin
TSH	Thyrotropin
Tucoprim	Trimethoprim + sulfadiazine
Tumil-K	Potassium gluconate
Tums	Calcium carbonate
Tylan	Tylosin
Tylenol	Acetaminophen
Tylenol with codeine	Acetaminophen + codeine
Tylocine	Tylosin
UlcerGard	Omeprazole
Ultiva	Remifentanyl
Ultralente insulin	Insulin
Ultram	Tramadol
Ultramectin	Ivermectin
Ultrase	Pancrelipase
Unasyn	Ampicillin + sulbactam
Uniprim	Trimethoprim + sulfadiazine
Uracid	Racemethionine
Urecholine	Bethanechol chloride
Urex	Methenamine
UriCon	Phenylpropanolamine hydrochloride
Urocit-K	Potassium citrate
Uroze	Racemethionine
Ursodeoxycholic acid	Ursodiol
Valbazen	Albendazole
Valium	Diazepam
Valproate sodium	Valproic acid
Vancocin	Vancomycin
Vancoled	Vancomycin
Vantin	Cefpodoxime proxetil
Vasodilan	Isoxsuprine
Vasotec	Enalapril maleate
Vasotop	Ramipril
Vasoxyl	Methoxamine
Veda-K1	Vitamin K
Velban	Vinblastine sulfate
Vetipulmin	Clenbuterol
Ventolin	Albuterol sulfate
Veraflox	Pradofloxacin
Vercom	Febantel
Verdisol	Dichlorvos
Vermox	Mebendazole
Versed	Midazolam hydrochloride
Vesprin	Triflupromazine hydrochloride
Veta-K1	Phytonadione; vitamin K
Vetalar	Ketamine hydrochloride
Vetalog	Triamcinolone
Vetergesic	Buprenorphine hydrochloride
Vetisulid	Sulfachlorpyridazine
Vetmedin	Pimobendan

Continued

List of Trade and Brand Names Cross-Referenced to Drug Names

Trade Names and Other Names	Drug Name as Listed in Handbook
Vetoryl	Trilostane
Vetsulin (porcine insulin zinc)	Insulin
Vfend	Voriconazole
Viagra	Sildenafil
Vibramycin	Doxycycline
Vincasar	Vincristine sulfate
Viokase	Pancrelipase
Virbagen	Interferon
Vitamin B ₁	Thiamine hydrochloride
Vitamin B ₂	Riboflavin
Vitamin B ₃	Niacinamide
Vitamin B ₁₂	Cyanocobalamin; cobalamin
Vitamin C	Ascorbic acid
Vitamin K ₁	Phytonadione
Wellcovorin	Leucovorin calcium
Winstrol-V	Stanozolol
Wycillin	Penicillin G
Wymox	Amoxicillin
Xanax	Alprazolam
Xylocaine	Lidocaine hydrochloride
Yarvitan	Mitratipide
Yobine	Yohimbine
Zanosar	Streptozocin
Zantac	Ranitidine hydrochloride
Zebeta	Bisoprostol
Zegerid	Omeprazole
Zelnorm	Tegaserod
Zeniquin	Marbofloxacin
Zestril	Lisinopril
Zilmax	Zilpaterol
Zimecterin	Ivermectin
Zinecarp	Carprofen
Zithromax	Azithromycin
Zofran	Ondansetron hydrochloride
Zolazepam	Tiletamine + zolazepam
Zoletil	Tiletamine + zolazepam
Zometa	Zoledronate
Zonegran	Zonisamide
Zovirax	Acyclovir
Zosyn	Piperacillin sodium
Zubrin	Tepoxalin
Zyloprim	Allopurinol
Zyrtec	Cetirizine hydrochloride
Zyvox	Linezolid

Acepromazine Maleate

ayss-proe'meh-zeen mal'ee-ate

Trade and other names: ACE, Aceproject, Aceproctabs, Atravet, and Promace; it sometimes is called acetylpromazine.

Functional classification: Tranquilizer, phenothiazine tranquilizer

Pharmacology and Mechanism of Action

Phenothiazine tranquilizer and sedative. Acepromazine inhibits central dopaminergic receptors to produce sedation and tranquilization. Acepromazine also has antimuscarinic action and blocks norepinephrine at adrenergic receptors (e.g., alpha-receptors). Because of the blockade of alpha-receptors on vascular smooth muscle it also produces vasodilation.

Indications and Clinical Uses

Acepromazine is used as a sedative, a tranquilizer, a preanesthetic, and an anesthetic adjunct. In small animals, acepromazine can produce antiemetic effects. For some indications, the administration also produces vasodilation. In horses for treatment of laminitis, it has increased the arterial digital blood flow after a dose of 0.02-0.04 mg/kg.

Precautionary Information

Adverse Reactions and Side Effects

Sedation and ataxia are common side effects. Extrapyrimal effects (involuntary muscle movements), twitching, dystonia, or Parkinson-like effects are rare but are possible with the administration of phenothiazines to animals. Phenothiazines may produce excessive vagal tone in some animals. This may be especially prominent in brachycephalic breeds. Administration of atropine may be used to treat the signs of high vagal tone. Because of alpha-adrenergic antagonism, hypotension is possible in animals. In horses, persistent penile prolapse has been reported from use. This effect in horses is unpredictable and apparently not related to dose.

Contraindications and Precautions

Use cautiously in animals that are prone to seizures. However, a risk of seizures in animals from administration of acepromazine may not be as much of a risk as once thought. Seizures were not reported to be a clinical problem in retrospective studies of patients who had seizures.

Do not use in animals that have problems with dystonia or that have had extrapyramidal effects from use of phenothiazines.

Phenothiazines can cause hypotension (via alpha-receptor blockade); therefore, use cautiously with other hypotensive drugs or in conditions that may exacerbate hypotension.

In pregnancy it produced only minor reduction in blood flow and oxygen delivery to the fetus when used in late pregnancy in cows.

Drug Interactions

Acepromazine may potentiate other drugs that cause vasodilation. Acepromazine may increase the risk of seizures if administered with other drugs that lower seizure threshold, but this may not be as much of a risk as once thought. Acepromazine has been used to sedate dogs for glucose tolerance testing (0.1 mg/kg), without adversely affecting the results.

2 Acetaminophen

Instructions for Use

Acepromazine can be administered PO, IV, or IM. When used with general anesthetics, lower doses of general anesthetics can be used, especially when administering barbiturates and inhalant anesthetics. Clinical signs from acepromazine administration are most prominent during the first 3-4 hours after administration but may persist for 7 hours.

Patient Monitoring and Laboratory Tests

Monitor blood pressure in animals susceptible to hypotension. Acepromazine does not affect adrenal function testing in dogs.

Formulations

Acepromazine is available in 5-, 10-, and 25-mg tablets and in a 10 mg/mL injection. Acepromazine oral granules and powder are available in Canada.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been investigated.

Small Animal Dosage

Dogs

- 0.025-0.1 mg/kg IM, IV, or SQ in a single dose (most common is 0.025 mg/kg). Do not exceed 3 mg total in dogs.
- Sedation: 0.5-2.2 mg/kg q6-8h PO.

Cats

- 0.025-0.1 mg/kg IM, IV, or SQ in a single dose.
- Sedation: 1.1-2.2 mg/kg q6-8h PO.

Large Animal Dosage

Horses

- 0.04-0.1 mg/kg IM, q 6-12h, but frequent dosing is not recommended and an interval of 36-48 hours between doses is recommended. For perioperative use, 0.01-0.05 mg/kg, IM, SQ, or IV.

Cattle

- 0.13-0.26 mg/kg PO, 0.03-0.1 mg/kg IM, or 0.01-0.02 mg/kg IV.

Pigs

- Adult: 0.03-0.2 mg/kg IV, IM, SQ (single dose).

Regulatory Information

Withdrawal times: There are no withdrawal times established in the US. It has been estimated that for extralabel use, establish a withdrawal time of at least 7 days for meat and 48 hours for milk.

Canada: 7 days for meat; 48 hours for milk.

RCI Classification: 3

Acetaminophen

ah-seet-ah-mee'noe-fen

Trade and other names: Tylenol and generic brands

Functional classification: Analgesic

Pharmacology and Mechanism of Action

Analgesic drug. Exact mechanism of action is not known; however, acetaminophen probably inhibits centrally mediated pain transmission. The centrally mediated analgesia may occur via inhibition of COX-3, a variant of COX-1 found in the central nervous system. Other evidence indicates that acetaminophen may inhibit prostaglandins in some cells and tissue in which low concentrations of arachidonic acid are present. The site of acetaminophen action may be the peroxidase enzyme component of prostaglandin H₂ synthase. Therefore, COX inhibition may occur at site-specific tissues, sparing the gastrointestinal mucosa, platelets, and kidneys but acting centrally. Other evidence suggests that acetaminophen can stimulate inhibitory pain pathways mediated by serotonin (5-HT₃). This evidence suggests that acetaminophen may directly activate serotonin receptors.

In canine studies it has not produced anti-inflammatory action but has been effective as an analgesic agent.

Indications and Clinical Uses

Acetaminophen is used as an analgesic and for pain control in dogs. Do not use in cats. It is considered relatively weak as an analgesic. Often used in combination with an opiate (e.g., codeine).

Precautionary Information

Adverse Reactions and Side Effects

Acetaminophen is well tolerated in dogs at doses listed; however, high doses have caused liver toxicity. It causes severe toxicosis in cats because of their inability to excrete metabolites. Clinical signs of toxicity include methemoglobinemia, acute hepatic toxicosis, swelling of paws, and Heinz body anemia.

Contraindications and Precautions

Do not administer to cats. In people, toxic episodes are more likely when administered with drugs that alter the activity of hepatic drug enzymes. Such a reaction also is possible in animals.

In cats, treatment of intoxication requires prompt treatment with acetylcysteine (see monograph for acetylcysteine) and monitoring.

Drug Interactions

In people, other drugs (especially alcohol) will increase risk of hepatotoxicosis. It is not known if other drugs increase this risk in animals.

Instructions for Use

Many non-prescription (OTC) formulations are available. Acetaminophen with codeine may have greater analgesic efficacy in some animals. See other entries for formulations that contain codeine.

Patient Monitoring and Laboratory Tests

Monitor liver enzyme levels periodically to look for evidence of hepatotoxicity. In cats that have received acetaminophen, there is a high risk of toxicity and careful monitoring of liver enzymes and blood cell parameters is needed. Many human hospitals and some diagnostic laboratories can measure acetaminophen concentrations in plasma. In people, treatment is initiated if plasma/serum concentrations are above 200 mcg/mL 4 hours after ingestion.

4 Acetaminophen + Codeine

Formulations

Acetaminophen is available in 120-, 160-, 325-, and 500-mg tablets.

Stability and Storage

Acetaminophen is stable in aqueous solutions. Maximum stability is at pH of 5-7.

Small Animal Dosage

Dogs

- 15 mg/kg q8h PO.

Cats

- Contraindicated.

Large Animal Dosage

Calves

50 mg/kg PO, followed by 30 mg/kg PO q6h.

No other doses have been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Acetaminophen + Codeine

ah-seet-ah-mee'noe-fen + koe'deen

Trade and other names: Tylenol with codeine and many generic brands

Functional classification: Analgesic, opioid

Pharmacology and Mechanism of Action

Analgesic agent. Exact mechanism of action for acetaminophen is not known; however, as discussed previously, a centrally mediated mechanism is likely, either via inhibition of central prostaglandin synthesis or effects on serotonergic inhibitory pain pathways. In this formulation, the opiate codeine is added to enhance analgesia. Effects of codeine are not established in animals. Systemic absorption of codeine from oral administration is small in dogs, and codeine may play only a minor role in analgesia.

Indications and Clinical Uses

Acetaminophen + Codeine is used for analgesia in dogs (e.g., postoperative use). Codeine or codeine with acetaminophen is indicated for treatment of moderate pain.

Codeine formulations have also been used as an antitussive. Despite the widespread use of codeine in humans, the efficacy in animals for its antitussive use or analgesic use has not been established.

Oral absorption of codeine in dogs is low. Because codeine is converted to morphine (10% of dose) for its activity and the duration of morphine is short in dogs, the clinical effectiveness of codeine in dogs may be questionable.

Precautionary Information

Adverse Reactions and Side Effects

Acetaminophen + Codeine is well tolerated in dogs at doses listed; however, high doses have caused liver toxicity.

Contraindications and Precautions

Do not administer to cats because acetaminophen is known to be toxic to cats. Codeine is a Schedule II controlled substance.

Drug Interactions

In people, other drugs (especially alcohol) will increase risk of hepatotoxicity. It is not known if other drugs increase this risk in animals, but consider this possibility when administering other drugs that may affect hepatic metabolism (see Appendix F).

Instructions for Use

Many generic preparations are available. Consider that other ingredients may be present in some combination tablets (e.g., ibuprofen or caffeine).

Patient Monitoring and Laboratory Tests

Monitor liver enzyme levels periodically to look for evidence of hepatotoxicity caused by acetaminophen.

Formulations

Acetaminophen + Codeine is available in oral solution and tablets. A variety of formulations are available (e.g., 300-mg acetaminophen plus 15-, 30-, or 60-mg codeine).

Stability and Storage

Acetaminophen is stable in aqueous solutions. Maximum stability is at pH of 5-7.

Small Animal Dosage

Dogs

Follow dosing recommendations for codeine. Administer dose to deliver doses of codeine equivalent to 0.5-1.0 mg/kg q4-6h PO.

Cats

- Contraindicated.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Acetaminophen + Codeine is a Schedule III drug controlled by DEA. Do not administer to animals intended for food.

Acetazolamide

ah-seet-ah-zole'a-mide

Trade and other names: Diamox

Functional classification: Diuretic

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Pharmacology and Mechanism of Action

Carbonic anhydrase inhibitor. Acetazolamide, like other carbonic anhydrase inhibitors, produces a diuresis through inhibition of the uptake of bicarbonate in proximal renal tubules via enzyme inhibition. This action results in loss of bicarbonate in the urine and a diuresis. The action of carbonic anhydrase inhibitors results in urine loss of bicarbonate, alkaline urine, and water loss.

Indications and Clinical Uses

Acetazolamide is rarely used as a diuretic any longer. There are more potent and effective diuretic drugs available such as the loop diuretics (furosemide).

Acetazolamide, like other carbonic anhydrase inhibitors, is used primarily to lower intraocular pressure in animals with glaucoma. Methazolamide is used more often than acetazolamide for this purpose, and other treatment regimens are now used more often than carbonic anhydrase inhibitors.

Acetazolamide, like other carbonic anhydrase inhibitors, is sometimes used to produce more alkaline urine for management of some urinary calculi.

Precautionary Information

Adverse Reactions and Side Effects

Acetazolamide can potentially produce hypokalemia in some patients. Significant bicarbonate loss can occur with repeated administration. In dogs, a respiratory reaction has been observed, which is attributed to respiratory acidosis.

Contraindications and Precautions

Do not use in patients with acidemia. Use cautiously in any animal sensitive to sulfonamides.

Drug Interactions

Acetazolamide will produce alkaline urine, which may affect clearance of some drugs. Alkaline urine may potentiate the effects of some antibacterial drugs (e.g., macrolides and quinolones).

Instructions for Use

Acetazolamide, in combination with other agents, is usually used to decrease intraocular pressure in the treatment of glaucoma. Acetazolamide has been used to produce alkaline urine to prevent formation of some urinary calculi. However, unless there is supplementation with bicarbonate, the urine alkalization will not be sustained with repeated administration.

Patient Monitoring and Laboratory Tests

Monitor patient's ocular pressure when used to treat glaucoma.

Formulations

Acetazolamide is available in 125- and 250-mg tablets.

Stability and Storage

Stable if stored in tight containers. Compounded solutions are stable at least 60 days.

Small Animal Dosage

Dogs

- Glaucoma: 5-10 mg/kg q8-12h PO.
- Other diuretic uses: 4-8 mg/kg q8-12h PO.

Cats

- 7 mg/kg, q8h, PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Acetylcysteine

ah-see-til-sis'tay-een

Trade and other names: Mucomyst and Acetadote. Also referred to as N-acetylcysteine.

Functional classification: Mucolytic, antidote

Pharmacology and Mechanism of Action

Acetylcysteine decreases viscosity of secretions and is used as a mucolytic agent in eyes and in bronchial nebulizing solutions. Acetylcysteine is a sulfhydryl compound and acts to increase synthesis of glutathione in the liver. Glutathione subsequently acts as an antioxidant and facilitates conjugation to toxic metabolites, particularly the toxic metabolites of acetaminophen. The antioxidant effects also have been used to treat conditions associated with oxidative stress.

Indications and Clinical Uses

As a donor of the sulfhydryl group, it is used as an antidote for intoxications (e.g., acetaminophen toxicosis in cats). When treating poisoning, it is important that acetylcysteine be administered as soon as possible for optimum effectiveness. Acetylcysteine also has been used to prevent contrast medium-induced nephropathy. Acetylcysteine has been used as a treatment of oxidative stress because it is a scavenger of hydroxyl radicals and hypochlorous acid. Acetylcysteine will reduce cerebral edema.

Precautionary Information

Adverse Reactions and Side Effects

None reported in animals. Allergic reactions have been reported in people, which resemble anaphylactic reactions when it is given IV. These reactions are manifest as skin reactions, bronchospasm, tachycardia, and hypotension.

Contraindications and Precautions

Acetylcysteine may cause sensitization with prolonged topical administration. It may react with certain materials in nebulizing equipment.

Drug Interactions

Acetylcysteine acts to donate sulfhydryl groups and may facilitate drug conjugation.

Instructions for Use

Available as agent for decreasing viscosity of respiratory secretions, but most common use is as a treatment for intoxications. In cats, acetylcysteine is used to

8 Acyclovir

treat acetaminophen toxicosis. When treating an intoxication, doses are listed here, but consult a poison control center for specific guidelines. For treatment of oxidative stress, constant rate infusions have been used in which 50 mg/kg is diluted 1:4 in saline solutions and administered IV over the course of 1 hour.

Patient Monitoring and Laboratory Tests

When used to treat acetaminophen toxicity, monitor CBC and liver enzyme concentrations.

Formulations

Acetylcysteine is available in a 20% solution (200 mg/mL).

Stability and Storage

Acetylcysteine is unstable in air and easily oxidizes. It should be protected from light. Discard open vials after 96 hours.

Small Animal Dosage

Dogs and Cats

- Antidote: 140 mg/kg (loading dose) then 70 mg/kg q4h IV or PO for 5 doses.
- Eye solution: 2% solution topically q2h.
- To prevent contrast-medium nephropathy: 17 mg/kg IV bolus, followed by 17 mg/kg every 12 hours for 48 hours.
- Constant rate infusions have been used to treat oxidative stress (50 mg/kg diluted in saline infused over 1 hour).

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. However, because it is short-acting and is used primarily for treatment of intoxications, no withdrawal time is suggested. For further information contact FARAD at 1-888-USFARAD (1-888-873-2723).

Acyclovir

ay-sye'kloe-veer

Trade and other names: Zovirax and generic brands

Functional classification: Antiviral

Pharmacology and Mechanism of Action

Antiviral drug. Acyclovir is a synthetic purine analogue (acyclic nucleoside analogue). It has antiviral activity against herpes virus. The action is related to the affinity for the enzyme thymidine kinase (TK). However, resistance among some virus forms is possible because of changes in TK or in the DNA polymerase. It is used for treatment of various forms of herpes virus infection in humans and also has been used for treatment of viral infections in animals. However, feline herpes virus 1 (FHV1) is resistant to acyclovir and valciclovir, and studies are lacking on the susceptibility of other herpes viruses. The half-life is 9.6 hours for horses, 2.3 hours for dogs, and 2.6 hours for cats. By comparison, the half-life in humans is 2.5 hours. Unfortunately, it is not absorbed orally in horses (less than 3%), and there are

little data to confirm oral absorption in other species. In humans, oral absorption is only 10%. Other forms (e.g., pro-drugs and related compounds) are better absorbed in people, but these have been expensive to use in animals. Information on these drugs (penciclovir, valacyclovir, and famciclovir) can be found in other monographs.

Indications and Clinical Uses

Acyclovir is an antiviral drug. The use in veterinary medicine is limited because the activity against some viruses (e.g., FHV1) is either poor or unknown. In cats, acyclovir had poor absorption and produced toxicity. Acyclovir is able to inhibit replication of equine herpes virus (EHV1) in vitro. However, acyclovir oral absorption in horses was poor and inconsistent and intravenous treatment is needed for treatment of EHV1 infection.

Precautionary Information

Adverse Reactions and Side Effects

The most serious adverse effect in humans is acute renal insufficiency. This may be prevented by slow intravenous infusion and proper hydration. Phlebitis can occur with intravenous administration. No adverse effects were identified in limited studies performed in horses. In cats, significant adverse effects have been observed, which included myelosuppression, hepatotoxicity, and nephrotoxicity.

Contraindications and Precautions

Do not use in animals with compromised renal function.

Drug Interactions

Do not mix with biological solutions (e.g., blood products). Do not mix with fluids that contain bacteriostatic preservatives. Do not use with other nephrotoxic drugs.

Instructions for Use

To prepare injectable formulation, dilute each vial with 10 or 20 mL of water to make 50 mg/mL. Do not use bacteriostatic water that contains benzyl alcohol or parabens. Further dilute solution to at least 100 mL to a concentration of 7 mg/mL or less.

Patient Monitoring and Laboratory Tests

Monitor BUN and creatinine during use. In horses, doses should be administered to maintain plasma concentrations above 0.3 mcg/mL.

Formulations

Acyclovir is available in 400- and 800-mg tablets, 200-mg capsules, 1-g and 500-mg vials for injection (50 mg/mL), and 40-mg/mL oral suspension.

Stability and Storage

After reconstitution of solution, at 50 mg/mL, it is stable for 12 hours at room temperature. More dilute solutions are stable for 24 hours. If refrigerated, a precipitate will form, which should be redissolved at room temperature before use. Store tablets and capsules in a tightly sealed container, protected from light, and at room temperature.

10 Aglepristone

Small Animal Dosage

Dogs and Cats

- Systemic doses have not been determined. Doses have been extrapolated from human use: 3 mg/kg PO 5 times daily for 10 days, up to 10 mg/kg PO 5 times daily for 10 days. Alternatively 10-20 mg/kg IV q8h (slow infusion for 1 hour).

Large Animal Dosage

Horses

- 10 mg/kg q12h IV infused over one hour. Even after 20 mg/kg, oral acyclovir is not absorbed in horses well enough for systemic treatment.

Regulatory Information

Because of mutagenicity, it should not be administered to animals intended for food.

Aglepristone

Trade and other names: Alizine

Functional classification: Hormone, antiprogestin

Pharmacology and Mechanism of Action

Aglepristone (RU 46534) is a synthetic steroid antiprogestin related to mifepristone (RU 38486). It has an affinity for progesterone receptors that is three times that of progesterone, without producing the same effects as progesterone. When administered, it binds to progesterone receptors to produce an antiprogestin effect and to interrupt and terminate pregnancy.

Indications and Clinical Uses

Aglepristone has also been used to terminate pregnancy in animals, treat mammary hyperplasia in cats, induce parturition in dogs and cats, and treat pyometra.

Precautionary Information

Adverse Reactions and Side Effects

After termination of pregnancy in dogs, mucoïd discharge may be observed. Other side effects include slight depression, transient anorexia, and mammary gland congestion. Otherwise, there have been no significant adverse effects reported in animals.

Contraindications and Precautions

Aglepristone will terminate pregnancy. It should be handled with caution by women. Owners should be cautioned about risks during pregnancy.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

For treatment of pyometra, it should be administered on days 1, 2, 7, and 14 by SQ injection.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Aglepristone is not available in the US at this time. In some European countries it is available as a 30-mg/mL injection.

Stability and Storage

Store at room temperature protected from light.

Small Animal Dosage

Dogs

- Terminate pregnancy: Two doses of 10 mg/kg (0.33 mL/kg) once daily for 2 days.

Cats

- Treatment of pyometra: 10 mg/kg SC, on days 1, 2, 7, and 14.

Large Animal Dosage

Large Animals

No large animal doses are available.

Regulatory Information

Do not administer to food-producing animals.

Albendazole

al-ben'dah-zole

Trade and other names: Valbazen

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Benzimidazole antiparasitic drug. Albendazole binds to intracellular beta-tubulin in parasites and prevents the microtubule formation for cell division.

Indications and Clinical Uses

Albendazole is used to treat a variety of intestinal helminth parasites. It has been used for treating parasitic infections of the respiratory tract, including *Capillaria aerophilia*, *Paragonimus kellicotti*, *Aelurostrongylus abstrusus*, *Filaroides* spp., and *Oslerus osleri*. It is also effective for treatment of *Giardia* in small animals. However, because albendazole has been associated with bone marrow suppression in dogs and cats, other drugs have been used for *Giardia*.

Precautionary Information

Adverse Reactions and Side Effects

Leukopenia and thrombocytopenia are possible in dogs and cats. Albendazole has an affinity for rapidly dividing cells and may cause toxicity to bone marrow and intestinal epithelium. High doses have been associated with bone marrow toxicity (*J Am Vet Med Assoc*, 213: 44-46, 1998) in dogs and cats, and it should be used cautiously in small animals. In other species, at approved doses, there is a

12 Albuterol Sulfate

wide margin of safety. Adverse effects can include anorexia, lethargy, and bone marrow toxicity.

Contraindications and Precautions

Adverse effects are more likely when administered for longer than 5 days. Avoid high doses. Pregnancy caution: Do not use during first 45 days of pregnancy.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Used primarily as antihelmintic but also has demonstrated efficacy for giardiasis.

Patient Monitoring and Laboratory Tests

Monitor CBC in animals experiencing signs suspicious of adverse effects. If high doses are accidentally administered to small animals, CBC should be examined for evidence of suppression.

Formulations

Albendazole is available in a 113.6-mg/mL suspension and 300-mg/mL paste.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been investigated.

Small Animal Dosage

- Anthelmintic dose: 25-50 mg/kg q12h PO for 3 days.
- Respiratory parasites: 50 mg/kg q24h PO for 10-14 days.
- Giardia: 25 mg/kg q12h PO for 2 days.

Birds

50-100 mg/kg once per day for 2-9 days.

Large Animal Dosage

Cattle

- Antiparasitic: Single dose of 10 mg/kg oral paste or 10 mg/kg (suspension) PO.

Horses

- *Dictyocaulus arnfieldi*: 25 mg/kg q12h for 5 days.
- *Strongylus vulgaris*: 50 mg/kg q12h for 2 days.

Sheep and Goats

- Single dose of 7.5 mg/kg oral suspension.

Regulatory Information

Cattle withdrawal time: 27 days meat. Do not use in lactating dairy cattle. Sheep withdrawal time: 7 days meat.

Albuterol Sulfate

al-byoo'ter-ole sul'fate

Trade and other names: Proventil, Ventolin, and Torpex equine inhaler. Also known as Salbutamol outside the US.

Functional classification: Bronchodilator, beta-agonist

Pharmacology and Mechanism of Action

Beta₂-adrenergic agonist. Albuterol stimulates beta₂-receptors to relax bronchial smooth muscle. It may also inhibit release of inflammatory mediators, especially from mast cells. This mechanism of action has been beneficial to relax bronchial smooth muscle to relieve bronchospasm and bronchoconstriction.

Indications and Clinical Uses

Albuterol is indicated in a variety of airway diseases for bronchodilation. Except for equine use, doses are primarily derived from extrapolation of human dose. Efficacy studies for small animal use are not reported. Onset of action is 15-30 minutes, and duration of action may be as long as 8 hours.

Albuterol is used as an inhaler (Torpex) in horses for treatment of airway disease. It provides immediate relief of bronchospasm and bronchoconstriction in horses.

Precautionary Information

Adverse Reactions and Side Effects

Excessive beta-adrenergic stimulation at high doses results in tachycardia and muscle tremors. Arrhythmias are possible with high doses. All beta₂-agonists will inhibit uterine contractions at the end of gestation in pregnant animals. High doses of beta₂-agonists can lead to hypokalemia because they stimulate Na⁺-K⁺-ATPase and increase intracellular K⁺, while decreasing serum K⁺ and producing hyperglycemia. Treatment consists of KCl supplement at a rate of 0.5 mEq/kg/hr.

Contraindications and Precautions

Avoid use in pregnant animals. IM or SQ injections can be painful.

Drug Interactions

All beta-agonists will interact with, and potentiate other drugs that act on, beta-adrenergic receptors.

Instructions for Use

Administration to horses requires an adaptor to facilitate a metered-dose inhaler. For horses, each valve actuation (puff) of the device delivers 120 micrograms of albuterol sulfate. One dose is three puffs, totaling 360 micrograms. For injection, dilute solution to 0.01 mg/mL (10 mcg/mL) before injection and further dilute to 50/50 with saline or 5% dextrose before injection. When used for bronchoconstriction, it is helpful for acute exacerbations, used intermittently, with other drugs (e.g., corticosteroids) administered for maintenance.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm in animals with cardiovascular disease. Monitor potassium concentrations for evidence of hypokalemia if high doses are administered. Monitor glucose for evidence of hyperglycemia.

Formulations

Albuterol is available in 2-, 4-, and 5-mg tablets and 2-mg/5-mL syrup. Solutions for inhalation are 0.83 mg/mL and 5 mg/mL. Equine formulation contains 6.7 grams of formulated albuterol sulfate in a pressurized aluminum canister. This formulation delivers 120 micrograms of albuterol sulfate. One dose is three puffs, totaling 360 micrograms.

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Stability and Storage

Store in well-closed containers and protected from light. Aqueous solutions are stable if kept at an acidic pH (2.2-5).

Small Animal Dosage

Dogs and Cats

- 20-50 mcg/kg q6-8h, oral, up to a maximum of 100 mcg/kg q6h.

Large Animal Dosage

Horses

- 120-mcg albuterol per actuation. Administer 3 actuations, up to a maximum of 6, actuations per each dose four times daily.
- Foals: 0.01-0.02 mg/kg, q8-12h, PO.

Regulatory Information

Do not administer to animals intended for food.

When treating horses, allow 48 hours or longer for urine clearance in performance animals that may be tested.

RCI Classification: 3

Alendronate

ah-len'droe-nate

Trade and other names: Fosamax

Functional classification: Antihypercalcemic

Pharmacology and Mechanism of Action

Bisphosphonate drug. Drugs in this class include pamidronate, risedronate, zoledronate, and etidronate. This is a group of drugs characterized by a germinal bisphosphonate bond. They slow the formation and dissolution of hydroxyapatite crystals. Their clinical use is in their ability to inhibit bone resorption. These drugs decrease bone turnover by inhibiting osteoclast activity, retarding bone resorption, and decreasing the rate of osteoporosis. Alendronate is 100-1000 times more potent than older drugs such as etidronate. Unfortunately, alendronate is poorly absorbed orally (3%-7%), and use of oral formulations in animals may not be effective. In dogs, half-life in plasma is short (1-2 hours), but there is prolonged uptake bone in which the half-life is 300 days.

Indications and Clinical Uses

Alendronate, like other bisphosphonate drugs, is used in people to treat osteoporosis and treatment of hypercalcemia of malignancy.

In animals, alendronate is used to decrease calcium in conditions that cause hypercalcemia, such as cancer and vitamin D toxicosis. It may be helpful for managing neoplastic complications associated with pathologic bone resorption. It also may provide pain relief in patients with pathologic bone disease. Most experimental work performed in dogs has been performed with pamidronate rather than alendronate.

Precautionary Information

Adverse Reactions and Side Effects

No serious adverse effects have been identified; however, use in animals has been uncommon. In people, esophageal injury and erosion are important problems.

When administering to animals, ensure that the entire medication is swallowed and followed with water.

Contraindications and Precautions

Do not administer with foods or medications containing calcium. Food will decrease absorption.

Drug Interactions

Do not mix with a solution containing calcium (e.g., Lactated Ringer's solution). Do not give with foods containing calcium.

Instructions for Use

When administering oral medication, ensure that the drug is not trapped in the esophagus. Food will significantly reduce oral absorption. Wait at least 30 minutes before feeding.

Patient Monitoring and Laboratory Tests

Monitor serum calcium and phosphorus.

Formulations

Alendronate is available in 5-, 10-, 35-, 40-, and 70-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 0.5-1 mg/kg q24h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Alfaxalone

Al-FAX-ah-lone

Trade and other names: Alfaxan (previous name was alphaxalone)

Functional classification: Anesthetic agent

Pharmacology and Mechanism of Action

Alfaxalone is chemically alfaxalone-2-hydroxypropyl-beta-cyclodextrin (HPCD). It is a synthetic neuroactive steroid that interacts with GABA receptors in the central nervous system to produce anesthesia and muscle relaxation. Alfaxalone is related to an older

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formulation (Saffan) first introduced in 1971, which was alfaxalone plus alfadolone in a combination of neurosteroids. This older formulation was in a castor oil formulation that induced mast cell degranulation and histamine release and produced swollen extremities, anaphylactic reactions, and other signs of histamine release. This new formulation (Alfaxan) overcomes the formulation issue by using a cyclodextrin solubilizing vehicle. The half-life is short in animals (less than 1 hour) but it exhibits nonlinear pharmacokinetics and may be eliminated slower with high doses.

Indications and Clinical Uses

Alfaxalone is used as a general anesthetic agent. It can be injected directly into the cephalic vein or delivered via constant rate infusion. If injected directly, administer over 60 seconds to allow enough time to cross the blood-brain barrier. It has been used safely with other anesthetic agents (e.g., propofol), and in combination with premedications (e.g., opiates, atropine, phenothiazines, benzodiazepines, and NSAIDs).

Precautionary Information

Adverse Reactions and Side Effects

As an anesthetic agent, CNS depression, respiratory depression, and some blood pressure decrease are expected after administration. At constant rate infusion doses >0.1 mg/kg/min it will produce noticeable hypotension and hypoventilation.

Drug Interactions

No drug interactions are reported in animals. However, do not mix with other drugs in the same syringe unless specific compatibility information is available.

Instructions for Use

For induction of anesthesia, use with appropriate monitoring equipment and ventilatory support.

Patient Monitoring and Laboratory Tests

Monitor character and depth of anesthesia during use. Monitor blood pressure and respiratory rate during infusions.

Formulations

Alfaxalone is not available in the US at this time.

Stability and Storage

Store at room temperature protected from light.

Small Animal Dosage

Dogs

- Induction: 1-1.2 mg/kg (up to 2 mg/kg) for each 10 minutes of anesthesia. Deliver dose over 60 seconds.
- Constant rate infusion: 6-7 mg/kg/hour (suitable to use with other anesthetic agents).

Cats

- Induction: 1-1.3 mg/kg IV (up to 5 mg/kg) delivered over 60 seconds, followed by sequential doses of 2 mg/kg as needed.
- Constant rate infusion: 7-8 mg/kg/hour.

Large Animal Dosage

Large Animals

No large animal doses are available.

Regulatory Information

Do not administer to food-producing animals.

Allopurinol

al-oh-pyoo'rih-nole

Trade and other names: Lopurin, Zyloprim, and Allopur (Europe)

Functional Classification: Anti-inflammatory

Pharmacology and Mechanism of Action

Purine analogue. Allopurinol decreases the production of uric acid by inhibiting enzymes responsible for uric acid synthesis. The other use of allopurinol is treating leishmaniasis. In parasites, allopurinol is metabolized to products that disrupt RNA synthesis and interfere with protein synthesis. Allopurinol does not eliminate *Leishmania* or cure the disease, but it may improve cutaneous lesions and induce remission.

Indications and Clinical Uses

Allopurinol is indicated to decrease formation of uric acid uroliths in at-risk animals. Allopurinol also is used to treat clinical signs associated with leishmaniasis. When used for leishmaniasis it is administered with pentavalent antimonial compounds such as meglumine antimonite (Glutamine) or sodium stibogluconate (Pentosan). With chronic treatment, allopurinol will produce progressive remission and improvement in clinical signs associated with leishmaniasis, which include decreasing the damaging effects of *Leishmania* on the animal's kidneys by decreasing proteinuria and preventing deterioration of GFR.

Precautionary Information

Adverse Reactions and Side Effects

Allopurinol may cause skin reactions (hypersensitivity). In dogs that were treated for leishmaniasis for several months, no adverse effects were reported.

Contraindications and Precautions

No contraindications reported for animals.

Drug Interactions

Allopurinol may inhibit drug metabolism of certain drugs. Do not use with azathioprine because it interferes with xanthine oxidase, an important enzyme for metabolizing azathioprine, and will enhance toxicity.

Instructions for Use

In people, allopurinol is used primarily for treating gout.

In animals, it is used to decrease formation of uric acid uroliths and for treating signs associated with leishmaniasis. No single drug or combination is completely effective for treating leishmaniasis, but allopurinol will improve skin lesions.

Allopurinol is usually administered with other drugs for leishmaniasis. For example,

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it has been administered with either amphotericin B or pentavalent antimonial compounds such as meglumine antimonite (Glutamine) or sodium stibogluconate (Pentosan).

Patient Monitoring and Laboratory Tests

Dose adjustments for treating leishmaniasis are based on monitoring clinical signs. Allopurinol will not cure the underlying disease, but it will decrease some clinical signs.

Formulations

Allopurinol is available in 100- and 300-mg tablets.

Stability and Storage

Store in well-closed containers at room temperature. Allopurinol is stable for at least 60 days in compounded formulations. Maximum stability in solutions at pH of 3-3.4.

Small Animal Dosage

Dogs

- Urate urolith prevention: 10 mg/kg q8h PO, then reduce to 10 mg/kg q24h PO.
- Leishmaniasis: 10 mg/kg q12h PO for at least 4 months and as long as 6 months. For leishmaniasis, some clinicians have used 15 mg/kg q12h, and then if there is a response, administer 7-10 mg/kg q12-24h PO.

Large Animal Dosage

Horses

- 5 mg/kg PO.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Alprazolam

al-pray/zoe-lam

Trade and other names: Xanax and Niravam

Functional classification: Tranquilizer, CNS depressant

Pharmacology and Mechanism of Action

Benzodiazepine. Central-acting central nervous system (CNS) depressant. Mechanism of action appears to be via potentiation of GABA-receptor mediated effects in CNS. A drug that has similar effects is diazepam.

Indications and Clinical Uses

Alprazolam is used to treat behavior problems in dogs and cats, particularly those associated with anxiety. Alprazolam has been used in dogs for the short-term treatment of anxiety states, such as noise phobias and thunderstorm phobia. For thunderstorm phobia, it may be more effective if combined with long-term clomipramine treatment.

Precautionary Information

Adverse Reactions and Side Effects

Sedation is the most common side effect, but alprazolam may also cause paradoxical excitement in dogs. It also causes polyphagia. In cats, idiopathic fatal hepatic necrosis has been reported from diazepam, but this has not been reported from alprazolam, probably because of differences in metabolism. Alprazolam is not as extensively metabolized as diazepam. Chronic administration in any species may lead to dependence and a withdrawal syndrome if discontinued.

Contraindications and Precautions

No serious contraindications. In rare individuals, benzodiazepines have caused paradoxical excitement.

Drug Interactions

Other drugs may decrease hepatic metabolism (e.g., ketoconazole, chloramphenicol, and itraconazole).

Instructions for Use

Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Duration of effect is only 2-3 hours in many dogs. Therefore, if needed, more frequent administration may be required.

When treating thunderstorm phobia, it is helpful in some dogs to administer 0.02 mg/kg of clomipramine 1 hour before a storm, in addition to alprazolam.

The Niravam tablets (see formulation section) are rapidly dissolving and may be easier to administer to animals that are difficult to medicate. Tablets easily dissolve on the tongue without requiring water and can be cut for accurate dosing.

Patient Monitoring and Laboratory Tests

Monitor hepatic enzymes in animals with chronic use.

Formulations

Alprazolam is available in 0.25-, 0.5-, 1-, and 2-mg tablets and 1- and 2-mg scored tablets.

Rapidly dissolving tablets (Niravam) are available in 0.25, 0.5, 1, and 2 mg that can be cut for accurate dosing.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Drug is stable in some compounded formulations for 60 days.

Small Animal Dosage

Dogs

- 0.025-0.1 mg/kg q8h PO. Administration more frequently (q4-6h) has been used in some patients.

Cats

- 0.125 mg per cat q12h PO (1/2 of 0.25 mg tablet) or 0.0125-0.025 mg/kg q12h PO, and up to q8h.

Large Animal Dosage

No dose has been reported for large animals.

20 Altrenogest

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Altrenogest

al-tren'-oh-jest

Trade and other names: Regu-Mate, Matrix

Functional classification: Hormone

Pharmacology and Mechanism of Action

Altrenogest is an active synthetic progestin hormone. As a progesterone agonist, it is primarily used to suppress estrus in animals. Suppression of estrus allows for a predictable occurrence of estrous activity after the drug is discontinued. Therefore, it is used to induce a normal cycle of estrous activity to facilitate scheduled breeding. When treatment is initiated, 95% of the mares will have an estrous cycle suppressed in 3 days.

Indications and Clinical Uses

Altrenogest is indicated to suppress estrus in animals to facilitate induction of normal estrous cycle activity. It is used in mares to facilitate scheduled breeding activity. It is also used to suppress estrous behavior in performance horses. When treatment is discontinued, mares exhibiting regular estrous cycles return to estrus within 4 to 5 days following treatment and continue to cycle normally.

In swine altrenogest is used for synchronization of estrus in sexually mature gilts that have had at least one estrous cycle. Do not use in gilts having a previous or current history of uterine inflammation (i.e., acute, subacute, or chronic endometritis).

Precautionary Information

Contraindications and Precautions

Do not administer to pregnant animals. Humans handling altrenogest, particularly women, should wear gloves and avoid contact because altrenogest can be absorbed in humans through intact skin. Altrenogest should not be used in mares or in gilts with a previous history of uterine problems (metritis).

Instructions for Use

Administer altrenogest 1 dose daily for 15 days, orally on grain or directly on the horse's tongue. In pigs administer as a top dressing or with feed.

Patient Monitoring and Laboratory Tests

Monitor for signs of estrous activity. Monitor CBC in cases of overdose.

Formulations

Altrenogest is available in an oil solution of 0.22% (2.2 mg/mL).

Stability and Storage

Store in well-closed containers at room temperature.

Small Animal Dosage

- No dose available.

Large Animal Dosage

Horses

- 0.044 mg/kg (or 1 mL per 110 pounds) orally once per day for 15 days.

Swine

Administer 6.8 mL (15 mg altrenogest) per gilt once daily for 14 consecutive days by top-dressing on a portion of each gilt's daily feed.

Regulatory Information

Do not use in horses intended for food. In pigs, gilts must not be slaughtered for human consumption for 21 days after the last treatment. Do not administer to other food-producing animals.

Aluminum Hydroxide and Aluminum Carbonate

ah-loo'mih-num hye-droks'ide, ah-loo'mih-num kar'boe-nate

Trade and other names: Aluminum hydroxide gel (Amphogel) and aluminum carbonate gel (Basalgel)

Functional classification: Antacid

Pharmacology and Mechanism of Action

Aluminum is an antacid and phosphate binder in intestine. It is used in both the aluminum hydroxide and aluminum carbonate formulations.

Indications and Clinical Uses

A common use of aluminum hydroxide is for its antacid properties to treat or manage gastrointestinal ulcers. Also, it is used as a phosphate binder. It is indicated in animals with hyperphosphatemia associated with chronic renal failure, often in combination with phosphorus-restricted diets. Because of the decreased availability of products containing aluminum, other drugs are used to decrease hyperphosphatemia in patients, such as calcium carbonate and calcium citrate.

Precautionary Information

Adverse Reactions and Side Effects

These aluminum-containing compounds are generally safe. However, there has been some concern expressed that these drugs may increase the systemic levels of aluminum, which may lead to some forms of aluminum toxicoses. The evidence for this as a clinical problem in veterinary medicine is lacking.

Contraindications and Precautions

Aluminum decreases oral absorption of some drugs (e.g., fluoroquinolones, tetracyclines). If fluoroquinolone antimicrobials are used concurrently, separation of oral doses should be considered.

Drug Interactions

Aluminum will bind and chelate some drugs and prevent the gastrointestinal absorption. Drugs bound to aluminum include tetracyclines and quinolone antibiotics.

Instructions for Use

Antacid doses are designed to neutralize stomach acid, but duration of acid suppression is short. Although aluminum hydroxide is often used to prevent hyperphosphatemia, this drug may not be available in some pharmacies. A substitute for this indication is calcium citrate or calcium carbonate.

Patient Monitoring and Laboratory Tests

Phosphate plasma levels should be monitored to determine success of therapy.

Formulations

Aluminum hydroxide gel is available in a 64-mg/mL oral suspension and 600-mg tablet. Aluminum carbonate gel is available in capsules (equivalent to 500 mg aluminum hydroxide). Note: Products containing aluminum may no longer be available from many sources.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- Aluminum hydroxide gel: 10-30 mg/kg q8h PO (with meals).
- Aluminum carbonate gel: 10-30 mg/kg q8h PO (with meals).

Cats

- Aluminum hydroxide gel: 10-30 mg/kg q8h PO (with meals).
- Aluminum carbonate gel: 10-30 mg/kg q8h PO (with meals).

Large Animal Dosage

Horses

- Antacid: 60 mg/kg q8h PO.

Regulatory Information

No regulatory information is available. Residues from administration to food-producing animals ordinarily are not a concern. However, for extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Amantadine

ah-man'tah-deen

Trade and other names: Symmetrel and generic brands

Functional classification: Antiviral

Pharmacology and Mechanism of Action

Amantadine is an antiviral drug. The action against viruses is not entirely known. For treating other conditions in people (Parkinson's disease) its effects are attributed to an increase in dopamine in the central nervous system (CNS). However it also is an N-methyl-D-aspartate (NMDA) receptor antagonist. As an NMDA antagonist, it will decrease tolerance to other analgesic drugs (e.g., opiates), but it probably does not possess many analgesic properties when used alone. Pharmacokinetics have not

been investigated for veterinary uses, but this drug is completely absorbed from oral administration in people and crosses the blood–brain barrier.

Indications and Clinical Uses

Amantadine is an antiviral drug used to treat influenza infections in people. It also is used in people to treat Parkinson's disease and extrapyramidal reactions, especially those that are drug induced. It also has been used to manage muscular weakness in humans with multiple sclerosis. However, its use in veterinary medicine has primarily been for treating pain in dogs and cats. It is used for treating pain when other drugs have been ineffective or when it is desirable to use in combination with multiple drugs in multimodal therapy analgesic protocols.

Precautionary Information

Adverse Reactions and Side Effects

Toxicity has not been seen in dogs and cats until doses are exceeded by at least two times. Rarely, the side effects of anxiety states and dry mouth have been observed. Dizziness, confusion, and other CNS disturbances have been reported in people.

Contraindications and Precautions

Pregnancy caution: Amantadine is embryotoxic and teratogenic at high doses in laboratory animals. Avoid its use in pregnancy.

Drug Interactions

Do not use with other drugs that increase dopamine concentrations (e.g., selegiline). If used with other CNS stimulants, it may enhance the effects.

Instructions for Use

Amantadine for treatment of pain may not be effective when used alone. Administer with another analgesic agent (e.g., NSAID) for best results. Antiviral effects have not been adequately explored in animals. In people, antiviral dose is 1.5–3 mg/kg once or twice a day.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Amantadine is available in 100-mg capsules, 100-mg tablets, and 10-mg/mL syrup.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

3 mg/kg q24h PO for treatment of pain, up to a dose of 5 mg/kg in some cases. In surgical patients it has been used for 21 days after surgery.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

This drug should not be administered to food-producing animals, and no regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Amikacin

am-ih-kay'sin

Trade and other names: Amiglyde-V (veterinary preparation), Amikin (human preparation), and generic brands

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Aminoglycoside antibiotic. Action is to inhibit bacteria protein synthesis via binding to 30S ribosome. Amikacin is bactericidal with a broad spectrum of activity except against streptococci and anaerobic bacteria. Amikacin may have activity against many bacteria, especially gram-negative bacilli, that are resistant to other drugs. Amikacin may be more active than gentamicin against many gram-negative bacteria, especially enteric species. In most animals, the half-life is short (1-2 hours), and volume of distribution reflects extracellular body water (e.g., 200-250 mL/kg). Amikacin is not absorbed from oral administration.

Indications and Clinical Uses

Amikacin is indicated in bacterial infections, especially for treatment of serious infections caused by gram-negative bacteria. When resistance to gentamicin is anticipated, amikacin is often used in its place. In horses, amikacin also is used for local administration as an intrauterine lavage to treat metritis and other infections of the genital tract caused by gram-negative bacteria. In horses, amikacin also is used for regional limb perfusion.

Precautionary Information

Adverse Reactions and Side Effects

Nephrotoxicity is the most dose-limiting toxicity. Ensure that patients have adequate fluid and electrolyte balance during therapy. Ototoxicity and vestibulotoxicity also are possible.

Contraindications and Precautions

Do not use in animals with renal insufficiency or renal failure. Do not use in dehydrated animals.

Drug Interactions

Do not mix in vial or syringe with other antibiotics. Amikacin is incompatible with other drugs and compounds when mixed in the same vial or syringe. This effect is particularly important when mixing with other antibiotics. When used with anesthetic agents, neuromuscular blockade is possible.

Instructions for Use

Once-daily doses are designed to maximize peak-to-minimum inhibitory concentration (MIC) ratio. Consider therapeutic drug monitoring to decrease risk of renal toxicosis. Activity against some bacteria (e.g., *Pseudomonas*) is enhanced when combined with a beta-lactam antibiotic. Nephrotoxicity is increased with persistently high trough concentrations.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI MIC break point is ≤ 16 mcg/mL. Monitor BUN, serum creatinine, and urine for evidence of renal toxicity. Plasma or serum drug

concentrations can be monitored to measure for problems with systemic clearance. When monitoring trough levels in patients during once-daily administration, the trough levels should fall below the limit of detection. Alternatively, the half-life and clearance can be measured from samples taken at 1 hour and 2 to 4 hours post-dosing. Clearance in most animals should be above 1.0 mL/kg/min and half-life should be <2 hours.

Formulations

Amikacin is available in 50- or 250-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Amikacin will be unstable if mixed with other drugs.

Small Animal Dosage

Dogs

- 15-30 mg/kg q24h IV, IM, or SQ.

Cats

- 10-14 mg/kg q24h IV, IM, or SQ.

Large Animal Dosage

Horses

- Adult: 4.4-6.6 mg/kg q12h IM or IV or 10 mg/kg q24h IV or IM.
- Foal: 20-25 mg/kg q24h IV or IM or 6.6 mg/kg q8h IV or IM.
- Intrauterine use: Administer 2 g (8 mL) diluted in 200-mL sterile saline solution in uterus once per day for 3 days.
- Regional limb perfusion: Doses have ranged from 125 mg to 500 mg per limb, diluted in 60 mL saline.

Cattle

- Adult: 10 mg/kg q24h IM, IV, or SQ.
- Calf (<2 weeks of age): 20 mg/kg q24h IV or IM.

Regulatory Information

Withdrawal times have not been established for extralabel use in animals used for food. Long persistence of drug in tissues (renal) is expected after administration. Amikacin, like other aminoglycoside antibiotics, should not be administered to animals that produce food because of a risk of residue problems. If extralabel doses have been administered, the meat withdrawal time may be as long as 18 months. Contact FARAD at 1-888-USFARAD (1-888-873-2723) for specific withdrawal time information.

Amino Acid Solution

Trade and other names: Travasol

Functional classification: Amino acid solution

Pharmacology and Mechanism of Action

Amino acid solutions are intended to provide amino acid supplement to animals with amino acid deficiency or with liver disorders. This particular solution contains

26 Aminopentamide

leucine, phenylalanine, lysine, methionine, isoleucine, valine, histadine, threonine, tryptophan, alanine, glycine arginine, proline, tyrosine, and serine.

Indications and Clinical Uses

In animals amino acid solutions are infused to provide supplement, particularly for treatment of liver disease.

Precautionary Information

Adverse Reactions and Side Effects

A hyperosmolar state can be induced if the infusion is too aggressive. If neurologic signs appear, the infusion should be stopped. In patients with liver disease or renal failure, hepatic encephalopathy or increases in BUN are possible.

Instructions for Use

10% solution may be diluted in 5% dextrose solution for peripheral vein administration. Otherwise, it should be administered via a central vein.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

10% solution.

Stability and Storage

Store at room temperature protected from light.

Small Animal Dosage

Dogs

- 25 mL of a 10% solution (diluted appropriately) infused IV via a central vein. Administer infusion over 6-8 hours and repeat at 7- to 10-day intervals. Solutions without electrolytes are preferred for treating hepatocutaneous syndrome.

Large Animal Dosage

Large Animals

- No dose reported.

Regulatory Information

There is no withdrawal time necessary for food animals.

Aminopentamide

ah-mee-noe-pent'ah-mide

Trade and other names: Centrine

Functional classification: Anticholinergic

Pharmacology and Mechanism of Action

Antidiarrheal drug. Anticholinergic (blocks acetylcholine at parasympathetic synapse). Like other anticholinergic drugs in this class, aminopentamide blocks

muscarinic receptors. As a result of blockade, effects of acetylcholine are blocked to inhibit gastrointestinal secretions and smooth muscle motility. Glandular, respiratory, and other physiologic functions also can be affected. Aminopentamide is an older drug that is not often used as a treatment of diarrhea or gastrointestinal diseases today.

Indications and Clinical Uses

Aminopentamide has been used to decrease GI motility and decrease GI secretions in animals. It also has been used to treat diarrhea, but long-term use for this purpose is not recommended.

Instructions for Use

Dosing guidelines based on manufacturer's recommendation.

Patient Monitoring and Laboratory Tests

Monitor for problems caused by intestinal stasis because of anticholinergic effect.

Formulations

Aminopentamide is available in 0.2-mg tablets and 0.5-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 0.01-0.03 mg/kg q8-12h IM, SQ, or PO.

Cats

- 0.1 mg/cat q8-12h IM, SQ, or PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Aminophylline

am-in-off'ih-lin

Trade and other names: Generic brands

Functional classification: Bronchodilator

Pharmacology and Mechanism of Action

Bronchodilator. Aminophylline is a salt of theophylline, formulated to enhance oral absorption without gastric side effects. It is converted to theophylline after ingestion. The mechanism of action and other properties are the same as theophylline. Consult the theophylline monograph for more details. Theophylline's action is to inhibit phosphodiesterase (PDE) and increase cyclic AMP. Other antiinflammatory mechanisms also may play a role in its clinical effects.

Indications and Clinical Uses

Aminophylline is indicated for control of reversible airway constriction, to prevent bronchoconstriction, and as an adjunct with other respiratory disease treatment. The uses are similar to the indications for theophylline because it is a salt form of theophylline. It is used for inflammatory airway disease in cats (feline asthma), dogs, and horses. In dogs, the uses include collapsing trachea, bronchitis, and other airway diseases. It has not been effective for respiratory diseases in cattle.

Precautionary Information

Adverse Reactions and Side Effects

Aminophylline causes excitement and possible cardiac side effects with high concentrations. Cardiac adverse effects include tachycardia and arrhythmias. Gastrointestinal adverse effects include nausea, vomiting, and diarrhea. Central nervous system adverse effects include excitement, tremors, and seizures.

Contraindications and Precautions

Although adverse effects appear more common in people than small animals, use cautiously in animals with cardiac arrhythmias. Use cautiously in animals prone to seizures. Horses may become excited from IV administration.

Drug Interactions

Use cautiously with other phosphodiesterase inhibitors such as sildenafil (Viagra) and pimobendan. Many drugs will inhibit the metabolism of theophylline and potentially increase concentrations (e.g., cimetidine, erythromycin, fluoroquinolones, and propranolol). Some drugs will decrease concentrations by increasing metabolism (e.g., phenobarbital and rifampin).

Instructions for Use

Therapeutic drug monitoring of theophylline is recommended for accurate dosing during chronic therapy. When dosing with salts or other formulations of theophylline, adjust dose for the amount of the parent drug.

Patient Monitoring and Laboratory Tests

Plasma concentrations of theophylline should be monitored in patients receiving therapy with aminophylline. Targeted plasma concentrations range from 10 to 20 mcg/mL, but clinical effects may occur as low as 5 mcg/mL.

Formulations

Aminophylline is available in 100- and 200-mg tablets and 25-mg/mL injection. A dose of 25 mg/mL of anhydrous aminophylline is equivalent to 19.7 mg of anhydrous theophylline per mL.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Compounded oral formulations have been stable for 60 days.

Small Animal Dosage

Dogs

- 10 mg/kg q8h PO, IM, or IV.

Cats

- 6.6 mg/kg q12h PO.

Large Animal Dosage

Horses

- Treatment of recurrent airway obstructions: 12 mg/kg initial dose, followed by 5 mg/kg q12h PO. Although aminophylline has been administered IV to horses, this administration has caused transient excitement and restlessness. Give intravenous administration slowly.

Cattle

- 10 mg/kg q8h IV or 23 mg/kg PO, administered once as a single dose.

Regulatory Information

Cattle: No withdrawal times have been established for food animals.

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Amiodarone Hydrochloride

ah-mee-oe'dah-rone

Trade and other names: Cordarone

Functional classification: Antiarrhythmic

Pharmacology and Mechanism of Action

Antiarrhythmic drug, Class III. Antiarrhythmic effects are primarily caused by blocking the outward potassium channel in cardiac tissues. Amiodarone prolongs the action potential, delays myocardial repolarization, and delays the refractory period in cardiac tissues. It also may have some alpha-adrenergic receptor, beta-adrenergic receptor, and calcium-channel blocking properties. Half-life is several days in duration, and in some animals the half-life may be as long as 100 days with chronic therapy. In horses the terminal half-life was 38-84 hours. The intravenous formulation of amiodarone uses Polysorbate 80 to enhance solubility, which may be responsible for some of the adverse reactions. There is a new non-iodinated derivative, dronedarone (Multaq), that is less lipophilic, has a shorter half-life, and may be safer, but there has been no use reported in animals.

Indications and Clinical Uses

Amiodarone is used to treat refractory ventricular arrhythmias. It is reserved for treating life-threatening arrhythmias that have been refractory to other treatments. It has been used as a last resort for recurrent hemodynamically unstable ventricular tachycardia.

In horses, IV amiodarone has been used to treat atrial fibrillation.

Precautionary Information

Adverse Reactions and Side Effects

Most common effect in dogs is decreased appetite. Prolonged Q-T interval is a concern. Other adverse effects include bradycardia, CHF, hypotension, AV block, thyroid dysfunction (decreased T3 and T4), pulmonary fibrosis, neutropenia, and

anemia. Hepatopathy is a serious concern and has been reported in dogs. Doberman dogs were particularly affected by amiodarone when treated for arrhythmias; there was a high incidence of adverse effects that included anorexia, lethargy, hepatic toxicity, and vomiting. In one study, doses up to 12.5 mg/kg IV produced no acute cardiovascular reactions; however, with acute intravenous administration, severe cardiac reactions, hypotension, vasodilation, pruritus, and edema (including swollen extremities) are possible. Adverse effects caused by IV treatment may be caused by the drug vehicle included to enhance solubility, Polysorbate 80, which is known to elicit allergic-type adverse events caused by histamine release. Pre-treatment with antihistamines may help to decrease adverse events caused by IV treatment.

No adverse clinical signs were observed in horses after single administration IV, but for treating atrial fibrillation, mild signs of shifting weight and hind limb weakness were reported.

Contraindications and Precautions

Severe reactions including hepatopathy and cardiac arrhythmias have been seen in dogs. Use only when arrhythmia has been refractory to other treatments or when dogs are at risk for sudden death.

Drug Interactions

Use amiodarone with beta blockers, calcium-channel blockers, and digoxin cautiously because it may slow conduction. Do not mix intravenous solution with mixtures containing bicarbonate.

Instructions for Use

Typically, loading doses are administered, followed by maintenance dose. Oral dosing in dogs has used 10-15 mg/kg q12h for 1 week, then 5-7.5 mg/kg q12h for 2 weeks, followed by maintenance dose of 7.5 mg/kg q24h. If intravenous therapy is used, doses should be given slowly; initial infusion rate should not exceed 30 mg per minute. Prior to IV treatment, administer antihistamines to prevent allergic-type reactions.

Patient Monitoring and Laboratory Tests

Because of a concern for adverse effects caused by amiodarone in dogs, therapy should be monitored carefully. It is highly recommended to monitor CBC for anemia and neutropenia and monitor hepatic indices with biochemical profile during treatment. Monitor ECG during treatment as prolonged Q-T interval may occur. Monitor thyroid function during treatment. Drug monitoring may be available from some hospitals. Therapeutic range of amiodarone in plasma is 1-2.5 mcg/mL.

Formulations

Amiodarone is available in 100-, 200-, 300-, and 400-mg tablets and 50-mg/mL injection. A new formulation (PM101) uses a different vehicle to enhance solubility, rather than Polysorbate 80. This vehicle, beta-cyclodextrin (Captisol), forms a hydrophilic central core and is less likely to elicit an allergic-type reaction.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- Ventricular arrhythmias: 10-15 mg/kg q12h PO for 1 week, then 5-7.5 mg/kg q12h for 2 weeks, followed by maintenance dose of 7.5 mg/kg q24h.
- Refractory arrhythmias: 25 mg/kg q12h PO for 4 days, followed by 25 mg/kg q24h PO.
- Atrial fibrillation: 15 mg/kg loading dose for 5 days, followed by 10 mg/kg per day, PO, thereafter.
- Boxer or Doberman: 200 mg q12h for 1 week, PO, followed by 200 mg once daily thereafter. Doses as high as 2× these rates have been administered, but with a higher risk of toxicity.

Cats

No dose has been reported for cats.

Large Animal Dosage

Horses

Treatment of atrial fibrillation: 5 mg/kg/hr for 1 hour, followed by 0.83 mg/kg/hr for 23 hours IV. Oral absorption was low and inconsistent and has not been recommended.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Amitraz

am'ih-traz

Trade and other names: Mitaban

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic drug for ectoparasites. Amitraz inhibits monoamine oxidase (MAO) in mites. Mammals are resistant to this inhibition. However, administration of amitraz can interact with other MAO inhibitors (MAOIs).

Indications and Clinical Uses

Amitraz is indicated for the topical treatment of mites, including Demodex. It is applied topically as a dip or sponge-on. It should not be administered systemically. The approved dose is effective in many animals; however, in more resistant cases of Demodex, higher doses have been applied. As the dose increases, the risk of adverse effects also increases.

Precautionary Information

Adverse Reactions and Side Effects

Amitraz causes sedation in dogs caused by the agonist activity on alpha₂-adrenergic receptors, which may be reversed by yohimbine or atipamezole. When high doses are used, other side effects reported include pruritus, polyuria/

32 Amitriptyline Hydrochloride

polydipsia, bradycardia, hypotension, heart block, hypothermia, hyperglycemia, and (rarely) seizures.

Contraindications and Precautions

Adverse effects are more common when high doses are administered.

Drug Interactions

Do not administer with MAOIs, such as selegiline (Deprenyl, Anipryl). Do not administer with other α_2 -agonists.

Instructions for Use

Manufacturer's dose should be used initially, but for refractory cases, this dose has been exceeded to produce increased efficacy.

Patient Monitoring and Laboratory Tests

Monitor by performing periodic skin scrapings and examining for presence of mites.

Formulations

Amitraz is available in 10.6-mL concentrated dip (19.9%).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 10.6 mL/7.5 L water (0.025% solution). Apply 3-6 topical treatments every 14 days. For refractory cases, this dose has been exceeded to improve efficacy. Doses that have been used include 0.025%, 0.05%, and 0.1% concentration applied once or twice per week. For refractory cases, a dose of 0.125% has been used by applying to only one half of the dog's body one day, then to the other half of the body the following day. This alternating schedule has been repeated every day for 4 weeks and up to 5 months to achieve cures but should be considered only in extreme cases.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Amitriptyline Hydrochloride

am-ih-trip'tih-leen hye-droe-klor'ide

Trade and other names: Elavil and generic brands

Functional classification: Behavior modification, tricyclic antidepressant (TCA)

Pharmacology and Mechanism of Action

TCA drug. Amitriptyline, like other TCAs, acts via inhibition of uptake of serotonin and other transmitters at presynaptic nerve terminals. The action in cats for treating

cystitis is unknown but may be either through reducing anxiety, behavior modification, or via anticholinergic effects.

Indications and Clinical Uses

Like other TCAs, amitriptyline is used in animals to treat a variety of behavioral disorders (e.g., anxiety). However, there are few studies documenting efficacy in animals. For treatment of some disorders, such as obsessive compulsive disorder (1 mg/kg q12h up to 2 mg/kg), it was not as effective in animals as clomipramine. For treatment of aggressive behavior in dogs (2 mg/kg q12h) there was no difference between amitriptyline and placebo.

Amitriptyline has been used in cats for chronic idiopathic cystitis. However, when used for short-term treatment of idiopathic cystitis (10 mg per cat, q24h) it was not effective. In another study, at 5 mg/cat per day for 7 days (0.55-1.2 mg/kg), there was no difference on recovery from hematuria and pollakiuria between amitriptyline and placebo, leading to a conclusion that short-term treatment is not helpful.

Precautionary Information

Adverse Reactions and Side Effects

Amitriptyline has a bitter taste and is difficult to administer orally. Multiple side effects are associated with TCAs, such as antimuscarinic effects (dry mouth and rapid heart rate) and antihistamine effects (sedation). High doses can produce life-threatening cardiotoxicity. In cats, reduced grooming, weight gain, and sedation are possible.

Contraindications and Precautions

Use cautiously in patients with heart disease.

Drug Interactions

Do not use with other behavior modification drugs, such as serotonin reuptake inhibitors. Do not use with monoamine oxidase inhibitors (MAOIs).

Instructions for Use

Doses are primarily based on empiricism. There are no controlled efficacy trials available for animals. There is evidence for success treating idiopathic cystitis in cats (J Am Vet Med Assoc, 213: 1282-1286, 1998). Amitriptyline was not effective for treatment of aggressive behavior in dogs, compared to behavior modification alone (J Am Anim Hosp Assoc, 37: 325-330, 2001). Amitriptyline applied transdermally is not systemically absorbed in cats.

Patient Monitoring and Laboratory Tests

Monitor patient's cardiovascular status during therapy, such as heart rate and rhythm. Like other TCAs, amitriptyline may decrease total T4 and free-T4 concentrations in dogs.

Formulations

Amitriptyline is available in 10-, 25-, 50-, 75-, 100-, and 150-mg tablets injection off market in US.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

34 Amlodipine Besylate

Small Animal Dosage

Dogs

- 1-2 mg/kg q12-24h PO.

Cats

- 2-4 mg per cat/day PO (0.5-1.0 mg/kg PO per day). The dose for cats may be divided into 12-hour intervals.
- Idiopathic cystitis: 2 mg/kg/day PO, or a range of 2.5-7.5 mg/cat/day.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Amlodipine Besylate

am-loe'dih-peen bess'ih-late

Trade and other names: Norvasc

Functional classification: Calcium-channel blocker

Pharmacology and Mechanism of Action

Calcium-channel blocking drug. Amlodipine is a calcium-channel blocker of the dihydropyridine class. It decreases calcium influx in cardiac and vascular smooth muscle. Its greatest effect is on vascular smooth muscle, acting as a vasodilator. Hypertension in cats has been defined as systolic blood pressure >190 mm Hg and diastolic pressure >120 mm Hg.

Indications and Clinical Uses

In cats and dogs it is used to treat systemic hypertension (high blood pressure). Amlodipine is considered the drug of choice by many clinicians for treating hypertension in cats. By comparison, angiotensin-converting enzyme (ACE) inhibitors are less effective in cats. Amlodipine may improve survival in cats with hypertensive kidney disease. In cats, addition of a beta blocker to slow heart rate may also be beneficial.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects can include hypotension and bradycardia. In dogs, gingival hyperplasia has been observed but through an unknown mechanism.

Contraindications and Precautions

Use cautiously in animals with poor cardiac reserve and that are prone to hypotension. Do not use in dehydrated animals.

Drug Interactions

Use cautiously with other vasodilators. Drug interactions are possible from concurrent use with phenylpropanolamine, theophylline, and beta-agonists.

Instructions for Use

In cats, efficacy has been established at 0.625 mg/cat once daily. If cats are large size (>4.5 kg) or refractory, increase dose to 1.25 mg/cat q24h PO (J Vet Intern Med, 12: 157-162, 1998). In some cats, addition of a beta blocker to slow heart rate may be indicated.

Patient Monitoring and Laboratory Tests

Monitor patient's blood pressure if possible. Cats with high pressures of systolic 160-190 mm Hg and diastolic 100-120 mm Hg should be considered at risk of clinical effects from hypertension.

Formulations

Amlodipine is available in 2.5-, 5-, and 10-mg tablets. (Tablets are difficult to split for small animals.)

Stability and Storage

Amlodipine is an unstable drug and potency and stability are not assured if the original formulation is disrupted or compounded. Store in a tightly sealed container and protect from light.

Small Animal Dosage

Dogs

- 2.5 mg/dog or 0.1 mg/kg q24h PO.

Cats

- 0.625 mg/cat initially q24h PO and increase if needed to 1.25 mg/cat. Average recommended dose for most cats is 0.18 mg/kg; once daily for hypertension.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Ammonium Chloride

ah-moe'nee-um klor'ide

Trade and other names: Generic brands

Functional classification: Acidifier

Pharmacology and Mechanism of Action

Urine acidifier. After oral administration, ammonium chloride induces acidic urine.

Indications and Clinical Uses

Compounds containing ammonium are administered to patients to acidify the urine, primarily to manage cystic calculi or chronic UTIs.

Precautionary Information

Adverse Reactions and Side Effects

Ammonium chloride has a bitter taste when added to food. It may cause acidemia in some patients if administered at high doses.

Contraindications and Precautions

Do not use in patients with systemic acidemia. Use cautiously in patients with renal disease. It may be unpalatable when added to some animals' food.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Doses are designed to maximize urine acidifying effect.

Patient Monitoring and Laboratory Tests

Monitor patient's acid/base status.

Formulations

Ammonium is available as crystals.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 100 mg/kg q12h PO.

Cats

- 800 mg/cat (approximately 1/3 to 1/4 tsp) mixed with food daily.

Large Animal Dosage

Horses

- Acidifier: 100-250 mg/kg q24h PO.

Regulatory Information

No regulatory information is available. It is not expected to pose a residue risk and no withdrawal is recommended for food animals.

Amoxicillin

ah-moks-ih-sill'in

Trade and other names: Amoxicillin: Amoxi-Tabs, Amoxi-Drops, Amoxi-Inject, Robamox-V, Biomox, and other brands. Amoxil, Trimox, Wymox, Polymox (human preparation), and Amoxicillin trihydrate

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Amoxicillin inhibits bacterial cell wall synthesis.

Amoxicillin generally has a narrow spectrum of activity that includes streptococci,

non-beta-lactamase-producing staphylococci, and other gram-positive cocci and bacilli. Many *Staphylococcus* strains are resistant owing to beta-lactamase production. Most enteric gram-negative bacilli of the Enterobacteriaceae are resistant. Susceptible gram-negative bacteria include some species of *Proteus*, *Pasteurella multocida*, and *Histophilus*. Resistance among gram-negative bacteria is common.

In dogs the peak concentration, half-life, volume of distribution (VD/F), and clearance (CL/F) are 11 mcg/mL, 1.3 hours, 0.72 L/kg, and 6.5 mL/kg/min, respectively. In cats, these values are 12 mcg/mL, 1.4 hours, 1.05 L/kg, and 7.8 mL/kg/min, respectively. Amoxicillin oral absorption in small animals is higher than ampicillin (two times higher in some animals). Amoxicillin oral absorption in adult horses is <10% and is not recommended.

Indications and Clinical Uses

Amoxicillin is used for a variety of infections in all species, including urinary tract infection, soft tissue infections, and pneumonia. It is generally more effective for infections caused by gram-positive bacteria. Because of a short half-life, frequent administration is needed for treating gram-negative infections. In addition, break point for susceptibility is higher for gram-negative versus gram-positive organisms. Oral absorption in horses is <10%, and it is not suitable for treatment of adult horses. However, oral absorption in foals is 36%-43%. Oral absorption in small animals is 50%-60%.

Precautionary Information

Adverse Reactions and Side Effects

Amoxicillin is usually well tolerated. Allergic reactions are possible. Diarrhea and vomiting are common with oral doses. Oral administration to horses or cattle can cause diarrhea and/or enteritis.

Contraindications and Precautions

Use cautiously in animals allergic to penicillin-like drugs.

Drug Interactions

Do not mix with other drugs in compounded formulations.

Instructions for Use

Dose recommendations vary depending on the susceptibility of bacteria and location of infection. Generally, more frequent or higher doses are needed for gram-negative infections.

Patient Monitoring and Laboratory Tests

Susceptibility testing: For testing for susceptibility, the CLSI recommends using ampicillin to test for amoxicillin susceptibility. The CLSI break point for sensitive organisms is ≤ 0.25 mcg/mL for staphylococci, streptococci, and gram-negative bacilli. For canine urinary tract pathogens, use a break point of ≤ 8 mcg/mL. For cattle pathogens, use a break point of ≤ 0.25 mcg/mL. For equine respiratory pathogens (streptococci), use a break point of ≤ 0.25 mcg/mL.

Formulations

Amoxicillin is available in 50-, 100-, 150-, 200-, and 400-mg tablets and 250- and 500-mg capsules (human preparations).

Amoxicillin trihydrate is available in 50-, 100-, 200-, and 400-mg tablets, 50-mg/mL amoxicillin trihydrate oral suspension, and 250-mg/mL amoxicillin trihydrate for injection.

Stability and Storage

Store in a tightly sealed container at room temperature. Oral liquid suspensions are stable for 14 days. Other formulations should be protected from moisture. Optimum stability is at pH 5.8-6.5. Above this pH, hydrolysis occurs.

Small Animal Dosage

Dogs and Cats

- 6.6-20 mg/kg q8-12h PO.

Large Animal Dosage

Calves

- Nonruminating: 10-22 mg/kg q8-12h PO.

Cattle and Horses

- 6.6-22 mg/kg q8-12h PO (suspension). Note: Oral doses in large animals are not well absorbed (except in foals), and amoxicillin is generally not administered via this route.

Regulatory Information

Withdrawal time: (Cattle only) 25 days meat, 96 hours milk. Amoxicillin intramammary infusion: withdrawal time 12 days meat, 60 hours milk.

Amoxicillin + Clavulanate Potassium

ah-mox-ih-sill'in + klav-yoo-lan'ate poe-tah'see-um

Trade and other names: Clavamox (veterinary preparation) and Augmentin (human preparation)

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Beta-lactam antibiotic + beta-lactamase inhibitor (clavulanate potassium). Amoxicillin activity and spectrum are as described for amoxicillin. Clavulanate has no antibacterial effects alone, but it is a strong inhibitor of the beta-lactamase enzyme that causes resistance among gram-positive and gram-negative bacteria. By adding clavulanate to amoxicillin, the spectrum is extended to include beta-lactamase-producing strains of *Staphylococcus* (non-methicillin resistant) and many strains of gram-negative bacilli.

Indications and Clinical Uses

Amoxicillin + clavulanate is a broad-spectrum antibacterial drug used for skin and soft tissue infections, UTIs, wound infections, and respiratory infections. It is indicated for treatment of bacterial infections (gram-positive and gram-negative) that may otherwise be resistant to amoxicillin owing to bacterial beta-lactamase production.

Precautionary Information

Adverse Reactions and Side Effects

It is usually well tolerated. Allergic reactions are possible. Diarrhea is common with oral doses and has also caused vomiting in some animals. As the dose of clavulanate increases because of a high proportion of clavulanate in some formulations, vomiting is more likely.

Contraindications and Precautions

Use cautiously in animals allergic to penicillin-like drugs. Oral administration to horses and ruminants may produce diarrhea.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Dose recommendations vary depending on the susceptibility of bacteria and location of infection. Generally, more frequent or higher doses are needed for gram-negative infections. It has been the experience of many veterinarians that an oral dose of double the manufacturer's recommendation should be used for treating skin infections (i.e., 25 mg/kg q12h). Oral human dose forms are sometimes substituted for veterinary drugs. Note that veterinary dose formulations contain amoxicillin and clavulanate in a 4:1 ratio. Human dose forms (Augmentin) contain these drugs in ratios of 2:1 to as high as 7:1.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is $\leq 0.25/0.12$ mcg/mL for staphylococci, streptococci, *E. coli*, and *Pasteurella multocida*. (The “/” distinguishes the amoxicillin from the clavulanate concentrations.)

Formulations

Amoxicillin + clavulanate is available in veterinary dose form: 62.5-, 125-, 250-, and 375-mg tablets and 62.5-mg/mL suspension in a ratio of amoxicillin/clavulanate of 4:1. Amoxicillin + clavulanate is available in human dose form: 250/125-, 500/125-, and 875/125-mg tablets. Amoxicillin + clavulanate is available in 125/31.25-, 200/28.5-, 250/62.5-, and 400/57-mg chewable tablets and oral suspension 125/31.25-, 200/28.5-, 250/62.5-, and 400/57-mg per 5 mL.

Stability and Storage

Store in a tightly sealed container, protected from light, and below 24°C. Avoid exposure to humidity or moisture. Reconstituted oral products are stable for 10 days.

Small Animal Dosage

Dogs

- 12.5-25 mg/kg q12h PO. (Dose is based on combined ingredients: amoxicillin and clavulanate.)

Cats

- 62.5 mg/cat q12h PO. Consider administering these doses every 8 hours for gram-negative infections.

Large Animal Dosage

Amoxicillin + clavulanate is only available in an oral formulation. Because these components are not absorbed orally in large animal species, this drug is not recommended.

Regulatory Information

No regulatory information is available. However, it is anticipated that withdrawal times will be similar to those of amoxicillin.

Amphotericin B

am-foe-tare'ih-sin

Trade and other names: Fungizone (traditional formulation) and liposomal forms of Amphotec, ABLC, ABCD, Abelcet, and AmBisome

Functional classification: Antifungal

Pharmacology and Mechanism of Action

Antifungal drug. Amphotericin B is a fungicidal agent for systemic fungi. Amphotericin B binds to ergosterol in the fungal cell membrane, producing a loss of membrane integrity, leakiness, and cell death. Amphotericin is active against most fungi and some protozoa. There is a conventional formulation of amphotericin B deoxycholate that has been used most often in veterinary medicine. It is the least expensive but the most toxic. Lipid formulations of amphotericin B are now available. They are widely used in people but have not gained widespread use in veterinary medicine because of their high cost. The advantage of liposomal formulations over the traditional formulations is that they are less toxic. These new formulations are lipid-based complexes or cholesteryl complexes of amphotericin B that allow higher doses to be administered with less nephrotoxicity. Amphotericin B lipid complex (Abelcet, ABLC) is a suspension of amphotericin B complexed with two phospholipids at a concentration of 100 mg/20 mL. This formulation was shown to be safe and effective for treating blastomycosis in dogs at a cumulative dose of 8-12 mg/kg by administering 1 mg/kg every other day. Amphotericin B cholesteryl sulfate complex (Amphotec, ABCD) is a colloidal dispersion of amphotericin B. It has been effective in studies in which it was administered at doses higher than the traditional amphotericin B formulation. The liposomal complex of amphotericin B (AmBisome) is a unilaminar liposomal formulation. When reconstituted, it produces small vesicles of encapsulated amphotericin B. This formulation has been used safely and effectively in some dogs for blastomycosis.

Indications and Clinical Uses

Amphotericin B is indicated in patients with a variety of systemic mycoses. It is used to treat blastomycosis, coccidioidomycosis, and histoplasmosis. It also has been used to treat leishmaniasis in dogs. It may be administered for treatment of aspergillosis, but this is not a common use in veterinary medicine and some species of *Aspergillus* are resistant.

Precautionary Information

Adverse Reactions and Side Effects

Amphotericin B produces a dose-related nephrotoxicity. It also produces fever, phlebitis, and tremors. Renal toxicity is dose-dependent and cumulative. It is more likely when cumulative doses approach, or exceed, 6 mg/kg. With repeated use, amphotericin B can cause renal potassium wasting because of loss of potassium in the collecting duct.

Contraindications and Precautions

Do not use in patients who have renal disease or where renal clearance is not known. Do not use in dehydrated animals or animals with electrolyte imbalances.

Drug Interactions

When preparing intravenous solution, do not mix Amphotericin B with electrolyte solutions; instead use 5% dextrose in water. Nephrotoxicity is increased when administered with aminoglycosides.

Instructions for Use

Administer IV via slow infusion diluted in 5% dextrose in water and monitor renal function closely. Administer sodium chloride fluid loading IV to patients before therapy to decrease risk of renal toxicosis. One study administered amphotericin B subcutaneously (Aust Vet J, 73: 124, 1996). Amphotericin B has been mixed as a solution of amphotericin B (one vial of 50 mg) with 40 mL of sterile water and 10 mL of Intralipid 10% (soybean oil). Doses of this mixture of 1-2 mg/kg have been used for treating systemic leishmaniasis. For other indications, this mixture has been administered at a dose of 1-2.5 mg/kg two times per week for 8-10 treatments. This liposomal complex of amphotericin B was used in a study for treatment of canine *Leishmania infantum* at a dose of 3-3.3 mg/kg. Although there was rapid clinical improvement, dogs remained positive for leishmaniasis. When administering proprietary forms of liposomal amphotericin B, follow instructions on label carefully. For administration of Abelcet, dilute in 5% dextrose to 1 mg/mL has been infused over 1-2 hours.

For intrathecal use, use the conventional formulation only. Start with 0.05 (total dose) every 48 hours, and increase to 0.1 and 0.2 mg (total dose) if the animal tolerates it well. Prepare intrathecal solution with a 5 mg/mL solution in sterile water further diluting to 0.25 mg/mL by adding 1 mL (5 mg) of the solution to another 19 mL of 5% dextrose and inject directly intrathecally.

Patient Monitoring and Laboratory Tests

Monitor renal function closely during treatment. After treatment many animals will have an elevated creatinine and blood urea nitrogen. Persistent azotemia may be a cause for discontinuation of treatment and replacement with another antifungal agent. Hypokalemia and hypomagnesemia may occur during use because of renal tubular acidosis.

Formulations

The conventional form of amphotericin B is available in a 50-mg injectable vial.

Stability and Storage

Stable if stored in original vial. Amphotericin B for intravenous infusion will react with light and should be protected from light during infusions. Store reconstituted solutions in refrigeration. However, unrefrigerated solutions may be stable for up to 1 week. Optimum pH is 6-7.

Small Animal Dosage

Dogs

Conventional formulation: 0.5 mg/kg q48 h IV (slow infusion) to a cumulative dose of 4-8 mg/kg. The liposomal formulations are administered at a dose of 3 mg/kg/day at a rate of more than 60-120 minutes for up to 9-12 treatments. This dose may be administered three times per week, rather than every day. A goal for the total cumulative dose for liposomal formulations is 24-27 mg/kg.

Intrathecal use: See previous instructions. Start with 0.05 (total dose) every 48 hours, and increase to 0.1 and 0.2 mg (total dose).

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Cats

- Cats have received similar regimens to those used for dogs (e.g., 0.25 mg/kg conventional formulation). However, many clinicians will start with lower doses in cats. For liposomal formulations in cats, use 1 mg/kg IV three times per week for up to 12 treatments.

Large Animal Dosage

Horses

- 0.3 mg/kg IV on day 1, followed by 3 consecutive days and repeat after a 24-48-hour drug-free interval. Expense has prevented common usage in horses.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Ampicillin, Ampicillin Sodium

am-pih-sill'in

Trade and other names: Omnipen, Principen, Totacillin, and Polycillin (human preparations), Omnipen-N, Polycillin-N, and Totacillin-N (injectable preparations) and Amp-Equine and Ampicillin trihydrate (Polyflex) (veterinary preparations)

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Ampicillin inhibits bacterial cell wall synthesis. Ampicillin has a narrow spectrum of activity that is similar to that of amoxicillin. Ampicillin generally has a spectrum of activity that includes streptococci, non-beta-lactamase-producing staphylococci, and many other gram-positive cocci and bacilli. Many staphylococci are resistant owing to beta-lactamase production. Most enteric gram-negative bacilli of the Enterobacteriaceae are resistant. Susceptible gram-negative bacteria include some species of *Proteus*, *Pasteurella multocida*, and *Histophilus*. Resistance among gram-negative bacteria is common. It generally has a broad spectrum of activity that includes both gram-positive and gram-negative bacteria. However, resistance is common, especially among enteric gram-negative bacilli and staphylococci.

Pharmacokinetics of ampicillin indicated that the half-life is approximately 1-1.5 hours in most animals. Half-life in horses is 0.6-1.5 hours after intravenous administration but longer after intramuscular injection. When the trihydrate formulation is injected IM, it produces a lower peak concentration but a longer half-life of 6.7 hours in cattle. Volume of distribution in most species is approximately 0.2 L/kg. Systemic clearance is approximately 3-5 mL/kg/min in most animals. Oral absorption is less than 50% in dogs and cats and less than 4% in horses.

Indications and Clinical Uses

Ampicillin is indicated in patients with infections caused by susceptible bacteria, such as skin and soft tissue infections, UTIs, and pneumonia. Gram-positive bacteria (except beta-lactamase-producing strains of *Staphylococcus*) are usually susceptible.

However, infections caused by most gram-negative bacteria (except *Pasteurella*) are usually resistant.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects of penicillin drug are most commonly caused by drug allergy. This can range from acute anaphylaxis when administered IV to other signs of allergic reaction when other routes are used. When used for prophylaxis during surgery, ampicillin can be administered IV to anesthetized patients without affecting cardiovascular parameters. Diarrhea is possible, when administered orally, especially with high doses.

Contraindications and Precautions

Use cautiously in animals allergic to penicillin-like drugs. Ampicillin contains 3 mEq of sodium per gram.

Drug Interactions

Do not mix in vials with other drugs.

Instructions for Use

Dose requirements vary depending on susceptibility of bacteria. It is absorbed approximately 50% less compared to amoxicillin when administered orally. More frequent administration may be needed, and higher doses may be required for gram-negative bacilli and enterococci.

When preparing injectable solutions, the stability is dependent on the concentration. Concentrated solutions (250 mg/mL) should be injected within one hour of reconstitution either IM, SC, or slowly (over 3 minutes) IV. Less concentrated solutions prepared in intravenous fluids (e.g., 30 mg/mL) are stable for longer periods. See Stability and Storage section below for more detail.

Patient Monitoring and Laboratory Tests

Susceptibility testing: For testing for susceptibility, CLSI break point for sensitive organisms is ≤ 0.25 mcg/mL for staphylococci, streptococci, and gram-negative bacilli. For canine urinary tract pathogens, use a break point of ≤ 8 mcg/mL. For cattle pathogens use a break point of ≤ 0.25 mcg/mL. For equine respiratory pathogens (streptococci) use a break point of ≤ 0.25 mcg/mL.

Formulations

Ampicillin is available in 250- and 500-mg capsules and 125-, 250-, and 500-mg vials of ampicillin sodium. Amp-Equine is available in 1- and 3-g vials for injection. (However, this formulation has been discontinued by some suppliers.) Ampicillin trihydrate (Polyflex) is available in 10- and 25-g vials for injection.

Stability and Storage

Store in a tightly sealed container at room temperature. After reconstitution of ampicillin sodium, stability is concentration-dependent. After reconstitution with sterile water at a concentration of 250 mg/mL, it is stable for 1 hour at room temperature. If diluted to a concentration of up to 30 mg/mL using 0.9% saline or lactated Ringer's solution (e.g., in intravenous fluids), stability is maintained for 8 hours at room temperature and 72 hours if refrigerated. If this concentration is prepared in 5% dextrose in water, stability is maintained for only 1 hour. Oral suspensions are stable for 14 days if refrigerated. Ampicillin trihydrate for injection is stable for 12 months refrigerated and 3 months at room temperature. Other

44 Ampicillin + Sulbactam

formulations should be protected from moisture. Optimum stability is at pH 5.8. Above this pH, hydrolysis occurs.

Small Animal Dosage

Dogs and Cats

- 10-20 mg/kg q6-8h IV, IM, or SQ or 20-40 mg/kg q8h PO. Doses as high as 100 mg/kg have been used for some resistant infections such as those caused by enterococci.

Ampicillin Trihydrate

Dogs

- 10-50 mg/kg q12-24h IM or SQ.

Cats

- 10-20 mg/kg q12-24h IM or SQ.

Large Animal Dosage

Horses

- 6.6 mg/kg up to 10-20 mg/kg q6-8h IM or IV.
- Refractory infections: up to 25-40 mg/kg q6-8h.

Cattle and Calves

Ampicillin Trihydrate

- 4.4 to 11 mg/kg q24h IM.

Regulatory Information

Cattle withdrawal time: 6 days meat; 48 hours milk (at 6 mg/kg).

Pig withdrawal time: In Canada, 6 days.

Ampicillin + Sulbactam

am-pih-sill'in + sul-bak'tam

Trade and other names: Unasyn

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

The ampicillin component has the same spectrum and mechanism of action as described for ampicillin previously. This formulation contains ampicillin plus a beta-lactamase inhibitor (sulbactam). Sulbactam has similar activity as clavulanate (ingredient in amoxicillin-clavulanate), but it is not as active as clavulanate against some gram-negative enzymes (e.g., TEM). Because of the addition of sulbactam, it has a broader spectrum of activity than ampicillin alone. The spectrum includes beta-lactamase-producing strains of *Staphylococcus* and gram-negative bacilli.

Indications and Clinical Uses

This combination is indicated for general bacterial infections. It has been used for acute infections such as pneumonia, sepsis, and prophylaxis in patients with neutropenia. Because of the addition of sulbactam, it has a broader spectrum than ampicillin alone. Therefore, it is used for treating infections for which ampicillin resistance may be expected. Ampicillin-sulbactam can only be administered by injection. For oral use, amoxicillin-clavulanate (e.g., Clavamox and Augmentin) may be used as an alternative.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects of penicillin drug are most commonly caused by drug allergy. This can range from acute anaphylaxis when administered to other signs of allergic reaction when other routes are used.

Contraindications and Precautions

Use cautiously in animals allergic to penicillin-like drugs.

Drug Interactions

Do not mix in vials with other drugs.

Instructions for Use

Dosage recommendations vary depending on the susceptibility of bacteria and location of infection. Generally, more frequent or higher doses are needed for gram-negative infections. When preparing injectable solutions, the stability is dependent on the concentration. Concentrated solutions (250 mg/mL) should be injected within one hour of reconstitution either IM, SC, or slowly (over 3 minutes) IV. Vials for IM use may be reconstituted in lidocaine hydrochloride to decrease pain from injection. Less concentrated solutions prepared in intravenous fluids (e.g., 45 mg/mL) are stable for longer periods. See Stability and Storage section below for more detail.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is $\leq 8/4$ mcg/mL for staphylococci and gram-negative bacilli. (The “/” distinguishes the ampicillin from the sulbactam concentrations.) However, CLSI has recently lowered the breakpoint for amoxicillin/clavulanate and it is possible that the ampicillin/sulbactam breakpoint should be lower.

Formulations

Ampicillin + sulbactam is available in a 2:1 combination for injection and 1.5- and 3-g vials.

Stability and Storage

Store vial in a tightly sealed container at room temperature. Vials may be reconstituted with sterile water for immediate use at an ampicillin concentration of 250 mg/mL. The vial should be used within 1 hour of reconstitution. When reconstituted vial is diluted with sterile water, or 0.9% sodium chloride, at a concentration of 45 mg/mL stability is maintained for 8 hours at room temperature and 48 hours if refrigerated. Stability is maintained for 8 hours at room temperature and 24 hours refrigerated if lactated Ringer's solution is used. Optimum stability is at pH 5.8. Above this pH, hydrolysis occurs.

Small Animal Dosage

Cats and Dogs

- Doses are similar to dose used for ampicillin (when dosed according to ampicillin component) 10-20 mg/kg q8h IV or IM.

Large Animal Dosage

Horses and Ruminants

(Doses used should be same as for ampicillin component.)

6.6 mg/kg up to to 10-20 mg/kg q6-8hr, IM or IV.

Regulatory Information

Withdrawal time exists for ampicillin but not sulbactam. Because sulbactam has a similar half-life and presents little risk for toxicity, the withdrawal times listed for ampicillin are suggested.

Cattle withdrawal time: 6 days meat; 48 hours milk (at 6 mg/kg).

Pig withdrawal time: In Canada, 6 days.

Amprolium

am-proe'lee-um

Trade and other names: Amprol and Corid

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiprotozoal drug. This drug is a vitamin B₁ or thiamine structural analogue. Amprolium antagonizes thiamine in parasites and is used for treatment of coccidiosis.

Indications and Clinical Uses

Amprolium is used to control and treat coccidiosis in calves, sheep, goats, puppies, and birds. It is administered orally, often mixed with food.

Precautionary Information

Adverse Reactions and Side Effects

Toxicity is observed only at high doses. CNS signs are caused by thiamine deficiency, which may be reversed by adding thiamine to the diet.

Contraindications and Precautions

Do not administer to debilitated animals.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Usually administered as feed additive to livestock. For dogs, 30 mL of 9.6% amprolium has been added to 3.8 L of drinking water for control of coccidiosis.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Amprolium is available in 9.6% (9.6 g/100 mL) oral solution and a soluble powder in a 22.6-g packet.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- Treatment of coccidiosis: Add 1.25 g of 20% amprolium powder to daily feed or 30 mL of 9.6% amprolium solution to 3.8 L of drinking water for 7 days.

Large Animal Dosage

Calves

- Prevention of coccidiosis: 5 mg/kg q24h for 21 days.
- Treatment of coccidiosis: 10 mg/kg q24h for 5 days PO.

Regulatory Information

Withdrawal time for cattle (meat): 24 hours before slaughter.

A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal.

Apomorphine Hydrochloride

ah-poe-mor'feen hye-droe-klor'-ide

Trade and other names: Apokyn and generic brands

Functional classification: Emetic

Pharmacology and Mechanism of Action

Emetic drug. Apomorphine is a potent lipophilic agent that crosses the blood-brain barrier and stimulates dopamine (D₂) receptors in the vomiting center. It promptly causes vomiting in dogs. Although it is easily absorbed from mucosal surfaces (e.g., conjunctiva of the eye), it is not absorbed orally because of first-pass effects.

Indications and Clinical Uses

Apomorphine is indicated for inducing emesis in animals that have ingested toxic agents. After subcutaneous administration, the onset of effect is 10 minutes or shorter. It is promptly effective for inducing vomiting in dogs but less so in cats. Apomorphine also is absorbed from mucosal administration after applying to the conjunctiva of the eye. Xylazine often is a more reliable emetic in cats.

Precautionary Information

Adverse Reactions and Side Effects

Apomorphine produces emesis before serious adverse effects can occur, but at higher doses (0.1 mg/kg) sedation can occur, which can mask the signs of some toxic agents. The hydrochloride salt of this formulation has a pH of 3-4 and can be irritating to the ocular conjunctival membranes. At high doses (1 mg/kg) excitement can occur, possibly via stimulation of dopamine (D₁ and D₂) receptors.

Contraindications and Precautions

Use cautiously in cats that may be sensitive to opiates.

Drug Interactions

No drug interactions are reported in animals. However, some drugs will diminish the emetic action of apomorphine (e.g., acepromazine, atropine, and other antiemetics).

Instructions for Use

Consult local poison center or pharmacist for availability. Apomorphine should be available in most emergency practices for prompt treatment of poisoning. Apomorphine can be administered IM, SC, or to the mucosa (e.g., in the

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conjunctival sac of the eye). In dogs, vomiting should occur within 3-10 minutes after administration. Limit administration to once.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. If used to induce vomiting from a toxicant, monitor for signs of toxicity because vomiting is able to eliminate less than half of the ingested toxicant.

Formulations

Apomorphine is available in 6-mg tablets that can be hydrolyzed prior to use or in a 10-mg/mL concentration in a 2-mL ampule or 3-mL preloaded syringes. It has also been prepared by compounding pharmacists.

Stability and Storage

Solutions decompose when exposed to air and light. A green color indicates decomposition. Store in a tightly sealed container at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.03-0.05 mg/kg IV or IM.
- 0.1 mg/kg SQ.
- Dissolve 6-mg tablet in 1-2 mL of saline and instill directly in conjunctiva of eye. After animal vomits, the conjunctiva may be rinsed of residual drug with an eye wash solution.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 1

Aprepitant

ap-reh'pīh-tant

Trade and other names: Emend

Functional classification: Antiemetic

Pharmacology and Mechanism of Action

Aprepitant is a centrally acting antiemetic. Aprepitant is a substance P/neurokinin 1 (NK₁) receptor antagonist, similar to maropitant (Cerenia). It is used primarily with drugs known to be highly emetic, such as cisplatin. This drug is effective because chemotherapy drugs and other emetic stimuli release NK₁, which is highly emetic. It also blocks vomiting from other stimuli. The use in small animals has been somewhat limited because of the high expense and limited formulations for animals. In dogs, aprepitant is extensively metabolized after administration.

Indications and Clinical Uses

Aprepitant is an effective antiemetic for people, particularly when used to treat vomiting associated with cancer chemotherapy. It may be used with corticosteroids

(dexamethasone) and serotonin (5HT₃) antagonists. However, despite its broad effects to decrease vomiting in people, there are no reports of effective use in dogs or cats. Instead, a similar-acting drug, maropitant (Cerenia), is used in dogs and cats and produces similar antiemetic effects.

Precautionary Information

Adverse Reactions and Side Effects

There are no reported adverse effects in animals.

Contraindications and Precautions

No contraindications reported for animals.

Drug Interactions

Drug interactions are possible because aprepitant is both an inducer and inhibitor of cytochrome P450 enzymes. Potent inhibitors of cytochrome P450 (see Appendix F) can potentially affect aprepitant clearance.

Instructions for Use

Use in patients refractory to other antiemetic drugs. It may be combined with other antiemetics.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Aprepitant is available in 80- and 125-mg capsules.

Stability and Storage

Do not crush or mix capsules. Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- Start with 1 mg/kg q24h PO and increase to 2 mg/kg in refractory patients.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Ascorbic Acid

ah-skor'biik ass'id

Trade and other names: Vitamin C and sodium ascorbate. There are many brand names available.

Functional classification: Vitamin

Pharmacology and Mechanism of Action

Ascorbic acid is vitamin C. It is an important cofactor in a variety of metabolic functions.

Indications and Clinical Uses

Ascorbic acid is used to treat vitamin C deficiency and occasionally used as urine acidifier. Dogs are capable of synthesizing vitamin C, but it is used as a supplement to improve health and performance. There are insufficient data to show that ascorbic acid is effective for preventing cancer, treating infectious diseases, or preventing cardiovascular disease.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. High doses may increase the risk of oxalate urolith formation.

Contraindications and Precautions

No contraindications reported for animals.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Not necessary to supplement in animals with well-balanced diets. However, high doses have been used as adjunctive treatment for some diseases. Evidence shows that at doses of 15 and 50 mg/kg in dogs, the increase in absorption was nonlinear. Therefore, higher doses may not produce proportionately higher blood levels to the lower doses. Comparison of crystalline ascorbic acid and the vitamin C product, Ester-C, produced similar levels of vitamin C in the plasma.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Ascorbic acid is available in tablets of various sizes and injections. Typically the injection form is 250 mg sodium ascorbate/mL. The formulation of Ester-C appears to be absorbed similarly to the crystalline form of vitamin C.

Stability and Storage

Light sensitive. It will oxidize, darken, and decompose when exposed to air and light. The injectable solution in a vial may build up pressure with storage, which may be decreased by storing in a refrigerator. Otherwise, store at room temperature protected from light.

Small Animal Dosage

Dogs and Cats

- Dietary supplementation: 100-500 mg/animal/day PO.
- Urinary acidification: 100 mg/animal q8h PO. Injectable dose ranges from 1-10 mL (250 mg per mL), depending on size of animal, IM or IV.
- For treatment of oxidative stress: Dogs: 500-1,000 mg per dog q24h, PO; Cats: 125 mg per cat, PO, q12h.

Guinea Pigs

- 16 mg/kg twice weekly IM, to treat vitamin deficiency.

Large Animal Dosage

Large Animals

- Vitamin C supplementation: 1-10 mL IM or IV. Repeat daily as needed.
- 1-2 g q24h PO.

Regulatory Information

Withdrawal time: 0 days for all animals intended for food.

Asparaginase (L-Asparaginase)

ah-spar'á-jin-aze

Trade and other names: Elspar and Asparaginase

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Neoplastic cells are deficient in asparagine synthase and require extracellular asparagine for DNA and RNA synthesis. L-asparaginase destroys asparagine. Normal cells are capable of synthesizing their own asparagine, but certain malignant cells, especially malignant lymphocytes, are not. Therefore, asparagine is an essential amino acid for cancer cell survival, particularly malignant lymphocytes. Because cancer cells in patients treated with L-asparaginase are depleted of asparagine, this treatment interferes with DNA, RNA, and protein synthesis in cancer cells. It is specific for the G1 phase of the cell cycle. In dogs it has a long half-life of 1-2 days.

Indications and Clinical Uses

Asparaginase has been used in some lymphoma protocols and has been effective for melanoma and mast cell tumors. It has been administered IV, IM, or SQ, but results of one study favored intramuscular administration over subcutaneous administration. In cats it also has been used in combination cancer protocols.

Precautionary Information

Adverse Reactions and Side Effects

The most common adverse effect is hypersensitivity (allergic) reactions. Asparaginase is a foreign bacterial protein and can cause allergic reactions. Patients have developed hypersensitivity to asparaginase with repeated administrations. Hepatotoxic reactions, pancreatitis, and hyperglycemia also have been reported.

Contraindications and Precautions

Do not use in animals with known sensitivity (allergic reaction).

Drug Interactions

No drug interactions are reported in animals. It has been used with other anticancer drugs.

Instructions for Use

Asparaginase is usually used in combination with other drugs in cancer chemotherapy protocols (e.g., doxorubicin). Studies have shown that intramuscular dosing is more effective than subcutaneous dosing in dogs with lymphoma (J Am Vet Med Assoc, 214: 353-356, 1999). Asparaginase has minimal effect on the bone marrow; therefore, it can be used in combination with other myelosuppressive drugs in a protocol. Although it has been used in anticancer protocols, it has shown no benefit when added to CHOP protocols for lymphoma. Tumor cells can develop resistance by developing a capacity to synthesize asparagine. In cats, it has been used

52 Aspirin

in combination protocols at a dose of 400 units per kg SQ on day one of protocols combined with doxorubicin.

Patient Monitoring and Laboratory Tests

Monitoring CBC during chemotherapy is recommended.

Formulations

Asparaginase is available in 10,000 units per vial for injection. (Distribution of this drug to veterinarians by the manufacturer may be limited.)

Stability and Storage

Stable if stored in manufacturer's original vial.

Small Animal Dosage

Dogs

- 400 units/kg SQ or IM, weekly.
- 10,000 units/m² weekly SQ or IM for 3 weeks.

Cats

- 400 units/kg weekly SQ or IM.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals that produce food because it is an anticancer agent.

Aspirin

as'pir-in

Trade and other names: ASA, acetylsalicylic acid, Bufferin, Ascriptin, and many generic brands

Functional classification: Nonsteroidal anti-inflammatory

Pharmacology and Mechanism of Action

Nonsteroidal anti-inflammatory drug (NSAID). Anti-inflammatory action is caused by inhibition of prostaglandins. Aspirin binds irreversibly to the cyclo-oxygenase (COX) enzyme in tissues to inhibit synthesis of prostaglandins. At low doses it may be more specific for COX-1 than COX-2. Anti-inflammatory effects are attributed to inhibition of COX, but other anti-inflammatory mechanisms—attributed to salicylates—may also contribute to the anti-inflammatory action, such as inhibition of NF kappa-B. Pharmacokinetics are variable in animals with a half-life that ranges from 1 hour in horses, 6 hours in pigs, 8.5 hours in dogs, to 38 hours in cats.

Indications and Clinical Uses

Aspirin is used as an analgesic, anti-inflammatory, and antiplatelet drug. At low doses, aspirin is a more specific COX-1 selective inhibitor and antiplatelet drug than other NSAIDs. Therefore, low doses have been used in animals specifically to prevent thromboemboli formation. Low doses of aspirin are routinely used for antiplatelet therapy, but aspirin does not provide complete inhibition of platelet stimulation. Addition of other antiplatelet drugs such as clopidogrel (Plavix)

provides more effective inhibition. Although aspirin has been available for many years, it is not registered by the FDA for use in any species. There are no published controlled studies to document efficacy. Use of aspirin in animals is primarily based on empiricism rather than on published data.

Precautionary Information

Adverse Reactions and Side Effects

Narrow therapeutic index. High doses frequently cause vomiting. Other GI effects can include ulceration and bleeding. Aspirin inhibits platelets and increases risk of bleeding.

Contraindications and Precautions

Cats are susceptible to salicylate intoxication because of slow clearance. Use cautiously in patients with coagulopathies because of platelet inhibition (e.g., von Willebrand's disease). Do not administer to animals prone to GI ulcers.

Drug Interactions

Do not administer with other ulcerogenic drugs such as corticosteroids. Do not administer with other drugs that may cause coagulopathy and increase risk of bleeding problems.

Instructions for Use

Analgesic and anti-inflammatory doses have primarily been derived from empiricism. Antiplatelet doses are lower because of prolonged effect of aspirin on platelets. Aspirin is only available in oral form. Because it is a weak acid, it is ordinarily absorbed best in the acidic environment of the upper GI tract; however, considerable absorption also takes place in the intestine. In dogs, enteric-coated aspirin reduces gastric irritation, but absorption from this form is erratic and often incomplete. Buffering does not affect absorption but may protect the stomach from injury when high doses are administered. Buffering has less of a beneficial effect when low doses are administered and is not expected to protect the stomach from the more serious effects of GI ulceration, bleeding, and perforations.

Patient Monitoring and Laboratory Tests

Monitor patients for signs of gastric upset, gastroduodenal ulcers, and bleeding. Effective plasma concentrations: 20-50 mcg/mL for pain and fever and 150-200 mcg/mL for inflammation. Aspirin decreased thyroid concentrations (T₄, T₃, and fT₄) in dogs after 2-4 weeks of dosing but returned to normal in 14 days.

Formulations

Aspirin is available in 81-mg (children's aspirin) and 325-mg tablets.

For large animals, aspirin is available in 240-grain bolus (14,400 mg) and 3.9-, 15.6-, and 31.2-g tablets.

Stability and Storage

Store in a tightly sealed container at room temperature. After exposure to moisture, it will decompose to acetic acid and salicylic acid. If stored at pH 7 at 25°C, it has a half-life of 52 hours.

Small Animal Dosage

Mild Analgesia

Dogs

- 10 mg/kg q12h PO.

54 Atenolol

Cats

- 10 mg/kg q48h PO.

Antiinflammatory

Dogs

- 20-25 mg/kg q12h PO.

Cats

- 10-20 mg/kg q48h PO.

Antiplatelet

Dogs

- Minimum of 1 mg/kg, and usually 5-10 mg/kg q24-48h PO.

Cats

- 80 mg/cat q48h PO.

Large Animal Dosage

Ruminants

- 100 mg/kg q12h PO. Doses as high as 333 mg/kg have been administered to cattle.

Swine

- 10 mg/kg q6-8h PO.

Horses

- 25-50 mg/kg q12h PO (up to 100 mg/kg PO, per day).

Regulatory Information

Extralabel use: Although considered extralabel in animals intended for food, consider a withdrawal time of at least 1 day for meat and 24 hours for milk.

RCI Classification: 4

Atenolol

(ah-ten'oe-lole)

Trade and other names: Tenormin

Functional classification: Beta-antagonist

Pharmacology and Mechanism of Action

Beta-adrenergic blocker. Relatively selective for beta₁-receptor. Atenolol is a water-soluble beta blocker and relies on the kidney for clearance. (By comparison, drugs such as propranolol and metoprolol are more lipophilic and rely on liver for clearance.) In dogs and cats, oral absorption is 90%. In cats the half-life is 3.7 hours.

Indications and Clinical Uses

Atenolol is one of the most commonly administered beta blockers for dogs and cats. Atenolol is used primarily as an antiarrhythmic or for other cardiovascular conditions in which it is needed to slow the sinus rate. In cats, this drug is commonly used to treat heart disease from cardiomyopathy or hyperthyroidism, but it should not be used as monotherapy to treat primary hypertension.

Precautionary Information

Adverse Reactions and Side Effects

Bradycardia and heart block are possible. Atenolol may produce bronchospasm in sensitive patients.

Contraindications and Precautions

Use cautiously in animals with airway disease, myocardial failure, and cardiac conduction disturbances. Use cautiously in animals with low cardiac reserve.

Drug Interactions

Use cautiously with other drugs that may decrease cardiac contraction or heart rate.

Instructions for Use

Atenolol is reported to be less affected by changes in hepatic metabolism than other beta blockers. Although not an FDA-approved drug for dogs and cats, dosing guidelines are based on published reports and experience of experts. In cats, amlodipine (calcium-channel blocker) may be used with atenolol to control hypertension. When administered as a transdermal gel to cats, it produced inconsistent and lower plasma concentrations compared to oral administration.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and rhythm.

Formulations

Atenolol is available in 25-, 50-, and 100-mg tablets. (Tablets can be split for small animals.)

Stability and Storage

Store in a tightly sealed container at room temperature. There are stability studies that indicate that extemporaneously prepared oral suspensions are stable for 14 days, and some compounded oral formulations have been stable for 60 days. Consult compounding pharmacist for beyond-use-day of prepared compounded formulations. Atenolol is water soluble.

Small Animal Dosage

Dogs

- 6.25-12.5 mg/dog q12-24h (or 0.25-1.0 mg/kg q12-24h) PO. Doses in dogs have been increased to 3 mg/kg q12-24h PO for some conditions.

Cats

- 1-2 mg/kg q12h, PO. However, because of tablet size a common dose is 6.25-12.5 mg/cat q12-24h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Atipamezole Hydrochloride

ah-tih-pam'eh-zole hye-droe-klor'ide

Trade and other names: Antisedan

Functional classification: Anesthetic

Pharmacology and Mechanism of Action

Alpha₂-antagonist. It binds to alpha₂-receptors to antagonize other drugs that act as agonists, such as dexmedetomidine, medetomidine and xylazine. Other alpha₂-antagonists include yohimbine, but atipamezole is more specific for the alpha₂-receptor.

Indications and Clinical Uses

Atipamezole is used to reverse alpha₂-agonists such as dexmedetomidine (Dexdomitor), medetomidine (Domitor), and xylazine. Arousal from sedation should occur within 5-10 minutes of injection. It also can be used to reverse sedation caused by amitraz intoxication.

Precautionary Information

Adverse Reactions and Side Effects

Atipamezole can cause initial excitement in some animals shortly after reversal. There may be a transient decrease in blood pressure after injection.

Contraindications and Precautions

No contraindications reported for animals.

Drug Interactions

Atipamezole is an alpha₂-antagonist. As such, it will antagonize other drugs that bind to the alpha-receptor and prevent their action. Such drugs that may be antagonized include xylazine, medetomidine, dexmedetomidine, detomidine, and some alpha₁-agonists.

Instructions for Use

When used to reverse dexmedetomidine or medetomidine, inject the same volume of atipamezole as the volume of dexmedetomidine or medetomidine that was administered.

Patient Monitoring and Laboratory Tests

Monitor cardiovascular status when using alpha₂-agonists. Providing oxygen during recovery may help recovery from alpha₂-agonists.

Formulations

Atipamezole is available in a 5-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

- Inject the same volume as used for dexmedetomidine or medetomidine. The range of doses is 0.32 mg/kg for small animals (4 kg, or 8.8 pounds),

0.23 mg/kg for medium-sized animals (11 kg, or 24 pounds), and up to 0.14 mg/kg for large-sized animals (45 kg or 100 pounds).

Large Animal Dosage

- 30-60 mcg/kg (0.03-0.06 mg/kg) IV. However, in horses, doses of 60-80 mcg/kg IV were more effective than smaller doses.

Regulatory Information

Do not administer to animals intended for food.

Atovaquone

a-TOE-va-KWONE

Trade and other names: Mepron

Functional classification: Antibacterial, antiprotozoal

Pharmacology and Mechanism of Action

Atovaquone is an antimicrobial agent, an analogue of ubiquinone, that inhibits mitochondrial transport in protozoa by targeting the cytochrome bc₁ complex. It also inhibits nucleic acid and ATP synthesis in susceptible cells. Atovaquone is active against protozoa such as *Pneumocystis*, for which it is used in people. In cats it is used to treat *Cytauxzoon felis*. It may not eradicate *Cytauxzoon*, but it will decrease the parasite burden. In dogs, it has been used to treat *Babesia gibsoni*. For treating these infections in dogs and cats, it appears to have an additive or synergistic effect when combined with azithromycin. It is highly lipophilic. Oral absorption in animals is almost 50% but is increased with feeding. The half-life in people is very long (67-77 hours) but is not reported for animals.

Indications and Clinical Uses

In people, atavaquone is an antiprotozoal that is primarily used in individuals who cannot tolerate sulfonamides. In animals, it has been used, often in combination with azithromycin, to treat refractory protozoan diseases and bloodborne pathogens.

Precautionary Information

Adverse Reactions and Side Effects

One formulation (Malarone) also contains proguanil HCl. It may increase the risk of diarrhea in dogs when combined with proquanil. Otherwise, adverse effects have not been reported in animals. In people, adverse reactions consist of skin rash, cough, and diarrhea.

Contraindications and Precautions

Avoid use in pregnancy.

Drug Interactions

No drug interactions are reported in animals. In people, coadministration with rifampin will decrease effective concentrations.

Instructions for Use

There has been only limited experience with use of atovaquone for treatment of infections in animals. A few clinical trials have shown efficacy when combined with azithromycin for treatment of protozoa infections.

58 Atracurium Besylate

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Atovaquone is available as a 750-mg per 5 mL liquid oral suspension (150 mg/mL). The 250-mg tablets have been discontinued.

Stability and Storage

Store at room temperature protected from light. Do not freeze.

Small Animal Dosage

Cats

- 15 mg/kg q8h, PO, in combination with azithromycin (10 mg/kg q24h).

Dogs

- 13.3 mg/kg q8h, PO for 10 days, usually in combination with azithromycin (10 mg/kg q24h, PO).

Large Animal Dosage

Large Animals

- No dose reported.

Regulatory Information

There is no withdrawal time established for food animals.

Atracurium Besylate

ah-trah-kyoor'ee-um bess'ih-late

Trade and other names: Tracurium

Functional classification: Muscle relaxant

Pharmacology and Mechanism of Action

Neuromuscular blocking agent (nondepolarizing). Atracurium competes with acetylcholine at the neuromuscular end plate. It is used primarily during anesthesia or other conditions in which it is necessary to inhibit muscle contractions. It has a shorter duration of action than pancuronium.

Indications and Clinical Uses

Atracurium is a paralytic agent used to paralyze skeletal muscle during surgery and mechanical ventilation.

Precautionary Information

Adverse Reactions and Side Effects

Atracurium produces respiratory depression and paralysis. Neuromuscular-blocking drugs have no effect on analgesia.

Contraindications and Precautions

Do not use in patients unless it is possible to provide ventilation support. The action of neuromuscular-blocking agents may be antagonized by acetylcholinesterase inhibitors.

Drug Interactions

Gentamicin (and possibly other aminoglycosides) potentiates neuromuscular blockade (gentamicin acts at the presynaptic site to decrease release of acetylcholine). No other drug interactions are reported in animals.

Instructions for Use

Administer only in situations in which careful control of respiration is possible. Doses may need to be individualized for optimum effect. Do not mix with alkalinizing solutions or lactated Ringer's solution.

Patient Monitoring and Laboratory Tests

Monitoring of respiratory and cardiovascular indices is critical during use. If possible, monitor oxygenation of patient during use.

Formulations

Atracurium is available in 10-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 0.2 mg/kg IV initially, then 0.15 mg/kg q30min.
- Constant rate infusion: 0.3-0.5 mg/kg IV loading dose, followed by 4-9 mcg/kg/min.

Large Animal Dosage

Horses

- 0.05-0.07 mg/kg IV.

Regulatory Information

Do not administer to animals intended for food.

Atropine Sulfate

ah'troe-peen sul'fate

Trade and other names: Generic brands

Functional classification: Anticholinergic

Pharmacology and Mechanism of Action

Anticholinergic agent (blocks acetylcholine effect at muscarinic receptors), parasympatholytic.

As an antimuscarinic agent, it blocks cholinergic stimulation and causes decrease in GI motility and secretions, decrease in respiratory secretions, increased heart rate (antivagal effect), and mydriasis.

Indications and Clinical Uses

Atropine is used primarily as an adjunct to anesthesia or other procedures to increase heart rate and decrease respiratory and GI secretions. Atropine is the drug of choice

60 Atropine Sulfate

to overcome excess vagal stimulation associated with some clinical conditions. Atropine is also used as an antidote for organophosphate intoxication.

Precautionary Information

Adverse Reactions and Side Effects

Side effects include xerostomia, ileus, constipation, tachycardia, and urine retention.

Contraindications and Precautions

Do not use in patients with glaucoma, intestinal ileus, gastroparesis, or tachycardia. Use high doses (e.g., 0.04 mg/kg) cautiously because it will increase oxygen demand.

Drug Interactions

Do not mix with alkaline solutions. Atropine will antagonize the effects of any cholinergic drugs administered (e.g., metoclopramide).

Instructions for Use

Atropine is used ordinarily as an adjunct with anesthesia or other procedures. Compared to lower doses, in dogs 0.06 mg/kg was more effective than 0.02 mg/kg (Am J Vet Res, 60: 1000-1003, 1999). Atropine may be used during cardiac resuscitation; however, high doses may cause sustained tachycardia and increased myocardial oxygen demand. During cardiac resuscitation, doses of 0.04 mg/kg IV may be used, but for treating sinus bradycardia, consider lower doses of 0.01 mg/kg.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and rhythm.

Formulations

Atropine is available in 400-, 500-, and 540-mcg/mL injection and 15-mg/mL injection.

Stability and Storage

Store in a tightly sealed container at room temperature.

Small Animal Dosage

Dogs

- 0.02-0.04 mg/kg q6-8h IV, IM, or SQ (complete dose range has been from 0.01 mg/kg to 0.06 mg/kg, depending on the indication).
- Sinus bradycardia: 0.005-0.01 mg/kg, but for use during CPR use up to 0.04 mg/kg.

Cats

- 0.02-0.04 mg/kg q6-8h IV, IM, or SQ.

Dogs

- For organophosphate and carbamate toxicosis: 0.2-0.5 mg/kg as needed, IV, IM, or SQ.

Cats

- For organophosphate and carbamate toxicosis: 0.2-0.5 mg/kg as needed, IV, IM, or SQ.

Large Animal Dosage

Note that in large animals, atropine has a potent effect on inhibiting GI motility.

Horses

- Antidote to organophosphates or cholinesterase inhibitors: 0.02-0.04 mg/kg IM or SQ, and repeat as needed.
- Recurrent airway obstruction (RAO, formerly called COPD): 0.022 mg/kg, once, IV.

Pigs

- Antidote to organophosphates or cholinesterase inhibitors: 0.1 mg/kg IV followed by 0.4 mg/kg IM.
- Anesthesia adjunct: 0.02 mg/kg IV or 0.04 mg/kg IM.

Ruminants

- Antidote to organophosphates or cholinesterase inhibitors: 0.1 mg/kg IV, followed by 0.4 mg/kg IM and repeat as needed.
- Anesthesia adjunct to prevent salivation: 0.02 mg/kg IV or 0.04 mg/kg IM.

Regulatory Information

- Withdrawal time: None established in US. The manufacturer of large animal products lists 0 days milk and meat; however, it is listed as 14 days for meat and 3 days for milk in the UK.

RCI Classification: 3

Auranofin

or-an'oe-fin

Trade and other names: Ridaura

Functional classification: Immunosuppressive

Pharmacology and Mechanism of Action

Used for gold therapy (chrysotherapy). Mechanism of action is unknown but may relate to immunosuppressive effect on lymphocytes.

Indications and Clinical Uses

Auranofin (gold therapy) is used primarily for immune-mediated diseases. It has been used with some success to control immune-mediated skin diseases, such as pemphigus and immune-mediated arthritis, but evidence of efficacy is lacking for small animal therapy. It has been suggested that this product (oral) is not as effective as injectable products such as aurothioglucose.

Precautionary Information**Adverse Reactions and Side Effects**

Adverse effects include dermatitis, nephrotoxicity, and blood dyscrasias.

Contraindications and Precautions

Do not use in animals with suppressed bone marrow or in animals already receiving bone marrow-suppressing agents.

Drug Interactions

No drug interactions are reported in animals.

62 Aurothioglucose

Instructions for Use

Use of this drug has not been evaluated in veterinary medicine. No controlled clinical trials are available to determine efficacy in animals.

Patient Monitoring and Laboratory Tests

Monitor patient's CBC periodically because gold salts have caused blood dyscrasias.

Formulations

Auranofin is available in 3-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 0.1-0.2 mg/kg q12h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Aurothioglucose

or-oh-thye-oe-gloo'kose

Trade and other names: Solganal

Functional classification: Immunosuppressive

Pharmacology and Mechanism of Action

Used for gold therapy (chrysotherapy). Mechanism of action is unknown but may relate to immunosuppressive effect on lymphocytes.

Indications and Clinical Uses

Aurothioglucose (gold therapy) is used primarily for immune-mediated diseases. It has been used with some success to control immune-mediated skin diseases, such as pemphigus and immune-mediated arthritis. However, because of a lack of controlled trials to demonstrate efficacy and adverse effects that have been observed, the use in veterinary medicine has been uncommon.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include dermatitis, nephrotoxicity, and blood dyscrasias.

Contraindications and Precautions

Do not use in animals with suppressed bone marrow or animals already receiving bone marrow-suppressing agents.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Use of this drug has not been evaluated in veterinary medicine. No controlled clinical trials are available to determine efficacy in animals. This drug is often used in combination with other immunosuppressive drugs such as corticosteroids.

Patient Monitoring and Laboratory Tests

Monitor patient's CBC periodically because gold salts have caused blood dyscrasias.

Formulations

Aurothioglucose has been discontinued and is no longer available. However, some forms still persist (e.g., from compounding pharmacies) in a 50-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. The stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Dogs <10 kg: 1 mg IM first week, 2 mg IM second week, 1 mg/kg/week maintenance. Dogs >10 kg: 5 mg IM first week, 10 mg IM second week, 1 mg/kg/week maintenance.

Cats

- 0.5-1 mg/cat every 7 days IM.

Large Animal Dosage

Horses

- 1 mg/kg per week IM.

Regulatory Information

Do not administer to animals intended for food.

Azathioprine

ay-za-thye'oe-preen

Trade and other names: Imuran and generic

Functional classification: Immunosuppressive

Pharmacology and Mechanism of Action

Thiopurine immunosuppressive drug. Acts to inhibit T-cell lymphocyte function. This drug is metabolized to 6-mercaptopurine (6-MP), which may account for immunosuppressive effects because 6-MP interferes with purine metabolism in lymphocytes. Other cells can use salvage pathways for purine synthesis, but stimulated lymphocytes are not capable of this synthesis.

Indications and Clinical Uses

Azathioprine is used to treat various immune-mediated diseases in animals, including immune-mediated hemolytic anemia, pemphigus, and inflammatory bowel disease. It is often administered with prednisone or prednisolone. Onset of action may be delayed for 4-6 weeks in some patients.

Precautionary Information

Adverse Reactions and Side Effects

Bone marrow suppression is the most serious concern. Additional adverse effects in dogs include diarrhea, increased risk of secondary infections, and vomiting. Hepatotoxicosis after administration of azathioprine also has been reported. One of the metabolites produced may be hepatotoxic. There has been some association with development of pancreatitis when administered with corticosteroids. Sensitivity to the adverse effects may be because of a deficiency of metabolizing enzymes, thiopurine methyltransferase (TPMT) in certain individuals. In people, about 10% are deficient. Some dogs and many cats are also deficient; however, in dogs toxicity has not yet been correlated with status of TPMT levels. Cats are particularly susceptible to toxicity and are reported to have low levels of TPMT. Individuals who have higher sensitivity to the suppressing effects of bone marrow should have dose reduced.

Contraindications and Precautions

Exercise extreme caution and careful monitoring when administering to cats.

Drug Interactions

Administer with caution with other drugs that may suppress the bone marrow (e.g., cyclophosphamide and anticancer drugs). There is some evidence that concurrent use with corticosteroids may increase risk of pancreatitis. Do not administer with allopurinol because antagonism of xanthine oxidase may interfere with metabolism.

Instructions for Use

Azathioprine is usually used in combination with other immunosuppressive drugs (e.g., corticosteroids) to treat immune-mediated disease. Cats are very sensitive to the bone marrow-suppressing effects of azathioprine. Doses of 2.2 mg/kg to cats have produced toxicity, but most experts recommend starting cats with doses of 0.3 mg/kg/day.

Patient Monitoring and Laboratory Tests

Monitor patient's CBC periodically because some animals are sensitive to the effects of azathioprine and its metabolite 6-MP. After 2 weeks of treatment, a CBC is essential. Because of risk of hepatotoxicity, monitor hepatic enzymes and bilirubin regularly.

Formulations

Azathioprine is available in 25-, 50-, 75-, and 100-mg tablets and 10-mg/mL for injection.

Stability and Storage

Store in a tightly sealed container at room temperature. Compounded oral suspensions are stable for 60 days.

Small Animal Dosage

Dogs

- 2 mg/kg q24h PO initially then 0.5-1 mg/kg q48h. In dogs, doses as high as 1.5 mg/kg q48h PO have been used with prednisolone.

Cats (use cautiously)

- Cats are sensitive to bone marrow-suppressing effects, and many clinicians avoid azathioprine in cats altogether. However, if administered to cats, one should start

with 0.3 mg/kg q24h PO and adjust dose to q48h, after careful monitoring. Tablet size may be as low as 1/30 to 1/50 of a tablet, which will require careful compounding.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Azithromycin

ay-zith-roe-my'sin

Trade and other names: Zithromax

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Azalide antibiotic. Similar mechanism of action as macrolides (e.g., erythromycin), which is to inhibit bacteria protein synthesis via inhibition of ribosome. Spectrum of activity is primarily gram-positive cocci, including streptococci and staphylococci. It also has good activity against *Mycoplasma*, *Chlamydia*, and some intracellular pathogens. The activity against *Toxoplasma* has been questionable. Pharmacokinetic data show extremely long plasma, tissue, and leukocyte half-lives in dogs, cats, and horses. Plasma half-life is 18 hours in horses, 35 hours in cats, and 30 hours in dogs. Volume of distribution also is large, with values exceeding 10 L/kg.

Indications and Clinical Uses

Azithromycin is indicated for treatment of bacterial infections. Antimicrobial spectrum is primarily gram-positive. Azithromycin is not recommended for serious gram-negative infections. It may be used to treat infections caused by *Mycoplasma* and other atypical organisms. Azithromycin has been used to treat intracellular organisms because of its ability to concentrate in leukocytes. One of the uses has been to treat infections caused by *Rhodococcus equi* in foals. However, in one comparative study, clarithromycin plus rifampin had better clinical success in foals than azithromycin plus rifampin. In foals, azithromycin, administered at a dose of 10 mg/kg q48h oral, administered during the first 2 weeks after birth, has been used prophylactically to decrease *Rhodococcus* infection in foals at high risk (farms with high endemic risk). In horses, azithromycin also has been used to treat proliferative enteritis caused by *Lawsonia intracellularis*. Azithromycin has been used in cats to treat upper respiratory infections. There are no controlled clinical trials to document success for this use; however, this treatment has been common among veterinarians. Azithromycin administered to cats with infections caused by *Chlamydophila felis* (formerly *Chlamydia psittaci*), at 10-15 mg/kg once daily for 3 days and thereafter two times per week, was not effective for eliminating the organism, although clinical signs improved. However, azithromycin was not effective in cats for treatment of *Mycoplasma hemofelis* (hemobartonellosis). When azithromycin was administered to dogs with pyoderma at a dose of either 10 mg/kg on day 1 followed by 5 mg/kg on days 2 through 5 or 5 mg/kg given 2 days per week for 3 weeks, the response was equal statistically to cephalixin at 22 mg/kg twice daily. In dairy calves, azithromycin administration significantly suppressed shedding of *Cryptosporidium parvum* and improved clinical signs.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects to azithromycin have not been reported in publications. However, vomiting is likely with high doses. Diarrhea may occur in some patients. Diarrhea has been reported in horses that were administered recommended doses.

Contraindications and Precautions

Use cautiously in animals with a history of vomiting. Administration to adult horses has been associated with diarrhea. Do not administer IV solution as a bolus or IM.

Drug Interactions

Drug interactions have not been reported in animals. This class of drugs has the potential to inhibit some cytochrome P450 enzymes that are involved in drug metabolism, but azithromycin is less likely than erythromycin or clarithromycin to interfere with cytochrome P450 enzymes.

Instructions for Use

Azithromycin may be better tolerated than erythromycin. A primary difference from other antibiotics is the high intracellular concentrations achieved and long half-life that allows for intermittent administration. Although azithromycin has been commonly used for infections in dogs and cats, there is insufficient clinical trial evidence for many uses. To prepare IV solution, add 4.8 mL sterile water to each 500-mg vial and shake. Further dilute this solution with either 500 or 250 mL diluent to a solution of 1 or 2 mg/mL. When administered IV, a 1-mg/mL solution should be administered over a 3-hour period or 2 mg/mL should be administered over 1 hour.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is ≤ 2 mcg/mL.

Formulations

Azithromycin is available in 250-mg capsules, 250- and 600-mg tablets, 100- and 200-mg/5 mL oral suspension, and 500-mg vials for injection. Also, 1-g packets are available for mixing with water.

Stability and Storage

Stable if maintained in manufacturer's original formulation. Stability has not been reported for compounded formulations. IV solution is stable after reconstitution for 48 hours at room temperature.

Small Animal Dosage

Dogs

- A range of doses has been used, starting with 10 mg/kg once daily, PO, for 5-7 days, then decreasing to every other day. Alternatively, 5 mg/kg per day has been used by some veterinarians, either once per day or once every other day.

Cats

- 5-10 mg/kg, once daily for 7 days, PO, followed by administration q48h; or 10-15 mg/kg daily for 3 days, followed by the same dose twice weekly, PO.
- Upper respiratory infection: 15 mg/kg q72h, PO.

Large Animal Dosage

Horses

- For *Rhodococcus equi*: 10 mg/kg q24h, PO, initially, then q48h after a response is seen.
- Foals: 10 mg/kg q48h, PO. For foals, the 1-g packet can be mixed with water to create suspension for oral administration.

Cattle

- 10 mg/kg IM.

Calves

- For cryptosporidiosis: 33 mg/kg once daily for 7 days, PO.

Regulatory Information

Withdrawal times have not been established for animals producing food, but when administered to cattle, it persisted in milk with a half-life of approximately 160 hours and persisted longer in mastitic milk than normal milk.

Benazepril Hydrochloride

ben-ay'zeh-pril hye-droe-klor'ide

Trade and other names: Lotensin (human preparation) and Fortekor, Benazecare (veterinary preparation)

Functional classification: Vasodilator, angiotensin-converting enzyme (ACE) inhibitor

Pharmacology and Mechanism of Action

ACE inhibitor. Inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and will also stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. The inhibition of aldosterone will decrease sodium and water retention. Benazepril, like other ACE inhibitors, will produce vasodilation and decrease aldosterone-induced congestion. ACE inhibitors also contribute to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins. Unlike enalapril, benazepril has a dual mode of elimination through the kidneys and liver. Duration of ACE-inhibiting action is 16-24 hours, despite a short plasma half-life, because of high-affinity binding to ACE.

Indications and Clinical Uses

Benazepril, like other ACE inhibitors, is used to treat hypertension and CHF. Evidence shows that it may decrease the likelihood of developing cardiomyopathy in some dogs, but other studies failed to show this benefit. For treatment of occult mitral valve disease in dogs, there has not been a benefit of therapy. It may benefit some cats in heart failure or with systemic hypertension; however, some cats with hypertension may not respond, and ACE inhibitors are not considered a primary treatment for hypertension in cats. Benazepril has limited antihypertensive effects in cats with naturally occurring renal disease but may be effective in slowing the progression of renal failure. In studies in which it has been used in cats with renal insufficiency, it was associated with a small reduction in systemic hypertension, reduced glomerular filtration pressure, decreased glomerular hypertension, reduction in urine protein loss, and an increase in glomerular filtration rate (GFR), but no overall benefits on survival. In dogs it produces similar benefits to animals with renal disease (decreased proteinuria, increased GFR, and lower blood pressure), but it does not increase survival.

Precautionary Information

Adverse Reactions and Side Effects

Benazepril has been well-tolerated in dogs and cats with chronic renal failure. However, benazepril may cause azotemia in some patients; carefully monitor renal parameters after initiation of treatment, particularly in patients receiving high doses of diuretics.

Contraindications and Precautions

Discontinue ACE inhibitors in pregnant animals. ACE inhibitors cross the placenta and have caused fetal malformations and death of the fetus.

Drug Interactions

Use cautiously with other hypotensive drugs and diuretics. Nonsteroidal anti-inflammatory drugs (NSAIDs) may decrease vasodilating effects.

Instructions for Use

Dose is based on approved use in dogs in Europe and Canada. Monitor renal function and electrolytes 3-7 days after initiating therapy and periodically thereafter. In studies in cats there was no benefit to doses higher than 0.5-1 mg/kg/day.

Patient Monitoring and Laboratory Tests

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

Formulations

Benazepril is available in 5-, 10-, 20-, and 40-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 0.25 to 0.5 mg/kg q12-24h PO (0.5 mg/kg q24h in most patients).

Cats

- Systemic hypertension and renal disease: 0.5-1 mg/kg/day PO.
Alternative dose for cats is 2.5 mg per cat per day, for cats up to 5 kg body weight, PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 3

Betamethasone

bay-tah-meth'ah-sonē

Trade and other names: Celestone, betamethasone acetate, and betamethasone benzoate

Functional classification: Corticosteroid

Pharmacology and Mechanism of Action

Potent, long-acting corticosteroid. Anti-inflammatory and immunosuppressive effects are approximately 30 times more than cortisol. Anti-inflammatory effects are complex but primarily occur via inhibition of inflammatory cells and suppression of expression of inflammatory mediators.

Indications and Clinical Uses

Betamethasone is used for treatment of inflammatory and immune-mediated disease. It is used for similar indications as prednisolone and dexamethasone.

Precautionary Information

Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic-pituitary-adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, increased risk of diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodex, toxoplasmosis, fungal infections, and UTIs. In horses, additional adverse effects may include risk of laminitis.

Contraindications and Precautions

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously in diabetic animals, animals with renal failure, or pregnant animals.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Betamethasone is used for similar indications as dexamethasone because of similar potency and duration of effect. Topical forms of betamethasone also are available.

Patient Monitoring and Laboratory Tests

Monitor CBC and plasma cortisol.

Formulations

Betamethasone is available in 600-mcg (0.6-mg) tablets and 3 mg/mL sodium phosphate injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- Anti-inflammatory effects: 0.1-0.2 mg/kg q12-24h PO.
- Immunosuppressive effects: 0.2-0.5 mg/kg q12-24h PO.

Large Animal Dosage

- 0.05-0.1 mg/kg q24h IM or PO.

Regulatory Information

No withdrawal times are established for animals intended for food (extralabel use). RCI Classification: 4

Bethanechol Chloride

beh-than'eh-kole klor'ide

Trade and other names: Urecholine

Functional classification: Cholinergic

Pharmacology and Mechanism of Action

Muscarinic, cholinergic agonist. Parasympathomimetic. Bethanechol stimulates gastric and intestinal motility. It also stimulates contraction of urinary bladder via muscarinic receptor activation. Bethanechol, like other carbamoyl esters, resists hydrolysis by acetylcholinesterase to produce a more sustained response. The onset of action is usually 10 minutes after injection and 30-60 minutes after oral administration. Duration of effect is 4-6 hours.

Indications and Clinical Uses

Bethanechol is used in small animals to increase contraction of urinary bladder. In large animals it may increase gastrointestinal motility, but the efficacy for treating GI stasis problems is questionable.

Precautionary Information

Adverse Reactions and Side Effects

High doses of cholinergic agonists will increase motility of GI tract and cause abdominal discomfort and diarrhea. Bethanechol can cause circulatory depression in sensitive animals.

Contraindications and Precautions

Do not use in patients with suspected GI or urinary obstruction.

Drug Interactions

Anticholinergic drugs (atropine, scopolamine, etc.) will antagonize effects of bethanechol.

Instructions for Use

Administer injection SQ only. Doses are derived from extrapolation of human doses or via empiricism. There are no well-controlled efficacy studies available for veterinary species.

Bethanechol is no longer available from commercial sources, but some veterinary compounding pharmacists may be able to supply veterinarians.

Patient Monitoring and Laboratory Tests

Monitor GI function.

Formulations

Bethanechol is available in 5-, 10-, 25-, and 50-mg tablets and 5-mg/mL injection. (Commercial preparations are no longer available but are available through some compounding pharmacies.)

Stability and Storage

Store in a tightly sealed container at room temperature. Compounded oral suspensions prepared from tablets are not stable.

Small Animal Dosage

Dogs

- 5-15 mg/dog q8h PO (2.5 mg per dog for small dogs).

Cats

- 1.25-5 mg/cat q8h PO.

Large Animal Dosage

Horses

- 0.025 mg/kg SQ.

Cattle

- 0.07 mg/kg SQ.

Regulatory Information

No withdrawal times are established for animals intended for food (extralabel use). However, FARAD (1-888-873-2723) recommends a 21-day withdrawal time for slaughter.

RCI Classification: 4

Bisacodyl

biss-ah-koe'dil

Trade and other names: Dulcolax

Functional classification: Laxative

Pharmacology and Mechanism of Action

Laxative/cathartic. Bisacodyl acts via local stimulation of GI motility, most likely by irritation of bowel.

Indications and Clinical Uses

Bisacodyl is used as a laxative or for procedures in which bowel evacuation is necessary. It may be used with polyethylene glycol electrolyte solution (e.g., Golytely) to cleanse the bowel prior to endoscopy or surgical procedures.

Precautionary Information

Adverse Reactions and Side Effects

Abdominal discomfort. Fluid and electrolyte loss. Avoid chronic use.

Contraindications and Precautions

Avoid use in patients with renal disease. Avoid overuse.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Bisacodyl is available as an OTC tablet. Doses are derived from extrapolation of human doses or via empiricism. There are no well-controlled efficacy studies available for veterinary species. Onset of action is approximately 1 hour after administration.

Patient Monitoring and Laboratory Tests

Monitor electrolytes in animals if used chronically.

Formulations

Bisacodyl is available in 5-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 5 mg/animal q8-24h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Bismuth Subsalicylate

biz'muth sub-sal-iss'ih-late

Trade and other names: Pepto-Bismol

Functional classification: Antidiarrheal

Pharmacology and Mechanism of Action

Antidiarrheal agent and GI protectant. Precise mechanism of action is unknown, but antiprostaglandin action of salicylate component may be beneficial for enteritis. The bismuth component is efficacious for treating infections caused by spirochete bacteria (*Helicobacter pylori* gastritis). Bismuth subsalicylate in Pepto-Bismol contains five sources of salicylate, which are absorbed systemically after oral administration. Bismuth subsalicylate also may be found in other antidiarrhea preparations, such as kaolin-pectin formulations (e.g., Kaopectate).

Indications and Clinical Uses

Bismuth subsalicylate is used for symptomatic treatment of diarrhea in small and large animals. Efficacy has not been established for animals. However, in people it has been shown effective for treating or preventing diarrhea caused by enterotoxigenic *Escherichia coli* (ETEC).

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are uncommon. Owners should be warned that bismuth will discolor stools black.

Contraindications and Precautions

Salicylate component is absorbed systemically, and overuse should be avoided in animals that cannot tolerate salicylates (such as cats and animals allergic to aspirin).

Drug Interactions

No drug interactions are reported in animals. However, it may possibly exacerbate effects of other nonsteroidal anti-inflammatory drugs (NSAIDs) administered to animals. The bismuth component may prevent oral absorption of some drugs.

Instructions for Use

Bismuth subsalicylate is available as an OTC product. Doses are derived from extrapolation of human doses or via empiricism. There are no well-controlled efficacy studies available for veterinary species.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

74 Bisoprolol fumarate

Formulations

Bismuth subsalicylate is available in oral suspension in 262 mg/15 mL or 525 mg/mL in extra-strength formulation and 262-mg tablets. Two tablespoons (30 mL) contain 270-mg salicylate.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 1-3 mL/kg/day (in divided doses) PO.

Large Animal Dosage

Calves

- 30 mL q30min for 8 doses PO.

Horses

- 1-2 mL/kg q6-8h PO.

Regulatory Information

No withdrawal times are established for animals intended for food (extralabel use). Because salicylate component may be systemically absorbed, withdrawal times should be considered for the salicylate component (similar to aspirin).

Bisoprolol fumarate

bis-oh'-proe-lol

Trade and other names: Zebeta

Functional classification: Antiarrhythmic, beta blocker

Pharmacology and Mechanism of Action

Bisoprolol is a synthetic beta₁-selective beta-adrenergic receptor blocker with a low affinity for beta₂-receptors in bronchial smooth muscle, blood vessels, and fat cells and no intrinsic sympathomimetic activity. Typical cardioselective effects include lower heart rate, decreased cardiac output, and inhibition of renin release by kidneys. At higher doses it will lose beta₁ selectivity and also inhibit some beta₂ receptors to affect bronchial and vascular smooth muscle. Clearance in dogs is balanced (60% metabolized by the liver and 40% excreted unchanged), distinguishing bisoprolol from lipophilic beta blockers such as carvedilol and metoprolol and hydrophilic beta blockers like atenolol. In dogs, bisoprolol has high and consistent oral absorption (91%) and a half-life of 4 hours. Although bisoprolol prolongs survival in human patients with heart failure, similar studies have not been conducted in dogs or cats.

Indications and Clinical Uses

Bisoprolol is a beta₁ blocker that is somewhat cardioselective and therefore is indicated for conditions that require a reduction in heart rate, heart conductivity, or contractility. Such conditions include tachyarrhythmias and atrial fibrillation. In people it is used to treat hypertension, but this use has not been explored in animals.

Precautionary Information

Adverse Reactions and Side Effects

Beta blockade will result in adverse effects that are attributed to decreased adrenergic tone in the heart. Bradycardia and heart block are possible. At high doses, or in sensitive doses, bisoprolol may produce bronchospasm. Treat bradycardia from overdose with atropine.

Contraindications and Precautions

Use cautiously in animals with airway disease, myocardial failure, and cardiac conduction disturbances. Use cautiously in animals with low cardiac reserve.

Drug Interactions

Use cautiously with other drugs that may decrease cardiac contraction or heart rate. Concurrent use of rifampin may increase the metabolic clearance of bisoprolol.

Instructions for Use

Dosing precautions are similar to other beta-blocking drugs.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm. Monitor blood pressure in patients prone to hypotension.

Formulations

Bisoprolol is available in 5- and 10-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 0.1-0.2 mg/kg q8-12h, PO.

Cats

- No dose has been established for cats.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Bleomycin Sulfate

blee-oh-mye'sin sul'fate

Trade and other names: Blenoxane

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer antibiotic agent. Exact mechanism of action is unknown, but it may bind to DNA and prevent synthesis.

Indications and Clinical Uses

Bleomycin is used for treatment of various sarcomas and carcinomas.

Precautionary Information

Adverse Reactions and Side Effects

Bleomycin causes local reaction at site of injection, pulmonary toxicity, fever, and chills in people. Side effects are not well documented in veterinary species.

Contraindications and Precautions

Do not use in animals with suppressed bone marrow.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Injectable solution usually used in combination with other anticancer agents. Consult anticancer protocols for details regarding use.

Patient Monitoring and Laboratory Tests

Monitor CBC during treatment.

Formulations

Bleomycin is available in 15-unit vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Refrigerate vials after opening. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 10 units/m² IV or SQ for 3 days, then 10 units/m² weekly. (Maximum cumulative dose 200 units/m².)

Cats

- No dose is available for cats.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. Because it is an anticancer agent, do not administer to food-producing animals.

Boldenone Undecylenate

bole'de-none un-de-sil-en'ate

Trade and other names: Equipoise

Functional classification: Hormone, anabolic agent

Pharmacology and Mechanism of Action

Anabolic steroid. Boldenone is a steroid ester designed to maximize anabolic effects while minimizing androgenic action (see also Methyltestosterone). Anabolic agents

have been used for reversing catabolic conditions, increasing weight gain, increasing muscling in animals, and stimulating erythropoiesis. Stanozolol is a similar drug used in horses. There are no documented differences in efficacy among the anabolic steroids.

Indications and Clinical Uses

Boldenone is an anabolic agent. It is used primarily in horses to improve nitrogen balance, reduce overexertion associated with exercise, and improve training. It may also improve appetite and improve weight gain when used with a well-balanced diet. Boldenone is a long-lasting agent, and effects may persist for 6 weeks after an intramuscular injection.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects from anabolic steroids can be attributed to the androgenic action of these steroids. Increased masculine effects are common. Increased aggressiveness may be observed. Increased incidence of some tumors has been reported in people and 17 alpha-methylated oral anabolic steroids (oxymetholone, stanozolol, and oxandrolone) are associated with hepatic toxicity.

Contraindications and Precautions

This drug is abused by humans to enhance athletic performance and is a controlled substance. Do not administer to animals intended for food. Do not administer to pregnant animals.

Drug Interactions

There are no significant drug interactions known; however, use cautiously with other drugs that may affect liver function.

Instructions for Use

For many indications, use in animals is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes for signs of hepatic injury (cholestatic) during treatment.

Formulations

Boldenone is available in 25- and 50-mg/mL injection in sesame oil.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze. Do not mix with aqueous solutions.

Small Animal Dosage

Doses have not been reported for small animals.

Large Animal Dosage

Horses

- 1.1 mg/kg IM. Injection may be repeated every 3 weeks.

Regulatory Information

Do not administer to animals intended for food.

Schedule III controlled drug

RCI Classification: 4

Bromide

broe'mide

Trade and other names: Potassium bromide and sodium bromide

Functional classification: Anticonvulsant

Pharmacology and Mechanism of Action

Anticonvulsant. Exact mechanism of action is uncertain. Anticonvulsant action is to stabilize neuronal cell membranes. By changing the chloride conductance in neuronal membranes, it may stabilize epileptic foci in the brain. In dogs oral absorption is 46%. It is not metabolized, and most is eliminated by the kidneys. The half-life is long—11 days in cats, and it has ranged from 25 days to 46 days in dogs. Bromide is available in two forms: sodium bromide (78% bromide) and potassium bromide (67% bromide).

Indications and Clinical Uses

Bromide ordinarily is used in patients with seizure disorders that have been refractory to phenobarbital. Usually, patients are treated with both phenobarbital and bromide. However, some patients have been treated with bromide as a single therapy for epilepsy. If bromide is added to phenobarbital therapy, it allows for a reduction in phenobarbital dose (reduce by 25% every 6 weeks). Bromide has not been as effective for treating cats with seizure disorders as in dogs. Cats have more adverse effects and are less well controlled.

Precautionary Information

Adverse Reactions and Side Effects

Common side effects include PU/PD, polyphagia, ataxia, sedation, and GI upset. More serious adverse effects are related to high levels of bromide (bromism) and are more specific for the CNS. Signs of toxicosis are CNS depression, delirium, hyperexcitability, weakness, and ataxia. Hind limb stiffness and abnormal gait also may be a sign of bromide toxicosis.

Nausea and pancreatitis have been reported in dogs, and there is evidence that a combination of bromide and phenobarbital in dogs may increase the risk of pancreatitis.

Some dogs show paradoxical excitement with bromide treatment. In many cats, bronchitis, resembling allergic airway disease, has been observed. In cats this may be characterized by coughing.

Contraindications and Precautions

Consider using sodium bromide, rather than potassium bromide, in patients with hypoadrenocorticism or in any patients in which potassium regulation is a problem. Likewise, consider the sodium content of administration in animals with CHF or hypertension. Diets high in chloride will cause a shorter half-life and need for a higher dose. Monitor plasma concentrations and adjust dose as necessary whenever changing diets because increasing chloride in the diet will shorten the half-life and vice versa. If diet is high in chloride (Hill's h/d, s/d, I/d, and others), higher starting doses may be necessary. Administration of bromide will interfere with some blood chemistry analysis (e.g., false elevation of chloride).

Drug Interactions

Diets high in chloride will cause a shorter half-life and need for a higher dose. Administration of bromide will interfere with some blood chemistry analysis (e.g., false elevation of chloride).

Instructions for Use

Bromide usually is administered in combination with phenobarbital. Sodium bromide can be substituted for potassium bromide. When considering doses for sodium bromide, slight dose adjustments should be considered. Potassium bromide is 67% bromide, and sodium bromide is 78% bromide. The dose of sodium bromide should be approximately 15% less (e.g., 30 mg/kg of potassium bromide is equivalent to 25 mg/kg of sodium bromide).

Patient Monitoring and Laboratory Tests

Monitor serum bromide concentrations to adjust dose. Effective plasma concentrations should be 1-2 mg/mL (100-200 mg/dL), but if used alone (without phenobarbital) higher concentrations of 2-2.5 mg/mL (200-250 mg/dL) and as high as 4 mg/mL may be needed. Most veterinary laboratories can perform a test for bromide in plasma or serum.

Formulations

Bromide is usually prepared as an oral solution. Although there are no commercial forms approved by the FDA, compounding pharmacists can prepare a solution. To prepare the oral solution, mix 25 g of potassium bromide with 60 mL of purified water, then add a sufficient quantity of corn syrup to make 100 mL. This formulation will result in a concentration of approximately 151-185 mg/mL. This solution is stable for 180 days. For sodium bromide oral solution, mix 21.6 g sodium bromide with 60 mL purified water, then add a sufficient quantity of corn syrup to make 100 mL. This formulation will result in a concentration of approximately 151-185 mg/mL. This solution is stable for 180 days.

A pharmacist should prepare the intravenous solution in sterile water and filter it to remove impurities. To prepare injectable solution, add 3.0 g of sodium bromide with a sufficient quantity of sterile water to make 100 mL. This formulation will result in a concentration of approximately 21-25.6 mg/mL. It is stable for 180 days and should be stored in the refrigerator to decrease the risk of microbial growth.

Stability and Storage

Store in a tightly sealed container. Compounded formulations in aqueous solutions are stable for at least 180 days. Refrigerate injectable solution to prevent bacterial growth. Do not mix with salt-containing flavorants or solutions.

Small Animal Dosage

Cats

- 30 mg/kg q24h PO.

Dogs

- 30-40 mg/kg q24h PO. If administered without phenobarbital, higher doses of up to 40-50 mg/kg may be needed. If animals are on diets high in chloride, higher doses may be needed. Adjust doses by monitoring plasma concentrations.
- Oral loading dose: 600 mg/kg divided over 3-5 days, PO. Alternatively, 60 mg/kg/day have been administered for 15 days to achieve a plasma concentration of 100 mg/dL, and 200 mg/dL by 60 days.

80 Bromocriptine Mesylate

- IV loading dose for sodium bromide: 800 to 1200 mg/kg infused over 8 hours (it is critical to use sodium bromide instead of potassium bromide for this use).

Large Animal Dosage

Horses

100 mg/kg loading dose, followed by 25 mg/kg q24h, PO.

No dose has been reported for other large animals.

Regulatory Information

Do not administer to animals intended for food.

Bromocriptine Mesylate

broe-moe-krip'teen mess'ih-late

Trade and other names: Parlodel

Functional classification: Dopamine agonist

Pharmacology and Mechanism of Action

Dopaminergic agonist. Antiprolactin agent. Bromocriptine is a lactation inhibitor. It reduces serum prolactin concentration by inhibition of release from anterior pituitary gland by binding to dopamine (D₂) receptors in the CNS. The binding of D₂ receptors restores hormonal function in the pituitary. Through the action on the dopamine pituitary receptors, bromocriptine may decrease corticotropin (ACTH) release and has been used in animals (especially horses) for treating pituitary-dependent hyperadrenocorticism (PDH). It has not been effective for treating canine pituitary-dependent hyperadrenocorticism (Cushing's syndrome). It also stimulates postsynaptic dopamine receptors and has been used to treat dopamine-deficient neurodegenerative diseases.

Indications and Clinical Uses

In people, bromocriptine is used for its antiparkinson effect and to inhibit lactation associated with excess prolactin. It also has been used to treat acromegaly. Bromocriptine has been used to treat disorders associated with dopamine deficiency in animals. In dogs, bromocriptine has been used to terminate pregnancy when used in combination with a prostaglandin (dinoprost or cloprostenol). In this combination, it was 100% effective for terminating pregnancy in dogs. In horses, bromocriptine may decrease ACTH release and has been used in treating equine pituitary pars intermedia dysfunction (Cushing's syndrome), but pergolide is usually a preferred treatment.

Precautionary Information

Adverse Reactions and Side Effects

Pyometra may occur in dogs after it has been used to induce abortion. Bromocriptine may cause mammary gland enlargement. When terminating pregnancy, bromocriptine is used in combination with prostaglandin F₂alpha. Adverse effects (vomiting, nausea, and retching) may occur as a result of the prostaglandin. Bromocriptine will inhibit lactation.

Contraindications and Precautions

Except when used for termination of pregnancy, do not use in pregnant animals. Do not use in nursing animals. Women handling bromocriptine should use caution to avoid exposure.

Drug Interactions

No drug interactions have been reported in animals. However, it will exacerbate the effects of selegiline. Do not administer with monoamine oxidase inhibitors (MAOIs).

Instructions for Use

Use of bromocriptine is limited to treatment of some endocrine disorders. Studies of efficacy are limited. Bromocriptine has been used to terminate pregnancy in dogs in combination with prostaglandin F₂alpha. For this use, administer 15 mcg/kg q12h PO on day 1, 20 mcg/kg 12h PO on days 2 and 3, and 30 mcg/kg q12h PO thereafter for an average of 4-5 days. Ten days may be needed in some dogs. A prostaglandin (cloprostenol sodium) should be used at a dose of 1 mcg/kg q48h SQ during this regimen.

Patient Monitoring and Laboratory Tests

Monitor pregnant animals carefully, especially if bromocriptine has been used to terminate pregnancy.

Formulations

Bromocriptine is available in 5-mg capsules and 2.5-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Termination of pregnancy: 15 mcg/kg q12h PO on day 1, 20 mcg/kg 12h PO on days 2 and 3, and 30 mcg/mkg q12h PO thereafter for an average of 4-5 days. For treatment success, it should be administered in combination with prostaglandin F₂alpha.
- Other conditions: 0.02-0.04 mg/kg q12h PO.

Cats

- 0.02-0.04 mg/kg q12h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Budesonide

byoo-dess'oh-nide

Trade and other names: Enterocort

Functional classification: Anti-inflammatory, corticosteroid

Pharmacology and Mechanism of Action

Budesonide is a locally acting corticosteroid but is 1000 times more active than prednisolone as a corticosteroid. It is approved for use in people, but there has been only limited use in small animals. Budesonide granules are contained in an ethylcellulose matrix that is coated with methacrylic acid polymer. This coating does not release the drug until the pH is >5.5. Therefore, the drug is not usually released until it reaches the distal GI tract. If any is absorbed, 80%-90% is inactivated by metabolism first-pass effects. Therefore, systemic glucocorticoid effects are minimized. In humans it has been as effective as other drugs for treatment of Crohn's disease.

Indications and Clinical Uses

In animals it has been used to treat inflammatory bowel disease. The most common use has been for treating colitis in dogs or inflammatory bowel disease in cats. There is only limited experience with budesonide in dogs and cats, and reports of successful treatment are mostly anecdotal.

Precautionary Information

Adverse Reactions and Side Effects

There is some systemic absorption, as evidenced by decreased response to ACTH and decreased cortisol after 30-day treatment to dogs at 3 mg/m², but other side effects were not observed and other variables (CBC, liver enzymes) were not affected.

Contraindications and Precautions

No known contraindications. However, some of the drug may be absorbed systemically; therefore, use with caution in animals that should not receive corticosteroids.

Drug Interactions

Do not administer with drugs that increase stomach pH (antacids, antisecretory drugs). Because budesonide is metabolized by cytochrome P450 enzymes, other drugs that inhibit these enzymes (see Appendix F) may inhibit metabolism.

Instructions for Use

Use in animals has been limited to anecdotal experience. The capsules should not be crushed or compounded for animals, unless action in the proximal portion of the intestine is desired.

Patient Monitoring and Laboratory Tests

Monitor corticosteroid effects and, preferably, conduct an ACTH-stimulation test to determine degree of adrenal suppression with chronic use.

Formulations

Budesonide is available in 3-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not crush capsules.

Small Animal Dosage

Dogs and Cats

- 0.125 mg/kg q8-12h PO. Dose interval may be increased to every 24 hours when condition improves.

- In dogs, intact 3-mg capsules, once per day, have been administered; but in cats, doses of 0.5 to 0.75 mg per cat per day are administered by reformulating capsules.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. Because of minimal systemic absorption expected, no withdrawal time is suggested.

RCI Classification: 4

Bunamidine Hydrochloride

byoo-nam'ih-deen hye-droe-klor'ide

Trade and other names: Scolaban

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Bunamidine hydrochloride damages the integrity of protective integument on cestode parasites. It is effective against various species of tapeworms in animals.

Indications and Clinical Uses

Bunamidine is used as an anticestodal agent to treat tapeworm infections in dogs and cats.

Precautionary Information

Adverse Reactions and Side Effects

Vomiting and diarrhea have occurred after use.

Contraindications and Precautions

Avoid use in young animals.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Do not break tablets. Administer tablets on empty stomach. Do not feed animal for 3 hours after administration.

Patient Monitoring and Laboratory Tests

Monitor fecal samples for evidence of parasites.

Formulations

Bunamidine is available in 400-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 20-50 mg/kg once PO.

84 Bupivacaine Hydrochloride

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Bupivacaine Hydrochloride

byoo-piv'ah-kane hye-droe-klar'ide

Trade and other names: Marcaine and generic brands

Functional classification: Local anesthetic

Pharmacology and Mechanism of Action

Local anesthetic. Bupivacaine inhibits nerve conduction via sodium channel blockade. Bupivacaine has a slow onset of action (20 minutes) but is longer acting (6-8 hours) and more potent than lidocaine or other local anesthetics. Epidural onset of action is approximately 15-20 minutes with a duration of 2-4 hours.

Indications and Clinical Uses

Bupivacaine is used for local anesthesia and epidural analgesia/anesthesia. It is administered by local infiltration or by epidural injection.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are rare with local infiltration. High doses absorbed systemically can cause nervous system signs (tremors and convulsions). The toxic dose in cats is 5 mg/kg. In cats, signs of toxicity include bradycardia, arrhythmias, tremors, muscle twitching, and seizures. After epidural administration, respiratory paralysis is possible with high doses.

Contraindications and Precautions

When using for epidural anesthesia, respiratory support should be available. Some formulations contain epinephrine (1:200,000) and should not be administered to animals that are prone to reactions from epinephrine.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Used for local infiltration or infusion into epidural space. For epidural injection, the volume of injection is approximately 0.2 mL/kg, or not to exceed 6 mL for large dogs. Ordinarily, the dose for a nerve block in small animals does not exceed 1 mg/kg. One may mix 0.1 mEq sodium bicarbonate per 10-mL solution to increase pH, decrease pain from injection, and produce a shorter onset of action. Use immediately after mixing with bicarbonate because of risk of precipitation. Increasing the pH will accelerate the onset of anesthetic action.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Bupivacaine is available in 0.25%, 0.5%, and 0.75% (2.5, 5 and 7.5 mg/mL) solution for injection.

Stability and Storage

Store in a tightly sealed container at room temperature. Avoid mixing with strongly acidic or alkaline solutions. If solutions change to a yellow, pink, or darker color, they should not be used. If pH is adjusted by mixing with alkalizing solutions (e.g., bicarbonate) the drug is stable but must be used soon after mixing.

Small Animal Dosage

Dogs and Cats

- Epidural dose: 1-1.5 mg/kg; for nerve blocks, usually 0.2 mL/kg of 0.5% solution is used.

Large Animal Dosage

- Limited to local infiltration for minor surgery.

Regulatory Information

No withdrawal times are established for animals intended for food (extralabel use). When used for local infiltration, clearance from animal is expected to be rapid. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USEFARAD (1-888-873-2723).

RCI Classification: 2

Buprenorphine Hydrochloride

byoo-preh-nor'feen hye-droe-klor'ide

Trade and other names: Buprenex (Vetergesic in the UK)

Functional classification: Analgesic, opioid

Pharmacology and Mechanism of Action

Opioid analgesic. Buprenorphine is a partial mu-receptor agonist and kappa-receptor antagonist. It is 25 to 50 times more potent than morphine. Buprenorphine may cause less respiratory depression than other opiates. The pharmacokinetics in dogs have been variable, depending on the study. The half-life in dogs has ranged from 4.5 hours to 9 hours, with a clearance from 5.4 to 24 mL/kg/min. In horses the half-life is 7 hours, with a clearance of 8 mL/kg/min. In horses the absorption from IM administration is highly variable (41%-93%).

Indications and Clinical Uses

Buprenorphine is an opiate analgesic that is used for pain control in dogs and cats. It has lower efficacy (lower ceiling) than pure mu-receptor agonists such as morphine. Buprenorphine has been shown to be effective in animal studies for treating postoperative pain. Duration of analgesia based on plasma values in animals is 3-4 hours, but it may be longer clinically because of slow dissociation from binding sites or longer half-life from CNS tissues and higher affinity for the mu-receptor. Duration of effect has not been established for all indications in well-controlled studies and has

been variable. In cats it has been administered for transmucosal absorption (buccal administration), in which high systemic absorption has been demonstrated. In dogs, absorption from transmucosal (gingival) administration is less complete (47%) and higher doses must be administered to achieve analgesic effects. In dogs, 120 mcg/kg administered transmucosal (gingiva) is equivalent to 20 mcg/kg intravenously. At these doses for dogs, the high volume increases the risk of drug loss from the mouth or from swallowing. In horses, the doses that are analgesic are likely to produce adverse effects (excitement and locomotor activity), which limits the uses in horses. The adverse effects in horses persist longer than the analgesic effects.

In people, buprenorphine analgesia has been enhanced with the addition of small doses of naloxone (0.001-0.1 mcg/kg), but this effect has not been investigated in animals.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are similar to other opiate agonists, except there may be less respiratory depression. Sedation is common. Dependency from chronic use of buprenorphine may be less than with pure agonists. Lethal dose in dogs is 80 mg/kg.

In horses, restlessness, excitatory reactions, head shaking, pawing, shifting leg movements, decreased intestinal motility, and increased locomotor activity are likely and may persist for several hours.

Contraindications and Precautions

Patients receiving buprenorphine may require higher doses of naloxone for reversal. IV dose in horses may cause behavior reactions (excitement, pacing).

Drug Interactions

As a partial agonist, it may reverse or antagonize some of the mu-receptor effects of other opiates, such as morphine or fentanyl.

Instructions for Use

Buprenorphine is used for analgesia, often in combination with other analgesics or in conjunction with general anesthesia. It is longer acting than morphine and only partially reversed by naloxone. When administration is intended to be buccal (transmucosal) it is important that the entire dose is applied to the oral mucosa and not swallowed. Ingested drug will not be effective (only 3%-6% oral absorption). Therefore, as the dose increases, the volume also increases and there is a higher likelihood that some of the drug will be lost from the mouth or swallowed (e.g., at a dose of 0.03 mg/kg to cats, the volume necessary for administration is 0.45 mL per average cat).

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, if necessary atropine can be administered. If serious respiratory depression occurs, the opioid can be reversed with naloxone. Patients receiving buprenorphine may require higher doses of naloxone for reversal.

Formulations

Buprenorphine is available in 0.3-mg/mL injection solution in a 1-mL vial. Two- and 8-mg sublingual tablets (Subutex and Suboxone with naloxone) have been used in people to treat substance abuse. Suboxone (with naloxone) is also available in a transmucosal/sublingual film.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Use sodium chloride for infusions. Stability of compounded formulations has not been evaluated. Schedule II drugs should be stored in locked compartment.

Small Animal Dosage

Dogs

- 0.006-0.02 mg/kg q4-8h IV, IM or SQ. For analgesia, doses have been increased to as high as 0.03-0.04 mg/kg SQ.
- Epidural: 0.003-0.006 mg/kg (3-6 mcg/kg)

Cats

- 0.005-0.01 mg/kg q4-8h IV or IM. For analgesia, a dose of 0.01 mg/kg IM is most common.
- Buccal (transmucosal) administration: 0.01-0.02 mg/kg q12h and as high as 0.03 mg/kg. 0.02 mg/kg (20 mcg/kg) is equivalent to 0.066 mL per kg. This may be applied to the cat's gingival or oral mucosa (i.e., sublingual). After initial response, the dose can be gradually tapered to 5-10 mcg/kg.
- Epidural: 12.5 mcg/kg diluted with saline to a volume of 0.3 mL/kg.

Large Animal Dosage

Horses

- 0.005-0.01 mg/kg (5-10 mcg/kg IM); short acting in horses.

Sheep

- 0.01 mg/kg (10 mcg/kg) IM, q6h.

Regulatory Information

The drug is controlled by the DEA. Do not administer to animals intended for food.

Schedule III controlled drug

RCI Classification: 2

Buspirone Hydrochloride

byoo-speer'own hye-droe-klor'ide

Trade and other names: BuSpar

Functional classification: Behavior modification

Pharmacology and Mechanism of Action

Antianxiety agent of the azapirone class. Buspirone acts as a direct-acting serotonin (5-HT_{1A}) agonist. By activating 5HT_{1A} receptors, buspirone and related drugs alter mood and anxiety. Buspirone is used to treat anxiety and other behavior problems. Other related drugs include gepirone and ipsapirone.

Indications and Clinical Uses

In veterinary medicine, buspirone has been primarily used for treatment of urine spraying (urine marking) in cats. In cats there are published studies demonstrating efficacy. However, some cats relapse after treatment is discontinued. Buspirone also has been used as an antiemetic in cats (4 mg/kg SQ). In dogs, it has occasionally been used to treat behavior problems, such as anxiety disorders.

Precautionary Information

Adverse Reactions and Side Effects

Few side effects are seen in cats compared to other drugs. Some cats show increased aggression; and some cats show increased affection and friendliness to owners. It may produce mild sedation.

Contraindications and Precautions

Do not use in animals with sensitivity to serotonin agonists.

Drug Interactions

Do not use with other serotonin antagonists, selective serotonin reuptake inhibitors (SSRIs), or monoamine oxidase inhibitors (MAOIs; e.g., selegiline).

Instructions for Use

Some efficacy trials suggest effectiveness for treating urine spraying in cats. There may be a lower relapse rate compared to other drugs.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Buspironone is available in 5-, 10-, 15- and 30-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Cats

- 2.5-5 mg/cat q12h PO, which may be increased to 5-7.5 mg per cat twice daily for some cats (0.5-1 mg/kg q12h PO).

Dogs

- 2.5-10 mg/dog q24h or q12h PO.
- 1 mg/kg q12h PO.

Large Animal Dosage

Horses

- 100-250 mg/horse q24h PO (0.5 mg/kg).

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 2

Busulfan

byoo-sul'fan

Trade and other names: Myleran

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Busulfan is a bifunctional alkylating agent and acts to disrupt DNA of tumor cells.

Indications and Clinical Uses

Busulfan is used primarily for lymphoreticular neoplasia.

Precautionary Information

Adverse Reactions and Side Effects

Leukopenia is the most severe side effect.

Contraindications and Precautions

Do not use in animals with suppressed bone marrow.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Busulfan is usually used in combination with other anticancer agents. Consult specific protocol for details.

Patient Monitoring and Laboratory Tests

Monitor CBC in animals during treatment.

Formulations

Busulfan is available in 2-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 3-4 mg/m² q24h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in food animals because it is an anticancer agent.

Butorphanol Tartrate

byoo-tor'fah-nole tar'trate

Trade and other names: Torbutrol and Torbugesic

Functional classification: Analgesic, opioid

Pharmacology and Mechanism of Action

Opioid analgesic. Opiate that acts as kappa receptor agonist and weak mu-receptor antagonist (some authorities classify the antagonist effect as a "partial agonist" effect). As a kappa-agonist, butorphanol produces sedation and analgesia in animals. It is considered a mild analgesic compared to pure mu-receptor opiates. It is often used in combination with other anesthetics. It has a short half-life in animals (1-2 hours) and a short duration of analgesia (1-2 hours).

Indications and Clinical Uses

Butorphanol is used for perioperative analgesia, for chronic pain, and as an antitussive agent. Butorphanol is considered a weak analgesic compared to drugs that are pure mu-receptor agonists and some of the observed effects may be caused by sedation, rather than analgesia. In dogs, at doses of 0.4 mg/kg, butorphanol produces analgesia for a duration of 1.0 hour or less. As an antitussive, it is more potent than morphine (4×) and codeine (100×). Duration of the antitussive effect is approximately 90 minutes, but the effect may persist for as long as 4 hours. In cats, butorphanol at 0.4 mg/kg may have an analgesic duration of effect for as long as 3 hours. In horses it may be administered IV, IM, and as constant rate infusion (CRI). CRI has been shown effective in controlled studies.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are similar to other opioid analgesic drugs. Sedation is common at analgesic doses. Respiratory depression can occur with high doses. Lethal dose in dogs (LD₅₀) is 20 mg/kg. Although bradycardia rarely needs to be treated when it is caused by an opioid, if necessary atropine can be administered. If serious respiratory depression occurs, the opioid can be reversed with naloxone. Dysphoric effects have been observed with agonist/antagonist drugs; this effect has been observed in cats. Decreased intestinal peristalsis and constipation may occur in some animals. A decrease in intestinal motility may be a particular concern in some horses.

Contraindications and Precautions

Schedule IV controlled substance. Butorphanol use in birds requires much higher doses than in mammals because of shorter half-life and rapid clearance (e.g., 2-4 mg/kg every 2-4 hours).

Drug Interactions

Butorphanol is compatible with many other analgesics and used in combination treatment for analgesia. Because butorphanol is an agonist/antagonist, it may antagonize some effects of drugs that are pure agonists (e.g., fentanyl, morphine, and oxymorphone). However, the clinical significance of this antagonism has been debated among experts. Do not mix with sodium barbiturates.

Instructions for Use

Butorphanol is often used in combination with anesthetic agents or in conjunction with other analgesic drugs. For most indications, a dose of 0.4 mg/kg is considered optimum, and there is no reason to increase the dose above 0.8 mg/kg because this is considered the ceiling dose. Butorphanol has a short duration of effect of less than 2 hours and usually only 1 hour. In horses, because butorphanol may cause increased locomotor activity and excitement, xylazine may be administered prior to buprenorphine.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration.

Formulations

Butorphanol is available in 1-, 5-, and 10-mg tablets and 0.5- and 1-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Antitussive: 0.055 mg/kg q6-12h SQ, 0.011 mg/kg IM, or 0.5-1 mg/kg q6-12h PO.
- Preanesthetic: 0.2-0.4 mg/kg (with acepromazine) IV, IM, or SQ.
- Analgesic: 0.2-0.4 mg/kg q2-4h IV, IM, or SQ or 1-4 mg/kg q6h PO.
- CRI: Loading dose of 0.2-0.4 mg/kg IV, followed by 0.1-0.2 mg/kg/hr.

Cats

- Analgesic: 0.2-0.8 mg/kg q2-6h IV or SQ or 1.5 mg/kg q4-8h PO.
- CRI: Loading dose of 0.2-0.4 mg/kg IV, followed by 0.1-0.2 mg/kg/hr.

Large Animal Dosage

Horses

- Pain: 0.2-0.4 mg/kg q3-4h IV. In some instances, lower doses of 0.02-0.1 mg/kg IV or 0.04-0.2 mg/kg IM have been used. Lower doses of 0.1 mg/kg IV have been used to minimize the decrease in intestinal motility.
- Sedation: 0.01-0.06 mg/kg IV.
- CRI: 13-24 mcg/kg/hr IV.

Ruminants

- 0.05-0.2 mg/kg IV.

Cattle

- In combination with xylazine: 0.01-0.02 mg/kg IV.

Regulatory Information

Drug controlled by DEA, Schedule IV.

Do not administer to animals intended for food.

RCI Classification: 2

Calcitriol

kal-sih-trye'ole

Trade and other names: Rocaltrol and Calcijex

Functional classification: Calcium supplement

Pharmacology and Mechanism of Action

Vitamin D analogue, also called 1,25-dihydroxycholecalciferol. Calcitriol is normally formed in the kidneys from 25-hydroxycholecalciferol. Action of calcitriol is to increase calcium absorption from the intestine and facilitate a parathyroid hormone (PTH) effect on bone. Low calcitriol levels in animals lead to decreased intestinal calcium absorption. Animals with chronic renal failure and hyperparathyroidism often have low calcitriol levels. Calcitriol can also inhibit synthesis and storage of PTH.

Indications and Clinical Uses

Calcitriol is used to treat calcium deficiency and diseases such as hypocalcemia associated with hyperparathyroidism. It is also used to increase calcium in cats that have had parathyroid glands removed. In this use, it is often administered with calcium supplements to the diet. It is used in dogs and cats to manage calcium and phosphorous balance with chronic kidney disease. Although used by veterinarians to reduce renal secondary PTH concentrations in animals with chronic renal disease, this benefit is more controversial and not supported by strong evidence. Calcitriol should not be used as a vitamin D supplement.

Precautionary Information

Adverse Reactions and Side Effects

Overdose can result in hypercalcemia.

Contraindications and Precautions

Do not use in patients that are at risk of hypercalcemia. Capsules made for humans may contain high overdoses for dogs and cats and should be reformulated.

Drug Interactions

Calcitriol may cause hypercalcemia if used with thiazide diuretics.

Instructions for Use

Doses should be adjusted in each patient according to response and monitoring calcium plasma concentration. Dose requirements may vary depending on the adjustment to calcium levels. For example, when used for treating dogs with chronic kidney disease, the dose was 2.5 ng/kg/day but ranged from 0.75 to 5 ng/kg/day based on adjustments from measuring calcium concentrations. When used in chronic renal failure, it is often used with intestinal phosphate binders (e.g., aluminum hydroxide) and dietary phosphorous restriction.

Patient Monitoring and Laboratory Tests

Monitor plasma ionized calcium concentration. Adjust doses as necessary to maintain normal calcium, phosphorous, and PTH concentrations.

Monitor serum PTH concentrations (assays are available in many diagnostic

laboratories). Monitor serum creatinine in animals when used to treat chronic kidney disease.

Formulations

Calcitriol is available as injection (Calcijex) in a 1- and 2-mcg/mL and in 0.25- and 0.5-mcg capsules and 1 mcg/mL oral solution (Rocaltrol).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Renal secondary hyperparathyroidism in chronic renal failure: 2.5 ng/kg, PO, once daily. Adjust dose with calcium and PTH measurements. If PTH concentrations remain elevated and calcium is not elevated, increase the dose to 3.5 ng/kg, once daily. The dose may be increased incrementally up to 5 ng/kg, once daily.

Cats

- Hypocalcemia (after removal of parathyroid glands): 0.25 mcg/cat q48h PO or 0.01-0.04 mcg/kg/day PO (10-40 ng/kg/day).
- Renal secondary hyperparathyroidism: 2.5 ng/kg, PO, once daily. Adjust dose with calcium and PTH measurements. If PTH concentrations remain elevated and calcium is not elevated, increase the dose to 3.5 ng/kg, once daily, and incrementally up to a dose of 5 ng/kg/day.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Calcium Carbonate

Trade and other names: Titalac, Calci-mix, Tums, and generic brands

Functional classification: Calcium supplement

Pharmacology and Mechanism of Action

Calcium supplement. Calcium is essential for the functional integrity of several body systems. Calcium carbonate is equivalent to 400 mg of calcium ion per gram. Calcium carbonate neutralizes stomach acid for treating and preventing stomach ulcers.

Indications and Clinical Uses

Calcium carbonate is used as an oral calcium supplement for hypocalcemia, sometimes used with vitamin D supplements or calcitriol. It is used as antacid to treat gastric hyperacidity and GI ulcers and as an intestinal phosphate binder for hyperphosphatemia associated with renal failure.

Precautionary Information

Adverse Reactions and Side Effects

Few side effects. High calcium concentrations are possible. With any calcium supplements, constipation and intestinal bloating can occur.

Contraindications and Precautions

Do not administer to animals predisposed to forming calcium-containing renal or cystic calculi. When calcium carbonate or calcium citrate are used as a phosphate binder to prevent hyperphosphatemia, caution is advised to avoid hypercalcemia in patients with renal failure.

Drug Interactions

Oral administration of calcium supplements may interfere with absorption of other drugs such as fluoroquinolones (e.g., enrofloxacin, orbifloxacin, marbofloxacin), bisphosphonates, zinc, iron, and tetracyclines. Use cautiously with thiazide diuretics because this could cause a high increase in calcium concentrations.

Instructions for Use

Calcium carbonate is equivalent to 400 mg of calcium ion per gram. Doses are primarily derived from extrapolation of human doses. When used as a calcium supplement, doses should be adjusted according to serum calcium concentrations. Some tablets also contain vitamin D. Doses are based on calcium carbonate, not the ion concentration (e.g., a 650-mg tablet contains 260 mg of calcium ion).

Patient Monitoring and Laboratory Tests

Monitor serum calcium levels, particularly if patients have renal failure.

Formulations

Calcium carbonate is available in tablets or oral suspension, most of which are OTC. One gram of calcium carbonate is equivalent to 400 mg of calcium ion. Calci-mix is available in 1.25 g capsules. OTC tablets are available in 500, 600 mg and 1, 1.25, and 1.5 g. Oral suspension (Titalac) is 1.25 g per 5 mL.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Do not mix with other compounds that may chelate with calcium.

Small Animal Dosage

Dogs and Cats

- Calcium supplementation: 70-185 mg/kg/day given with food PO.
- Phosphate binder: 60-100 mg/kg/day in divided doses usually given with food PO.

Large Animal Dosage

No dose has been reported for large animals. Usually other calcium salts are used for supplementation in cattle.

Regulatory Information

No withdrawal times are available. Because this is a normal dietary supplement with little risk from residues, no withdrawal time is suggested for animals intended for food.

Calcium Chloride

Trade and other names: Generic brands

Functional classification: Calcium supplement

C

Pharmacology and Mechanism of Action

Calcium supplement. Calcium is essential for the functional integrity of several body systems. Injection is 27.2 mg of calcium ion (1.36 mEq) per mL. Calcium chloride increases ionized calcium in blood greater than other calcium salts.

Indications and Clinical Uses

Calcium chloride is used in acute situations to supplement as electrolyte replacement or as a cardiotonic. It is administered to cows for hypocalcemia (milk fever).

Precautionary Information

Adverse Reactions and Side Effects

Overdose with calcium is possible. Do not administer intravenous solution SQ or IM because it may cause tissue necrosis.

Contraindications and Precautions

Do not administer by IV injection at a rapid rate. Rapid intravenous administration to cows can cause cardiac arrhythmias and even death.

Drug Interactions

Calcium chloride will precipitate with sodium bicarbonate. Do not mix with compounds known to chelate with calcium.

Instructions for Use

Injection is 27.2 mg of calcium ion (1.36 mEq) per mL. It is usually used in emergency situations. Intracardiac administrations have been performed, but avoid injections into the myocardium.

Patient Monitoring and Laboratory Tests

Monitor serum calcium concentration. Monitor heart rhythm during administration.

Formulations

Calcium chloride is available in a 10% (100 mg/mL) solution. This supplies 1.36 mEq calcium ion per mL. Preparations for cattle usually contain 8.5-11.5 g calcium per 500 mL. Many formulations also contain magnesium.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Do not mix with other compounds that may chelate with calcium.

Small Animal Dosage

Dogs and Cats

- 0.1-0.3 mL/kg IV (slowly).

Large Animal Dosage

Cows

- 2 g/100 kg body weight, IV at a rate of 1 g/min.

Horses

- 1-2 g per adult horse IV slowly.

Regulatory Information

No withdrawal times are available. Because this is a normal supplement with little risk from residues, no withdrawal time is suggested for animals intended for food.

Calcium Citrate

Trade and other names: Citracal (OTC)

Functional classification: Calcium supplement

Pharmacology and Mechanism of Action

Calcium supplement. Calcium is essential for the functional integrity of several body systems. It is administered orally to supply calcium to the diet.

Indications and Clinical Uses

Calcium citrate is used in the treatment of hypocalcemia, such as with hypoparathyroidism. It also is used as an intestinal phosphate binder for hyperphosphatemia associated with renal failure.

Precautionary Information

Adverse Reactions and Side Effects

Hypercalcemia is possible with oversupplementation. With any calcium supplements, constipation and intestinal bloating can occur.

Contraindications and Precautions

When calcium carbonate or calcium citrate are used as a phosphate binder to prevent hyperphosphatemia, caution is advised to avoid hypercalcemia in patients with renal failure.

Drug Interactions

Oral administration of calcium supplements may interfere with absorption of other drugs such as fluoroquinolones (e.g., enrofloxacin, orbifloxacin, marbofloxacin), bisphosphonates, zinc, iron, and tetracyclines.

Instructions for Use

Doses should be adjusted according to serum calcium concentration.

Patient Monitoring and Laboratory Tests

Monitor serum calcium levels, particularly if patients have renal failure.

Formulations

Calcium citrate is available in 950-mg tablets (contains 200 mg of calcium ion).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Do not mix with other compounds that may chelate with calcium.

Small Animal Dosage

Cats

- 10-30 mg/kg q8h (with meals) PO.

Dogs

- 20 mg/kg/day (with meals) PO.

Dogs and Cats

- Phosphate binder (to prevent hyperphosphatemia): 10-20 mg/kg per day in divided doses, with meals PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No withdrawal times are available. Because this is a normal dietary supplement with little risk from residues, no withdrawal time is suggested for animals intended for food.

Calcium Gluconate and Calcium Borogluconate

Trade and other names: Kalcinate, AmVet, Cal-Nate, and generic brands

Functional classification: Calcium supplement

Pharmacology and Mechanism of Action

Calcium supplement. Calcium is essential for the functional integrity of several body systems. It is administered orally to supply calcium to the diet, but injected for acute conditions in which a rapid increase in serum calcium is needed.

Indications and Clinical Uses

Calcium gluconate and calcium borogluconate are used in the treatment of hypocalcemia, such as with hypoparathyroidism. They are used in electrolyte deficiency. Calcium supplements are administered to cattle for treatment of hypocalcemia (milk fever).

Precautionary Information**Adverse Reactions and Side Effects**

Hypercalcemia is possible with oversupplementation. Calcium supplements may cause constipation. SQ or IM injections of calcium salts may cause tissue injury and necrosis at the site of injection.

Contraindications and Precautions

Avoid rapid intravenous administration. Avoid use in patients that are prone to calcium-containing renal or cystic calculi. Avoid administration of intravenous solution IM or SQ because it will cause tissue necrosis.

Drug Interactions

Do not mix with any bicarbonate (sodium bicarbonate) phosphates, sulfates, and tartrates because it may precipitate. Specific drugs that can precipitate with calcium gluconate include oxytetracycline, promethazine, sulfamethazine, tetracycline, cephalothin, and amphotericin B. Calcium supplements may interfere with the oral absorption of iron, tetracyclines, and fluoroquinolones.

Instructions for Use

The 500-mg tablets contain 45 mg of calcium ion. The 10% injection contains 97 mg (9.3 mg of calcium ion [0.47 mEq]) per mL.

Patient Monitoring and Laboratory Tests

Monitor serum calcium concentration. Monitor heart rate during intravenous administration.

Formulations

Calcium gluconate is available as 10% (100 mg/mL) injection. Calcium gluconate 10% contains 9.3 mg of calcium ion per mL, or 0.465 mEq per mL. Calcium gluconate is available in tablets in sizes of 325, 500, 650, 975 mg, and 1 g. Each gram contains 90 mg of calcium ion. Chewable tablets intended for human use are available in 650-mg and 1-g tablets.

Calcium borogluconate is available as 230 mg/mL (AmVet Calcium Gluconate 23% and Cal Nate).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Solutions should be clear. If crystals are present, warm vial up to 30-40°C (86-104°F) to dissolve crystals. Stability of compounded formulations has not been evaluated. Do not mix with other compounds that may chelate with calcium.

Small Animal Dosage

Dogs and Cats

- 75-500 mg IV, slowly.

Large Animal Dosage (use Calcium Borogluconate)

Cattle and Horses

- 5-12 g, diluted in 500 mL and infused IV, slowly.

Pigs and Sheep

- 5-1.5 g IV, slowly.

Dairy Cows

- 2 g/100 kg body weight, slowly, at a rate of 1 g/min.

Horses

- 50-70 mg/kg, diluted in 5% dextrose and infused slowly, IV.

Regulatory Information

No withdrawal times are available. Because this is a normal dietary supplement with little risk from residues, no withdrawal time is suggested for animals intended for food.

Calcium Lactate

Trade and other names: Generic brands

Functional classification: Calcium supplement

Pharmacology and Mechanism of Action

Calcium supplement. Calcium is essential for the functional integrity of several body systems. This oral supplement is used to provide animals with dietary calcium to prevent or treat a deficiency.

Indications and Clinical Uses

Calcium lactate is used in treatment of hypocalcemia, such as with hypoparathyroidism, and in electrolyte deficiency.

Precautionary Information

Adverse Reactions and Side Effects

Hypercalcemia possible with over supplementation.

Contraindications and Precautions

Avoid use in patients that are prone to calcium-containing renal or cystic calculi.

Drug Interactions

Calcium supplements may interfere with the oral absorption of iron, tetracyclines, and fluoroquinolones.

Instructions for Use

Calcium lactate contains 130 mg of calcium ion per gram.

Patient Monitoring and Laboratory Tests

Monitor serum calcium concentrations.

Formulations

Calcium lactate is available in 325-mg (42.25 mg of calcium ion) and 650-mg (84.5 mg of calcium ion) OTC tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Do not mix with other compounds that may chelate with calcium.

Small Animal Dosage

Dogs

- 0.5 g/day (in divided doses) PO.

Cats

- 0.2-0.5 g/day (in divided doses) PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No withdrawal times are available. Because this is a normal dietary supplement with little risk from residues, no withdrawal time is suggested for animals intended for food.

Captopril

kap'toe-pril

Trade and other names: Capoten

Functional classification: Vasodilator, angiotensin-converting enzyme (ACE) inhibitor

Pharmacology and Mechanism of Action

ACE inhibitor. Captopril inhibits conversion of angiotensin I to angiotensin II, leading to vasodilation. Angiotensin II is a potent vasoconstrictor and will stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. ACE inhibitors limit the ability of aldosterone to cause sodium and water retention that contribute to congestion. Captopril, like other ACE inhibitors, will cause

100 Captopril

vasodilation, but ACE inhibitors also contribute to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins.

Indications and Clinical Uses

Captopril, like other ACE inhibitors, is used to treat hypertension and CHF. It has been used primarily in dogs, but its use has declined. Captopril is the first ACE inhibitor available for clinical use but has been replaced by other ACE inhibitors such as enalapril, benazepril and lisinopril. Unlike benazepril and enalapril, it has not been studied for clinical use in dogs and cats.

Precautionary Information

Adverse Reactions and Side Effects

Hypotension is possible with excessive doses. Captopril may cause azotemia in some patients, especially when administered with potent diuretics (e.g., furosemide). GI side effects, predominantly anorexia, are common in dogs.

Contraindications and Precautions

Discontinue ACE inhibitors in pregnant animals; they cross the placenta and have caused fetal malformations and death of the fetus.

Drug Interactions

Use cautiously with diuretics and potassium supplements. Nonsteroidal anti-inflammatory drugs (NSAIDs) may diminish antihypertensive effect.

Instructions for Use

Use of captopril has been replaced by enalapril and benazepril in small animal practices, and most clinical experts recommend these other drugs instead of captopril.

Patient Monitoring and Laboratory Tests

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

Formulations

Captopril is available in 12.5-, 25-, 50-, and 100-mg tablets.

Stability and Storage

Store in a tightly sealed container at room temperature. More stable at acidic pH. Oral compounded solutions are stable for 30 days refrigerated. However, tap water should not be used; purified water is necessary to ensure stability.

Small Animal Dosage

Dogs

• 0.5-2 mg/kg q8-12h PO.

Cats

• 3.12-6.25 mg/cat q8h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 3

Carbenicillin

kar-ben-ih-sill'in

Trade and other names: Geopen and Pyopen Carbenicillin indanyl sodium (Geocillin)

Functional classification: Antibacterial

C

Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Carbenicillin has an action similar to ampicillin, which inhibits bacterial cell wall synthesis. Carbenicillin has a broad spectrum of activity that includes both gram-positive and gram-negative bacteria. However, resistance is possible, especially among beta-lactamase-positive strains. The difference between carbenicillin and ampicillin is that it is active against *Pseudomonas aeruginosa* and other gram-negative bacteria that are resistant to ampicillin and amoxicillin. Half-life is short and clearance is rapid in animals; therefore it requires frequent administration.

Indications and Clinical Uses

Carbenicillin is used to treat gram-negative infections in animals, including infections caused by *Pseudomonas aeruginosa*. The use of carbenicillin is uncommon in veterinary medicine and has been replaced by other drugs such as ticarcillin and cephalosporins. Indanyl sodium carbenicillin (Geocillin) is poorly absorbed orally and should not be used for systemic infections. However, this form may produce high enough urine concentrations for treating some infections of lower urinary tract.

Precautionary Information

Adverse Reactions and Side Effects

Carbenicillin, like other penicillin drugs, may cause allergy. Carbenicillin may cause bleeding problems in some animals by interfering with platelets.

Contraindications and Precautions

Use cautiously in patients sensitive to penicillins (e.g., allergy).

Drug Interactions

No drug interactions are reported in animals. Do not mix in vial with other drugs because inactivation may result.

Instructions for Use

Carbenicillin has a short half-life and should be administered frequently for optimum bactericidal effect. Carbenicillin injection often is administered with an aminoglycoside when treating *Pseudomonas* infections. Do not mix with aminoglycosides prior to administration or inactivation will result. Carbenicillin indanyl sodium is the oral formulation of carbenicillin but attains concentrations that are only sufficient for treating UTIs. Do not use for systemic infections.

Patient Monitoring and Laboratory Tests

Culture and sensitivity testing recommended to guide therapy. CLSI break points are ≤ 128 mcg/mL when testing for *Pseudomonas*-susceptible organisms and ≤ 16 mcg/mL for other gram-negative organisms.

Formulations

Carbenicillin has been unavailable because other drugs are used as a replacement. However, older formulations include 1-, 2-, 5-, 10-, and 30-g vials for injection and 500-mg tablets.

102 Carbimazole

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stable at pH of 6.5, but rate of degradation is greater at higher or lower pH. Use quickly after reconstitution of vials for injection.

Small Animal Dosage

Dogs and Cats

- Carbenicillin: 40-50 mg/kg and up to 100 mg/kg q6-8h IV, IM, or SQ.
- Carbenicillin indanyl sodium: 10 mg/kg q8h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Carbimazole

kar-bih'mah-zole

Trade and other names: Neomercazole, Vidalta

Functional classification: Antithyroid drug

Pharmacology and Mechanism of Action

Antithyroid drug similar to methimazole. It is a pro-drug converted to methimazole after administration. Like methimazole, the action is to serve as substrate for thyroid peroxidase (TPO) and inhibits it and decreases incorporation of iodide into tyrosine molecules. It also inhibits coupling of mono-iodinated and di-iodinated residues to form T4 and T3. Carbimazole has been preferred in some patients because, compared to methimazole, it may have fewer side effects, such as less frequent GI problems. Oral absorption (based on methimazole concentrations) is 88% in cats.

Indications and Clinical Uses

Carbimazole has been used for treating hyperthyroidism, primarily in cats. Carbimazole has been more readily available in Europe, where there is more clinical experience, than in the US. Experience in the US is limited because of lack of availability. Sustained-release formulation in Europe (Vidalta) administered to people as 15 mg once per day, followed by 10-25 mg once daily in people.

Precautionary Information

Adverse Reactions and Side Effects

In cats, lupus-like reactions are possible, such as vasculitis and bone marrow changes. In people, it has caused agranulocytosis and leukopenia. Other systemic effects reported for methimazole are expected to be similar for carbimazole (for example, bone marrow effects).

Contraindications and Precautions

Do not use in cats with bone marrow suppression or thrombocytopenia.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Carbimazole is used in Europe; clinical experience in US is limited. Otherwise, the clinical indications and use are similar as for methimazole.

Patient Monitoring and Laboratory Tests

Monitor thyroid concentrations to adjust dose. Monitor CBC periodically for evidence of bone marrow suppression.

Formulations

This drug has not been approved in the United States. This drug has been obtained in Europe.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Cats

- 5 mg/cat q8h (induction), followed by 5 mg/cat q12h PO. In Europe, Vidalta (a newer sustained release brand available) induction usually 15 mg once daily and maintenance dose ranges between 10 mg and 25 mg *once daily*.

Dogs

No dose has been established for dogs.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Carboplatin

kar-boe-plat' in

Trade and other names: Paraplatin

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Carboplatin is a second-generation platinum compound and is related to cisplatin. Action is similar to cisplatin. Its action is a bifunctional alkylating agent, which interrupts replication of DNA in tumor cells. It induces a non-cell cycle–dependent tumor cell lysis. Major route of elimination is via the kidneys. It has replaced cisplatin in some anticancer protocols because it may not be as toxic.

Indications and Clinical Uses

Carboplatin has been used for squamous cell carcinoma and other carcinomas, melanoma, osteosarcomas, and other sarcomas. When used in dogs, myelosuppression has been the most dose-limiting factor. Compared to cisplatin, carboplatin is better tolerated in cats and is preferred. However, bone marrow suppression is the dose-limiting toxicity in cats.

Precautionary Information

Adverse Reactions and Side Effects

Compared to cisplatin, carboplatin is less emetogenic and less nephrotoxic. In dogs, the other most common adverse effects relate to GI system toxicity (gastroenteritis, vomiting, anorexia, and diarrhea). The dose limiting effect is myelosuppression, anemia, leukopenia, or thrombocytopenia. In dogs, nadir of myelosuppression occurs at 14 days, but recovery occurs by 21-28 days. In cats, the nadir is 21 days and recovery occurs by 28 days. Vomiting is not as much of a problem as for cisplatin, but GI toxicosis is still a problem, especially in smaller dogs. Because it is excreted by the kidneys, animals with decreased renal function may have a higher rate of GI toxicosis.

Contraindications and Precautions

In one study, small dogs were more prone than larger dogs to adverse effects.

Drug Interactions

Do not use with other nephrotoxic drugs.

Instructions for Use

Available for reconstitution for injection. It is stable for 1 month when reconstituted with 5% dextrose. It may be frozen at -4°C to prolong the stability of a reconstituted vial. Do not use with administration sets containing aluminum because of incompatibility. It is usually administered in specific anticancer protocols; consult oncology protocols for regimen. In dogs, it has been dosed on a milligram per square meter dose, which has produced a higher incidence of adverse effects in smaller dogs compared to larger dogs; however, smaller dogs also were more likely to respond. Carboplatin is excreted by the kidneys; therefore, the dose should be decreased in proportion to reduced GFR and creatinine clearance.

Patient Monitoring and Laboratory Tests

Monitoring of CBC and platelets is recommended during treatment.

Formulations

Carboplatin is available in 50- and 150-mg vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stable for 1 month if reconstituted with 5% dextrose solution. It is stable if frozen at -4°C .

Small Animal Dosage

Dogs

- 300 mg/m², IV, every 3-4 weeks. Is also administered at 300 mg/m² for dogs less than 15 kg and 350 mg/m² for dogs greater than 15 kg.

Cats

- 200-227 mg/m², IV, every 4 weeks for four treatments; for a 4-kg cat, the dose is equivalent to 14.7 mg/kg.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Carprofen

car-proe'fen

Trade and other names: Rimadyl, Vetprofen, Zinecarp (Europe), and generic brands

Functional classification: NSAID

Pharmacology and Mechanism of Action

Carprofen is a nonsteroidal anti-inflammatory drug (NSAID). Like other drugs in this class, carprofen has analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by an NSAID is the cyclooxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. (There may be crossover of COX-1 and COX-2 effects in some situations.) Carprofen is relatively COX-1 sparing compared to older NSAIDs, but it is not known if the specificity for COX-1 or COX-2 determines efficacy or safety. In horses, carprofen is not as COX-2 selective as it is in dogs. As an analgesic agent the mechanism of action may involve other mechanisms other than inhibition of prostaglandin synthesis.

Indications and Clinical Uses

Carprofen is used primarily for treatment of musculoskeletal pain and acute pain related to surgery or trauma. It is used primarily for treatment of dogs. Long-term safe use in cats has not been established. However, it is registered in Europe for one-time administration in cats at 4 mg/kg injection. Although use in large animals is uncommon, in cattle, carprofen has been shown to reduce inflammation in cows associated with *Escherichia coli* mastitis at a dose of 0.7 mg/kg IV. Although carprofen has been used in horses, it does not show the same COX-2 selectivity of inhibition as in dogs. In cattle, carprofen is registered in Europe for treatment of fever associated with mastitis and used to reduce inflammation associated with bovine respiratory disease.

Precautionary Information

Adverse Reactions and Side Effects

Safety of carprofen in dogs was determined by the sponsor during preclinical studies. The most common adverse effect in dogs has been in the GI tract (vomiting, anorexia, and diarrhea). GI ulcers, perforation, and bleeding are uncommon in dogs. In rare cases, carprofen has caused idiosyncratic acute hepatic toxicity in dogs. Signs of toxicity usually appear 2-3 weeks after exposure. There were no adverse effects on kidneys when carprofen was evaluated in anesthetized dogs. Carprofen may lower total thyroid (T4) concentrations in

dogs but not free T4. Carprofen has produced toxicity in cats if administered at the same dose rates as for dogs.

Contraindications and Precautions

Do not use in cats at doses intended for dogs. Do not administer to animals prone to GI ulcers. Do not administer with ulcerogenic drugs such as corticosteroids. If a patient has had previous adverse effects from NSAIDs, carprofen should be used cautiously.

Drug Interactions

Use NSAIDs cautiously with other drugs known to cause GI injury (e.g., corticosteroids). The efficacy of angiotensin-converting enzyme (ACE) inhibitors and diuretics (e.g., furosemide) may be diminished when administered concurrently with NSAIDs.

Instructions for Use

Doses are based on clinical investigations in dogs with arthritis and for treatment of pain associated with surgery. Dogs may receive carprofen either once daily or twice daily with similar effectiveness. The only approved dose for cats is 4 mg/kg as a one-time injection for surgical pain. However, for long-term use, pharmacokinetic extrapolations suggest a long-term dose of 0.5 mg/kg q24h PO. Long-term safety at this dose has not been established.

Patient Monitoring and Laboratory Tests

After administration has begun, one should monitor hepatic enzymes for evidence of drug-induced hepatic toxicity approximately 7-14 days after treatment has started. If liver enzymes are elevated, discontinue the medication and contact the drug manufacturer.

Formulations

Carprofen is available in 25-, 75-, and 100-mg caplets; 25-, 75- and 100-mg chewable tablets; and injectable solution: 50 mg/mL.

(Zinecarp injection has also been available in Europe.)

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Carprofen has been compounded by mixing tablets with methylcellulose gel (1%), simple syrup, and a suspending and flavoring vehicle to make a 1.25-, 2.5- and 5-mg/mL suspension. This formulation was stable if stored in refrigerator or room temperature for 28 days.

Small Animal Dosage

Dogs

- 2.2 mg/kg, q12h PO or 4.4 mg/kg q24h PO.
- 2.2 mg/kg q12h SQ or 4.4 mg/kg q24h SQ.

Cats

- 4 mg/kg given once by injection or 0.5 mg/kg q24h PO for long-term use (safety for long-term use has not been established).

Large Animal Dosage

Carprofen is not approved in large animals; safety and efficacy studies have not been published

Horses

- 0.7 mg/kg q24h IV (in Europe oral granules: 0.7 mg/kg PO).

Cattle

- 1.4 mg/kg SQ, IV.

Regulatory Information

Withdrawal times have not been established for carvedilol in the US. It is suggested (based on European labeling) that the withdrawal time for meat is 21 days but zero days for milk. Caution is advised when considering carvedilol for cattle because it has a longer half-life in cows compared to other animals (30-40 hours).

RCI Classification: 4

Carvedilol

kar-ved' ih-lole

Trade and other names: Coreg

Functional classification: Antiarrhythmic

Pharmacology and Mechanism of Action

Antiarrhythmic. Nonselective beta-receptor blocker. Carvedilol is a third-generation adrenergic blocker. Carvedilol blocks both beta₁-receptors and beta₂-receptors in heart and other tissues. Carvedilol is unique because it also has alpha-receptor-blocking properties that will produce vasodilation. It also is reported to have antioxidant properties.

In dogs the half-life is short (1.2 hrs). Oral absorption is low and variable because of high systemic clearance and first-pass effects. Average oral absorption in one study was only 14% and highly variable, but in another study it was only 1.6% (range 0.4%-54%), making the oral use of carvedilol in dogs unpredictable. In people, it has been also shown to prolong survival in human patients with heart failure, but this effect has not been measured in animals.

Indications and Clinical Uses

Carvedilol has been used to treat arrhythmias in animals. It is also used to treat systemic hypertension and to block beta-cardiac receptors in animals with rapid heart rates. Efficacy has been based on anecdotal accounts, extrapolation from humans, and limited studies in healthy dogs. In healthy dogs, 0.2 mg/kg PO decreased heart rate and 0.4 mg/kg PO decreased heart rate and lowered blood pressure. At 0.4 mg/kg, the effects in healthy dogs persisted for 36 hours. In other studies, doses of 0.3 mg/kg were not effective. In clinical patients, the optimum dose is not known and long-term benefits have not been established. Because oral absorption is inconsistent in dogs (discussed in pharmacology section), the response may be variable. Elimination is rapid after oral administration to dogs, but clinical pharmacodynamic effects may persist for up to 12 hours, possibly from the metabolites.

Precautionary Information**Adverse Reactions and Side Effects**

Bradycardia can occur resulting from beta-receptor blockade. Carvedilol increases risk of myocardial depression and decreased cardiac output. Adverse effects from nonselective beta-receptor blockade are possible in other tissues.

Contraindications and Precautions

Use carefully in patients with limited cardiac reserve. Do not administer to dehydrated or hypotensive animals. Use carefully in patients with respiratory disease because the beta₂-blocking properties can worsen bronchoconstriction.

Drug Interactions

Use with other beta blockers will increase its effect. Do not administer with other drugs that may cause hypotension.

Instructions for Use

Doses in dogs established through clinical experience and limited trials. In a dose titration study in dogs, the effective dose was 0.2-0.4 mg/kg q24h, PO.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and rhythm carefully during treatment. During the initial phase of dosing, monitor patients for worsening of heart failure.

Formulations

Carvedilol is available in 3.125-, 6.25-, 12.5-, and 25-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Carvedilol is not soluble in water. Carvedilol compounded suspension has been prepared by adding 25-mg tablets to water to make a paste, then mixed with simple syrup to make a 2 mg/mL or 10 mg/mL suspension for oral administration. This suspension has been stable for 90 days at room temperature, protected from light.

Small Animal Dosage

Dogs

- Initial recommendations published were 0.2 mg/kg q24h PO, followed by gradually increasing the frequency to q12h, and followed by increases up to a maximum of 0.4 mg/kg q12h. More recent evidence suggests a dose of 1.5 mg/kg q12h PO is more effective, but even these doses have not been effective in some dogs.

Cats

Dose not established.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Cascara Sagrada

kass-kar'ah sah-grah'dah

Trade and other names: Nature's Remedy and generic brands

Functional classification: Laxative

Pharmacology and Mechanism of Action

Stimulant cathartic. Action is believed to be by local stimulation of bowel motility.

Indications and Clinical Uses

Laxative used to treat constipation or evacuate bowel for procedures.

Precautionary Information

Adverse Reactions and Side Effects

Overuse can cause electrolyte losses.

Contraindications and Precautions

Do not use in cases where there may be intestinal obstruction.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Available in various dietary supplements.

Patient Monitoring and Laboratory Tests

Monitor electrolytes with chronic therapy.

Formulations

Cascara sagrada is available in a variety of strengths, including tablets, capsules, and liquids.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 1-5 mg/kg/day PO.

Cats

- 1-2 mg/cat/day PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Castor Oil

kas'tar oil

Trade and other names: Generic brands

Functional classification: Laxative

Pharmacology and Mechanism of Action

Stimulant cathartic. Action is believed to be by local stimulation of bowel motility.

Indications and Clinical Uses

Castor oil is used as a laxative to treat constipation or to evacuate the bowel for procedures.

Precautionary Information

Adverse Reactions and Side Effects

Overuse can cause electrolyte losses. Castor oil has been known to stimulate premature labor in pregnancy.

Contraindications and Precautions

Do not use in pregnant animals. It may induce labor. Castor oil has been known to induce histamine release. Monitor patients for signs of histamine reaction.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Use in animals is strictly empirical. It is available as an OTC product. Pet owners should be discouraged from repeated administration to pets.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Castor oil is available in an oral liquid (100%).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 8-30 mL/day PO.

Cats

- 4-10 mL/day PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available.

Cefaclor

sef 'ah-klor

Trade and other names: Generic

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefaclor, like other second-generation cephalosporins, is more

active against gram-negative bacteria and has been used to treat infections caused by bacteria resistant to first-generation drugs.

Indications and Clinical Uses

Cefaclor is not used commonly in veterinary medicine because other cephalosporins are in more widespread use. However, it may be indicated for treatment of infections caused by bacteria that are resistant to first-generation cephalosporins. Although it has been used as oral therapy, the extent of oral absorption and efficacy information is not available for dogs or cats. Dosing regimens and indications are primarily derived from extrapolation and anecdotal information.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. Oral administration can potentially produce vomiting and diarrhea in small animals.

Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (less than 10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone. Oral absorption has not been measured in large animals, and cefaclor is not recommended unless information derived from pharmacokinetic or efficacy studies is available.

Drug Interactions

No drug interactions are reported in animals. However, do not mix with other drugs in a compounded formulation because inactivation may result.

Instructions for Use

It is used primarily when resistance has been demonstrated to first-generation cephalosporins and other alternatives have been considered.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible bacteria is ≤ 8 mcg/mL.

Formulations

Cefaclor is available in 250- and 500-mg capsules and 25-mg/mL oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 15-20 mg/kg q8h PO.

Cats

- 15-20 mg/kg q8h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of relatively short plasma half-life, residues should not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cefadroxil

sef-ah-drox'il

Trade and other names: Cefa-Tabs and Cefa-Drops (veterinary preparations) and Duricef and generic (human preparation)

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefadroxil is a first-generation cephalosporin, and activity and clinical use are similar to cephalexin. Like other first-generation cephalosporins, it is active against *Streptococcus* and *Staphylococcus* species and some gram-negative bacilli, such as *Pasteurella*, *Escherichia coli*, and *Klebsiella pneumoniae*. However, resistance is common among gram-negative bacteria. It is not active against *Pseudomonas aeruginosa*. Methicillin-resistant *Staphylococcus* (MRS) that are resistant to oxacillin will be resistant to first-generation cephalosporins.

Indications and Clinical Uses

Like other first-generation cephalosporins, it is indicated for treating common infections in animals, including UTIs, skin and soft tissue infections, pyoderma and other dermal infections, and pneumonia. Efficacy against infections caused by anaerobic bacteria is unpredictable. Adequate oral absorption has been shown for foals but not for adult horses.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. Cefadroxil has been known to cause vomiting after oral administration in dogs. Some estimates show that this can occur in up to 10% of treated dogs. If administered orally to adult horses, diarrhea is possible.

Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (less than 10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone.

Drug Interactions

No drug interactions are reported in animals. However, do not mix with other drugs in a compounded formulation because inactivation may result.

Instructions for Use

Spectrum of cefadroxil is similar to other first-generation cephalosporins. The FDA-approved label is appropriate for dosing ranges. For susceptibility test, use cephalothin as test drug.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 2 mcg/mL for all organisms. Cephalothin is used as a marker to test for sensitivity to cephalixin, cefadroxil, and cephradine.

Formulations

Cefadroxil is available in 50-mg/mL oral suspension and 50-, 100-, 200-, and 1,000-mg tablets for veterinary use. However, availability of veterinary-labeled tablets has been inconsistent. It is also available in 500-mg capsules and 25-, 50-, and 100-mg/mL suspension for human use.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Avoid moisture to prevent hydrolysis.

Suspension is stable for 14 days refrigerated and 10 days at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage**Dogs**

- 22 mg/kg q12h PO, up to 30 mg/kg q12h PO.

Cats

- 22 mg/kg q24h PO.

Large Animal Dosage**Foals**

- 30 mg/kg q12h PO. Note: Oral absorption is adequate only in foals and not in adults or ruminants.

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of relatively short plasma half-life, residues should not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cefazolin Sodium

sef-ah'zoe-lin so'dee-um

Trade and other names: Ancef, Kefzol, and generic brands

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibits synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefazolin is a first-generation cephalosporin. Like other first-generation cephalosporins, it is active against *Streptococcus* and *Staphylococcus* species and some gram-negative bacilli, such as *Pasteurella*, *Escherichia coli*, and *Klebsiella pneumoniae*. The difference between cefazolin and other first-generation cephalosporins is that it is slightly more active against gram-negative *Enterobacteriaceae* and its spectrum resembles some second-generation drugs. Nevertheless, resistance is common among gram-negative bacteria. It is not active against *Pseudomonas aeruginosa*. Methicillin-resistant *Staphylococcus aureus* and other staphylococci resistant to oxacillin will be resistant to first-generation cephalosporins. In dogs the half-life, clearance, and volume of distribution (V) are 1.04 hours, 2.9 mL/kg/min, and 0.27 L/kg, respectively. These values in horses are 0.62 hours, 5.07 mL/kg/min, and 0.27 L/kg, respectively.

Indications and Clinical Uses

Cefazolin, because it is injectable, is the most common drug to be administered prophylactically prior to surgery. It is one of the most frequently injected cephalosporin antibiotics used in small animals. Like other first-generation cephalosporins, it is indicated for treating common infections in animals, including UTIs, soft tissue infections, pyoderma and other dermal infections, and pneumonia. Efficacy against infections caused by anaerobic bacteria is unpredictable.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins; however, bleeding problems have not been observed from cefazolin. Some cephalosporins have caused seizures, but this is a rare problem. When administered during surgery it did not adversely affect cardiovascular function in dogs.

Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (less than 10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone.

Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

Instructions for Use

Cefazolin is a commonly used first-generation cephalosporin as injectable drug for prophylaxis for surgery and for acute therapy for serious infections. Use cephalothin to test susceptibility, although cefazolin is slightly more active against some gram-negative bacilli.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 2 mcg/mL for coagulase-positive staphylococci, *Pasteurella multocida*, streptococci beta-hemolytic group, and *Escherichia coli*.

Formulations

Cefazolin is available in 50 and 100 mg/50 mL for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. If slight yellow discoloration occurs, the solution is still stable. After reconstitution, it is stable for 24 hours at room temperature and 14 days refrigerated. It remains stable if frozen for 3 months.

Small Animal Dosage

Dogs and Cats

- 20-35 mg/kg q8h IV or IM.
- Constant rate infusion (CRI): 1.3 mg/kg loading dose, followed by 1.2 mg/kg/hr.
- Perisurgical use: 22 mg/kg IV every 2 hours during surgery.

Large Animal Dosage

Horses

- 25 mg/kg q6-8h IM or IV.

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of a relatively short plasma half-life, residues should not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cefdinir

sef 'dih-neer

Trade and other names: Omnicef

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibits synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. It is an oral third-generation cephalosporin and is active against staphylococci and many gram-negative bacilli.

Indications and Clinical Uses

Cefdinir is an oral third-generation cephalosporin used in people. Although it has been used as oral therapy, the extent of oral absorption and efficacy information is not available for dogs or cats. Dosing regimens and indications are primarily derived from extrapolation and anecdotal information. It has potential efficacy for infections

of the skin, soft tissues, and urinary tract; however, in most instances other cephalosporins such as cefpodoxime proxetil may be substituted instead.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. Oral cephalosporins can produce vomiting and diarrhea in small animals.

Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (less than 10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone. Oral absorption has not been measured in large animals, and cefdinir is not recommended unless information derived from pharmacokinetic or efficacy studies is available.

Drug Interactions

No drug interactions are reported in animals. However, do not mix with other drugs in a compounded formulation because inactivation may result.

Instructions for Use

Use in veterinary medicine has not been reported. Use and doses are extrapolated from human preparations.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 2 mcg/mL for all organisms.

Formulations

Cefdinir is available in 300-mg capsules and 25-mg/mL oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

Dose not established. Human dose is 7 mg/kg q12h PO, and similar doses of 10 mg/kg q12h PO have been used in animals.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of a relatively short plasma half-life, residues should not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cefepime

sef 'ah-peem

Trade and other names: Maxipime

Functional classification: Antibacterial

C

Pharmacology and Mechanism of Action

Antibacterial drug of the cephalosporin class. Action against bacterial cell walls is similar to other cephalosporins. Cefepime is one of the fourth-generation cephalosporins. It has an enhanced, extended spectrum that is beyond that of the older cephalosporins. Its activity includes gram-positive cocci and gram-negative bacilli. It has been active against organisms resistant to other beta-lactams such as *Escherichia coli* and *Klebsiella*. It is active against most *Pseudomonas aeruginosa*. It is not active against methicillin-resistant staphylococci, *Bacteroides fragilis*, or penicillin-resistant enterococci.

Indications and Clinical Uses

Cefepime is a fourth-generation cephalosporin. Although it has a broader spectrum than other cephalosporins, the use has been limited in veterinary medicine. Experimental studies have been conducted in foals, adult horses, and dogs to establish doses, but reports of efficacy are not available.

Precautionary Information

Adverse Reactions and Side Effects

Cefepime is generally safe. However, clinicians should consider the same possible side effects as for other cephalosporins, which include the possibility of bleeding disorders, allergy, vomiting, and diarrhea.

Contraindications and Precautions

Do not administer to patients with sensitivity or allergy to cephalosporins. Reduce dose to less frequent intervals (e.g., every 12 hours or every 24 hours) in patients with renal failure.

Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

Instructions for Use

Reconstitute with sterile water, sodium chloride, and 5% dextrose. It may be reconstituted with 1% lidocaine if pain from injection is a problem. Reconstituted solutions are stable for 24 hours at room temperature and 7 days in the refrigerator. Do not mix with other injectable antibiotics. Injection vials also contain L-arginine.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 8 mcg/mL for all organisms.

Formulations

Cefepime is available in 500-mg, 1-g, and 2-g vials for injection

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Observe manufacturer's recommendations for stability after vial is reconstituted.

Small Animal Dosage

Dogs

- 40 mg/kg q6h IM or IV.
- Constant rate infusion (CRI): 1.4 mg/kg loading dose, followed by 1.1 mg/kg/hr.

Large Animal Dosage

Foals

- 11 mg/kg q8h IV.

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of relatively short plasma half-life, residues should not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cefixime

sef-iks 'eem

Trade and other names: Suprax

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefixime is an oral third-generation cephalosporin but is not expected to have the same degree of activity against gram-negative bacilli as injectable third-generation cephalosporins such as cefotaxime. Against *Staphylococcus*, cefixime is less active than the oral drug cefpodoxime.

Indications and Clinical Uses

Cefixime is one of the few oral third-generation cephalosporins. It has been administered orally in dogs and cats to treat infections of the skin, soft tissues, and urinary tract. It is not as active as cefpodoxime against *Staphylococcus*, and because of availability of cefpodoxime for animals, it is substituted instead for most indications.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. Vomiting and diarrhea are possible from oral cephalosporins.

Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between

penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone. Oral absorption has not been measured in large animals, and cefixime is not recommended unless information derived from pharmacokinetic or efficacy studies is available.

Drug Interactions

No drug interactions are reported in animals. However, do not mix with other drugs in a compounded formulation because inactivation may result.

Instructions for Use

Although not approved for veterinary use, pharmacokinetic studies in dogs have provided recommended doses. Note that break point for sensitivity is lower than for other cephalosporins, indicating that organisms tested as susceptible to other cephalosporins may not be susceptible to cefixime.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 1 mcg/mL for all organisms.

Formulations

Cefixime is available in 20 or 40-mg/mL oral suspension and 400-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 10 mg/kg q12h PO.
- Urinary tract infection: 5 mg/kg q12-24h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of relatively short plasma half-life, residues should not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USEFARAD (1-888-873-2723).

Cefotaxime Sodium

sef-oh-taks'eem so'dee-um

Trade and other names: Claforan

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibits synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefotaxime is a third-generation cephalosporin. Like other third-generation cephalosporins, it has enhanced activity against gram-negative bacilli, especially *Enterobacteriaceae*, which may be resistant to first- and second-generation cephalosporins, ampicillin derivatives, and other drugs. It is active against *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacteriaceae*, Pasteurella species, and Salmonella species, among others. It is generally not active against *Pseudomonas aeruginosa*. It is active against streptococci, but *Staphylococcus* species are less susceptible. All methicillin-resistant strains of staphylococci will be resistant. Activity against anaerobic bacteria is unpredictable.

Indications and Clinical Uses

Cefotaxime is used when resistance is encountered to other antibiotics or when infection is in the CNS. Because it is injectable, is expensive, and must be administered frequently, it is not used for routine infections in veterinary medicine when other drugs will be active. Although cefotaxime is not FDA approved for use in animals, it is one of the most often used injectable third-generation cephalosporins used in small animals. The use in large animals is uncommon.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins.

Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (less than 10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone.

Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

Instructions for Use

Third-generation cephalosporin is used when resistance to first- and second-generation cephalosporins is encountered.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 2 mcg/mL for gram-positive and gram-negative bacteria.

Formulations

Cefotaxime is available in 500-mg and 1-, 2-, and 10-g vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Maximum stability is at pH of 5-7. Do not mix with alkaline solutions. Yellow or amber color does not indicate instability. After reconstitution, cefotaxime is stable for 12 hours at room temperature; it is stable 5 days when stored in plastic syringes or a vial if kept in refrigerator. It is stable for 13 weeks if frozen. IV solutions in 1000 mL are stable for 24 hours at room temperature or 5 days in refrigerator. Do not refreeze.

Small Animal Dosage

Dogs

- 50 mg/kg q12h IV, IM, or SQ.
- Constant rate infusion (CRI):
3.2 mg/kg loading dose, followed by
5 mg/kg/hr.

Cats

- 20-80 mg/kg q6h IV or IM.

Large Animal Dosage

Foals

- 40 mg/kg q6h IV.

Horses

- 25 mg/kg q6h, IV.

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of relatively short plasma half-life, residues should not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cefotetan Disodium

sef 'oh-tee-tan dye-soe' dee-um

Trade and other names: Generic

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefotetan has been listed with second-generation cephalosporins but is more properly considered with the cephamycin group of cephalosporins, which have greater stability against the beta-lactamases of anaerobic bacteria such as those of the *Bacteroides* group. It is slightly more active (lower minimum inhibitory concentration [MIC] values) compared to cefoxitin against many bacteria.

Indications and Clinical Uses

Cefotetan, a second-generation cephalosporin of the cephamycin group, has greater activity against anaerobic bacteria and gram-negative bacilli than other cephalosporins and also has activity against aerobic and facultatively anaerobic gram-negative bacilli. Therefore, it has been used to treat infections in dogs and cats in which enteric gram-negative bacilli or anaerobes are suspected, including abdominal infections, soft tissue wounds, and prior to surgery.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins.

Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone.

Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

Instructions for Use

Second-generation cephalosporin similar to cefoxitin but may have longer half-life in dogs.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 8 mcg/mL for gram-negative and gram-positive organisms.

Formulations

Cefotetan is available in 1-, 2-, and 10-g vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Observe manufacturer's recommendations for stability after vial is reconstituted.

Small Animal Dosage

Dogs and Cats

- 30 mg/kg q8h IV or SQ.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of relatively short plasma half-life, residues should not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cefovecin

sef-oh-ve'sin

Trade and other names: Convenia

Functional classification: Antibacterial

C

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefovecin is considered a third-generation cephalosporin but may not have the same activity as other injectable third-generation cephalosporins, such as cefotaxime. Cefovecin has good activity against streptococci, *Staphylococcus* species, and gram-negative bacilli. MIC values are lower for cefovecin than first-generation cephalosporins. Some *Enterobacteriaceae* can develop resistance. It is not active against *Pseudomonas aeruginosa*. Methicillin-resistant staphylococci are considered resistant to cefovecin. Activity against anaerobic bacteria is unpredictable. Cefovecin is greater than 99% protein bound in cats and greater than 98% in dogs, which is partly responsible for the long duration. The terminal half-life is approximately 7 days in cats and 5 days in dogs, and effective concentrations can be maintained in the tissue fluid of these species for 14 days.

Indications and Clinical Uses

Cefovecin is approved for use in dogs and cats. It is approved in the US for skin and soft tissue infections but also has been used to treat urinary tract infections, for which it is approved in some countries. The efficacy of cefovecin for treating infections in other sites, such as the respiratory tract, bone, and central nervous system, has not been established. Experience is limited to administration of cefovecin in dogs and cats; the use in other species, such as horses, large animals, birds, and reptiles, is not recommended until specific dosing recommendations are published.

Precautionary Information

Adverse Reactions and Side Effects

The animal safety studies have produced few serious adverse reactions. In dogs and cats, vomiting and diarrhea have been observed in a dose-related manner. With approved doses, mild GI upset may be observed for 2-3 days. Injection-site irritation and transient edema occurred with increasing frequency in a dose-related manner and with repeat injections. The long half-life indicates that drug concentrations will persist in animals for at least 60 days after an injection, but at this time, this has not produced adverse reactions attributed to a long persistence of drug in tissues.

Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small.

Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

Instructions for Use

The approved label in the US indicates that therapeutic concentrations are maintained for an interval of 7 days in dogs. However, pharmacokinetic studies indicated that drug concentrations persist long enough for a 14-day interval for some indications. In Canada and Europe, the approved label dose is 8 mg/kg SQ, once every 14 days and efficacy has been demonstrated with a 14-day interval for administration. The injection may be repeated for infections that require longer than 14 days for a cure (e.g., canine pyoderma).

Patient Monitoring and Laboratory Tests

Susceptibility testing: There is no CLSI approved break point for susceptibility testing, but a break point of ≤ 2 mcg/mL for gram-positive and gram-negative bacteria is suggested.

Formulations

Cefovecin is available in 10-mL vials containing 800 mg. When reconstituted it is 80 mg/mL.

Stability and Storage

Store in original vial in the refrigerator protected from light. Do not freeze. Once reconstituted, vial should be used within 28 days. The reconstituted solution may turn slightly yellow, which does not affect potency.

Small Animal Dosage

Dogs and Cats

- 8 mg/kg, SQ, every 14 days. For some indications, injections may be repeated at 7 days.

Large Animal Dosage

No dose has been established.

Regulatory Information

Withdrawal times are not established for animals that produce food and cefovecin should not be administered to food-producing animals.

Cefoxitin sodium

Se fox' i tin soe'dee-um

Trade and other names: Mefoxitin, Mefoxin, Cefoxil

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending

on spectrum of activity. Cefotetan has been listed with second-generation cephalosporins but is more properly considered with the cephamycin group of cephalosporins, which have greater stability against the beta-lactamases of anaerobic bacteria such as those of the Bacteroides group. In cats, the half-life is 1.6 hours, the volume of distribution is 0.3 L/kg, and the clearance is 2.3 mL/kg/min. In horses, these values are 0.82 hours, 0.12 L/kg, and 4.3 mL/min/kg, respectively. In dogs these values are 1.3 hours, 0.16 L/kg, and 3.2 mL/kg/min, respectively.

Indications and Clinical Uses

Cefoxitin, a cephalosporin of the cephamycin group, has greater activity against anaerobic bacteria and gram-negative bacilli than other cephalosporins. Therefore, it has been used to treat infections in dogs and cats in which enteric gram-negative bacilli or anaerobes are suspected, including abdominal infections and soft tissue wounds, and prior to surgery.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. Cefoxitin has been administered to dogs during surgery without adversely affecting their cardiovascular function.

Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone.

Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

Instructions for Use

Second-generation cephalosporin is often used when activity against anaerobic bacteria is desired.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is ≤ 8 mcg/mL for all organisms. Cefoxitin should not be used to test for methicillin-resistant strains of *Staphylococcus* from animals.

Formulations

Cefoxitin is available in 1- and 2-g vials for injection (20 or 40 mg/mL).

Stability and Storage

Store in a tightly sealed container, in the freezer at -25°C to -10°C , unless otherwise instructed by the manufacturer. Thaw at room temperature or in refrigerator to dissolve crystals before administration. Do not heat or place in microwave oven. After thawing, solution is potent for 24 hours at room

126 Cefpodoxime Proxetil

temperature or for 21 days in refrigerator. Protect from light. Once thawed, do not refreeze.

Small Animal Dosage

Dogs and Cats

- 30 mg/kg q6-8h IM or IV. 22 mg/kg IV for presurgical use.

Large Animal Dosage

Calves and Horses

- 20 mg/kg q4-6h IV or IM.

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of relatively short plasma half-life, residues should not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cefpodoxime Proxetil

sef-poe-doks'eem prahx 'ih-til

Trade and other names: Simplicef (veterinary preparation), Vantin (human preparation), and generic

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefpodoxime is a third-generation cephalosporin, which indicates greater activity against gram-negative bacilli compared to first-generation cephalosporins. However, cefpodoxime is not as active against many gram-negative bacilli as injectable third-generation cephalosporins such as cefotaxime or ceftazidime. Cefpodoxime has better activity against *Staphylococcus* than other oral third-generation cephalosporins. It is not active against *Enterococcus* spp., methicillin-resistant *Staphylococcus* spp., or *Pseudomonas aeruginosa*. Activity against anaerobic bacteria is unpredictable. It is one of the three currently available third-generation oral cephalosporins. It is combined with proxetil to produce an ester to improve oral absorption. Therefore, as the ester, it is actually a pro-drug that needs to be converted to the active cefpodoxime. Oral absorption in dogs was reported to be 35%. Half-life is 7.2 hours in horses and 5.7 hours in dogs. Protein binding in dogs is 83%.

Indications and Clinical Uses

Cefpodoxime is indicated for treatment of skin and other soft tissue infections in dogs caused by susceptible organisms. Efficacy has been established in dogs for treatment of skin and soft tissue infections. Cefpodoxime has greater activity against gram-negative bacilli than first-generation cephalosporins; therefore, it may be effective for some gram-negative infections. Although not currently registered for treatment of UTIs, approximately 50% of administered dose is excreted in urine and expected to be active for treating UTIs caused by common pathogens.

Although not registered for cats, or tested in cats, no adverse effects have been reported from occasional use. However, oral absorption in cats has not been examined.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. Vomiting and diarrhea can occur from oral administration of cephalosporins.

Contraindications and Precautions

This drug is best taken with food to improve oral absorption. Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone.

Drug Interactions

There are no important drug interactions reported for animals, but oral absorption of cefpodoxime in people is inhibited by H₂ blockers (e.g., cimetidine and ranitidine) and antacids, which can decrease oral absorption by 30%. Cephalosporins may be administered with other antibiotics to increase the spectrum of activity and produce a synergistic effect. However, do not mix with other drugs in a compounded formulation because inactivation may result.

Instructions for Use

FDA approval in dogs includes skin and soft tissue infections. It also has been used for urinary tract infections, and based on spectrum and tissue distribution, it has been used for other infections. There has also been occasional use in cats on an extralabel basis.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 2 mcg/mL for all organisms. Strains of *Escherichia coli* and *Klebsiella* that have extended spectrum beta lactamase (ESBL) may be clinically resistant.

Formulations

Cefpodoxime proxetil is available in 100- and 200-mg tablets and 10- and 20-mg/mL oral suspension (human preparation).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded tablets has not been evaluated. Avoid exposure to moisture.

Small Animal Dosage

Dogs

- 5-10 mg/kg q24h PO.

128 Cefquinome sulfate

Cats

A dose has not been established by the manufacturer for cefpodoxime proxetil. Some veterinarians have extrapolated from the canine dose.

Large Animal Dosage

Horses

- 10 mg/kg oral q6-12h. The 12-hour interval is appropriate for *Klebsiella*, *Pasteurella*, and streptococci. More frequent intervals may be needed for more resistant organisms.

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of a relatively short plasma half-life, residues should not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cefquinome sulfate

Sef' quin ome sul' fate

Trade and other names: Cobactan and Cephaguard

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Cefquinome, like other cephalosporins, inhibits synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefquinome is currently the only fourth-generation cephalosporin approved in any country for use in food animals. In contrast to other cephalosporins, cefquinome is not affected by chromosomal-mediated cephalosporinases of the Amp-C type or by plasmid mediated beta-lactamase from some gram-negative bacilli. Bacteria that produce extended spectrum beta-lactamases (ESBL) and methicillin-resistant *Staphylococcus* species will be resistant.

It is currently licensed in Europe but not the United States. Cefquinome has good activity against most gram-negative bacilli, especially *Enterobacteriaceae*. It has been shown to be active against bovine respiratory pathogens that include *Mannheimia haemolytica*, *Pasteurella multocida*, or *Histophilus somni*. It also is active against pathogens that cause mastitis in cows, including *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus dysgalactiae*, *Streptococcus agalactiae*, and *Streptococcus uberis*. Activity of cefquinome against equine pathogens includes gram-positive and gram-negative bacteria such as *Escherichia coli*, *Streptococcus equi subsp. zooepidemicus*, *Klebsiella pneumoniae*, *Enterobacter* spp., *Staphylococcus aureus*, *Streptococcus equi subsp. equi*, *Clostridium perfringens*, and *Actinobacillus equuli*.

In cattle, cefquinome has a half-life of 2.5 hours and is less than 5% protein bound. Cefquinome is not absorbed after oral administration. In pigs or piglets, the half-life is about 9 hours. Because of low protein binding, cefquinome penetrates into the cerebrospinal fluid (CSF) and the synovial fluid in pigs. In horses,

cefquinome has a half-life of 2 hours in adult horses and 1.4 hours in foals with protein binding less than 5%. Absorption from IM injection is almost 100% in adults and 87% in foals.

Indications and Clinical Uses

Cefquinome is used in cattle, pigs, and horses to treat infections caused by susceptible pathogens. It is registered in Europe for treatment of respiratory disease, *E. coli* sepsis in calves, and interdigital necrobacillosis (foot rot) in lactating cows in many countries. Cefquinome ointment has been administered intramammary for treatment of *E. coli* mastitis in dairy cattle. In Europe it is also registered for treatment of swine respiratory disease, arthritis, meningitis, and dermatitis caused by *Pasteurella multocida*, *Haemophilus parasuis*, *Actinobacillus pleuropneumoniae*, *Streptococcus suis*, *Staphylococcus hyicus*, and other cefquinome-sensitive organisms and mastitis-metritis-agalactia syndrome (MMA) with involvement of *E. coli*, *Staphylococcus* spp., *Streptococcus* spp., and other cefquinome-sensitive organisms. In horses, it is registered for respiratory infection caused by *Streptococcus equi* subsp. *zooepidemicus*, and systemic bacterial infection (sepsis) caused by *Escherichia coli* is involved. There is no use of cefquinome reported for small animals.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Cefquinome injection SQ may cause some injection reactions.

High doses may produce diarrhea in horses, but if doses are maintained within the range listed in the dosing section, it has been safe in most horses.

Contraindications and Precautions

Do not administer to animals prone to sensitivity to beta-lactams.

Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

Instructions for Use

Cefquinome is registered in Europe for treatment of infections in cattle, pigs, and horses. In the United States, without FDA approval, the use would be a violation. Cefquinome in cattle can be administered SQ or IM, depending on the formulation. In pigs it is administered IM. In horses the solution can be administered IV initially, then switched to IM injections.

Patient Monitoring and Laboratory Tests

Monitor CBC if high doses are administered for long periods. Susceptibility testing: CLSI guidelines for susceptible bacteria are not available.

Formulations

In countries in which cefquinome is available, it is a 7.5% (75 mg/mL) injectable suspension, 2.5% (25 mg/mL) injectable suspension, a powder for reconstitution to be used IV in horses and foals (4.5% or 45 mg/mL in a 30 mL or 100 mL vial), and as an intramammary ointment (75 mg in an 8-g syringe).

Stability and Storage

After container is opened, the shelf-life is 28 days. For the 4.5% IV solution, the shelf life after reconstitution is 10 days when stored in a refrigerator (2°C-8°C).

Small Animal Dosage

Dose not established.

Large Animal Dosage (based on registration label in Europe)

Cattle

- Bovine respiratory disease (BRD): 2.5 mg/kg, IM, q48h (1 mL of 7.5% suspension per 30 kg).
- Respiratory disease and foot rot: 1 mg/kg (2 mL per 50 kg of 2.5% suspension) IM once daily for 3-5 days.
- Mastitis (*E. coli*) systemic involvement: 1 mg/kg, (2 mL per 50 kg of 2.5% suspension) IM once daily for 2 days.
- Septicemia in calves (*E. coli*): 2 mg/kg (4 mL per 50 kg of 2.5% suspension), IM once daily for 3-5 days.

Pigs

- Respiratory infections: 2 mg/kg (2 mL of 2.5% suspension) IM once daily for 2 days.
- Meningitis, arthritis, or dermatitis in piglets: 2 mg/kg (2 mL of 2.5% suspension) once daily IM for 5 days.

Horses

- Respiratory infections caused by *Streptococcus equi*: 1 mg/kg (1 mL solution per 45 kg) of solution IV or IM, q24h, for 5-10 days.
- Systemic infection (especially septicemia in foals) caused by *E. coli*: 1 mg/kg (1 mL per 45 kg) IV or IM, q12h, for 6-14 days.

Regulatory Information

For cefquinome suspension, do not use in lactating cattle producing milk for human consumption (during lactation or the dry period). Do not use within 2 months prior to first calving in heifers intended for the production of milk for human consumption. In Europe, the meat withdrawal time is 13 days after 2.5 mg/kg SQ, 5 days after 1 mg/kg IM, and 3 days in pigs. Milk withdrawal time after systemic use is 24 hours. After intramammary administration the meat withdrawal time is 4 days and the milk discard is 5 days.

Ceftazidime

sef-tah' zih-deem

Trade and other names: Fortaz, Ceptaz, Tazicef, and Tazidime

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Ceftazidime is a third-generation cephalosporin. Not all third-generation cephalosporins are equal in activity. Ceftazidime is against many

gram-negative bacilli and more active against *Pseudomonas aeruginosa* than other third-generation cephalosporins. However, it may not be as active against some Enterobacteriaceae as cefotaxime.

Indications and Clinical Uses

Ceftazidime is a third-generation cephalosporin with activity against many gram-negative bacteria resistant to other drugs. Although it is not an FDA-approved drug for animals, it is used often in zoo, exotic, and companion animals because of its activity against many organisms that are resistant to other drugs. Its activity against *Pseudomonas aeruginosa* distinguishes it from other cephalosporins. Therefore, it has been used to treat infections in dogs and cats in which enteric gram-negative bacilli or *P. aeruginosa* are suspected, including abdominal infections, skin infections, soft tissue wounds, and prior to surgery.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins.

Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have a N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone.

Drug Interactions

Do not mix in a vial or syringe with other drugs because inactivation may result. In particular, there may be mutual inactivation if mixed with aminoglycosides. If mixed with vancomycin, precipitation may occur.

Instructions for Use

Ceftazidime may be reconstituted with 1% lidocaine for intramuscular injection to reduce pain. Ceftazidime contains l-arginine. To make up vials containing sodium carbonate, carbon dioxide will form on reconstitution. Venting may be necessary to release gas. Doses listed for dogs and cats are sufficient for treating infections caused by *P. aeruginosa*.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 8 mcg/mL for all organisms. Resistance to ceftazidime has been used to test for extended spectrum beta lactamase (ESBL) producing strains of *Escherichia coli* or *Klebsiella*.

Formulations

Ceftazidime is available in 0.5-, 1-, 2-, and 6-g vials reconstituted to 280 mg/mL.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Slight discoloration to yellow or amber may occur without losing potency. Do not mix in vial with other drugs, but it may be mixed with intravenous fluid solutions. After reconstitution, solutions are stable for at least 18 hours at room temperature

132 Cefotiofur Crystalline Free Acid

or 7 days if refrigerated. Solutions may be frozen at 20°C to retain potency for 3 months. Once thawed, it should not be refrozen. Thawed solutions are stable for 8 hours at room temperature and for 4 hours if refrigerated.

Small Animal Dosage

Dogs and Cats

- 30 mg/kg q6h IV or IM (interval as long as q8h for some indications).
- Dogs: 30 mg/kg q4-6h SQ.
- Constant IV infusion: Give loading dose of 1.2 mg/kg, followed by 1.56 mg/kg/hr delivered in IV fluids.

Large Animal Dosage

Horses

- 20 mg/kg q8h IV or IM.

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of a relatively short plasma half-life, residues should not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cefotiofur Crystalline Free Acid

sef' tee-oh-fer

Trade and other names: Excede, Naxcel XT

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Cefotiofur hydrochloride and cefotiofur sodium have similar action and spectrum. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefotiofur most closely resembles the activity of a third-generation cephalosporin. It has good activity against most gram-negative bacilli, especially *Enterobacteriaceae*. It has potent activity against bovine and swine respiratory pathogens such as *Mannheimia*, *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Salmonella choleraesuis*, *Haemophilus*, and *Streptococcus*. Cefotiofur has activity against some gram-positive cocci, such as streptococci, but activity against *Staphylococcus* is not as high as other cephalosporins. Cefotiofur is rapidly metabolized after administration to metabolites such as desfuoroylecefotiofur, which is active against bacteria, except that it is less active against *Staphylococcus* than other cephalosporins and the parent drug cefotiofur.

Indications and Clinical Uses

Cefotiofur crystalline free acid is indicated for treatment of swine respiratory disease (SRD) caused by *A. pleuropneumoniae*, *P. multocida*, *S. choleraesuis*, *Haemophilus parasuis*, and *Streptococcus suis*. In cattle, it is used for treatment of bovine respiratory disease (BRD) caused by *Mannheimia haemolytica*, *P. multocida*, and *Histophilus somni* (formerly *Haemophilus somnus*). It also can be administered to control respiratory disease in cattle at high risk of developing BRD (metaphylaxis) associated with *M. haemolytica*, *P. multocida*, and *H. somnus*. This formulation also is approved for treating foot rot in cattle (interdigital necrobacillosis) caused by

Fusobacterium necrophorum, *Porphyromonas levis*, *Bacteriodes melaninogenicus*.

This formulation also is approved for use in horses for treatment of respiratory tract infections caused by susceptible *Streptococcus equi* (*S. zooepidemicus*) after administration of two injections. Ceftiofur hydrochloride and ceftiofur crystalline free acid have also been administered extralabel intramammary to dairy cattle.

However, there are specific products designed for intramammary use (Spectramast).

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. For ceftiofur, doses that have exceeded the approved label recommendations have caused bone marrow suppression in dogs. Thrombocytopenia and anemia occurred at doses of 6.6 mg/kg and 11 mg/kg when administered to dogs. High doses have caused diarrhea in horses. Injections of the crystalline free acid formulation to small animals has caused injection site lesions in some animals and is generally not recommended.

Contraindications and Precautions

Do not administer this formulation (suspension) IV. Do not administer to animals prone to sensitivity to beta-lactams. Do not administer to animals at high doses. Ceftiofur crystalline free acid should not be used interchangeably with ceftiofur sodium or ceftiofur hydrochloride without consulting label information for difference in dosing and withdrawal times.

Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

Instructions for Use

Dosing information is available for pigs and cattle; it is not available for other animals. Ceftiofur sodium has been used in horses and dogs, but there is no information available on the use of ceftiofur crystalline free acid in these species.

Patient Monitoring and Laboratory Tests

Monitor CBC if high doses are administered for long periods. Sensitivity testing: CLSI guidelines for susceptible bacteria indicate that susceptible bacteria have minimum inhibitory concentration (MIC) values ≤ 2 mcg/mL. (Note that for some cephalosporins used in humans, the MIC values for susceptibility may be ≤ 8.0 mcg/mL.)

Formulations

Ceftiofur crystalline free acid is available in an injectable suspension for cattle at 200 mg/mL ceftiofur equivalents (CE).

Ceftiofur crystalline free acid is available in an injectable suspension for pigs at 100 mg/mL CE.

Stability and Storage

Store at room temperature. Shake well before administration. Protect from freezing. Contents should be used within 12 weeks after the first dose is removed.

Small Animal Dosage

Dogs and Cats

Dose not established for this product. See ceftiofur sodium for small animal dosage.

134 Cefotiofur Hydrochloride

Large Animal Dosage

Cattle

- 6.6 mg/kg, with a single SQ injection in the middle third of the posterior aspect of the ear.

Horses

- 6.6 mg/kg IM in neck muscle (15 mL per 1,000 pounds). Administer a second dose in 4 days. Do not administer more than 20 mL in one site.

Pigs

- 5.0 mg/kg IM injection in the postauricular region of the neck.

Regulatory Information

Pig withdrawal times: 14 days.

Cattle withdrawal time (slaughter): 13 days. A withdrawal period has not been established in preterminating calves. Do not use in calves to be processed for veal. Milk withdrawal: Zero days.

Cefotiofur Hydrochloride

sef 'tee-oh-fer hye-droe-klor 'ide

Trade and other names: Excenel

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Cefotiofur hydrochloride and cefotiofur sodium have similar action and spectrum. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefotiofur most closely resembles the activity of a third-generation cephalosporin. Cefotiofur has good activity against most gram-negative bacilli, especially *Enterobacteriaceae*. It has potent activity against bovine respiratory pathogens such as *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni* (formerly *Haemophilus somnus*). Cefotiofur has activity against some gram-positive cocci, such as streptococci, but activity against *Staphylococcus* is not as high as other cephalosporins. Cefotiofur is rapidly metabolized after administration to metabolites such as desfuroylcefotiofur, which is active against bacteria, except that it is less active against *Staphylococcus* than other cephalosporins and the parent drug cefotiofur.

Indications and Clinical Uses

Cefotiofur hydrochloride is used in cattle and pigs for treatment and control of infections caused by susceptible pathogens. It is registered for treatment of respiratory disease in cattle caused by *Mannheimia*, *P. multocida*, and *H. somni* (formerly *H. somnus*). It is used for interdigital necrobacillosis (foot rot) in cattle caused by *Fusobacterium necrophorum* or *Bacteroides melaninogenicus*. Cefotiofur hydrochloride has been shown to be effective for treatment of acute postpartum metritis in dairy cows when administered at 2.2 mg/kg or for treatment of retained fetal membranes by instilling into the uterus (1 g). Cefotiofur hydrochloride is used for treatment of swine respiratory disease (SRD) caused by *Actinobacillus*, *P. multocida*, *Salmonella choleraesuis*, and *Streptococcus suis*. Cefotiofur hydrochloride and cefotiofur crystalline free acid have also been administered via the intramammary

route to dairy cattle. For intramammary use, a specific formulation is recommended (Spectramast DC). Although ceftiofur sodium has been used in horses and dogs to treat infections, there is little experience with administration of ceftiofur hydrochloride in these species.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. For ceftiofur, doses that have exceeded the approved label recommendations have caused bone marrow suppression in dogs. Thrombocytopenia and anemia occurred at doses of 6.6 mg/kg and 11 mg/kg when administered to dogs. High doses have caused diarrhea in horses.

Contraindications and Precautions

Do not administer to animals prone to sensitivity to beta-lactams. Do not administer to animals at high doses. Ceftiofur hydrochloride is a sterile suspension and should not be used interchangeably with ceftiofur sodium, which is a solution.

Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

Instructions for Use

Dosing information is not available for species other than pigs and cattle. Dose in cattle may be extended beyond 3 days if necessary. Alternatively, doses have been administered to cattle for bovine respiratory disease (BRD) at 2.2 mg/kg at 48-hour intervals. Ceftiofur sodium has been used in horses and dogs, but there is no information available on the use of ceftiofur hydrochloride in these species.

Patient Monitoring and Laboratory Tests

Monitor CBC if high doses are administered for long periods. Susceptibility testing: CLSI guidelines for susceptible bacteria indicate that susceptible bacteria have minimum inhibitory concentration (MIC) values ≤ 2 mcg/mL. (Note that for some human-labeled cephalosporins, the MIC values for susceptibility may be ≤ 8.0 mcg/mL.)

Formulations

Ceftiofur hydrochloride is available in 50-mg/mL sterile suspension.

Stability and Storage

Store at room temperature. Shake well before administration. Protect from freezing.

Small Animal Dosage

Dogs and Cats

Dose not established for this product. See ceftiofur sodium for small animal dose.

Large Animal Dosage

Cattle

- 1.1-2.2 mg/kg q24h for 3 days IM or SQ.
- Intrauterine (retained fetal membranes): 1 g ceftiofur diluted in 20 mL sterile water infused in uterus once at 14-20 days after calving.

Dairy Cows

- Treatment of postpartum metritis: 2.2 mg/kg once daily for 5 days SQ or IM.

136 Cefotiofur Sodium

Pigs

- 3-5 mg/kg q24h for 3 days IM.

Regulatory Information

Cattle withdrawal time: 0 days for milk; 3 days for meat.

Pig withdrawal time: 4 days.

Cefotiofur Sodium

Sef' tee-oh-fer soe' dee-um

Trade and other names: Naxcel

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Cefotiofur hydrochloride and cefotiofur sodium have similar action and spectrum. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefotiofur most closely resembles the activity of a third-generation cephalosporin. Cefotiofur has good activity against most gram-negative bacilli, especially *Enterobacteriaceae*. It has potent activity against bovine and swine respiratory pathogens such as *Mannheimia*, *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Salmonella choleraesuis*, *Haemophilus*, and *Streptococcus*. Cefotiofur has activity against some gram-positive cocci, such as streptococci, but activity against *Staphylococcus* is not as high as other cephalosporins. Cefotiofur is rapidly metabolized after administration to metabolites such as desfuroylcefotiofur, which is active against bacteria, except that it is less active against *Staphylococcus* than other cephalosporins and the parent drug cefotiofur.

Indications and Clinical Uses

Cefotiofur sodium is used in cattle and pigs for treatment and control of infections caused by susceptible pathogens. It is registered for treatment of respiratory disease and interdigital necrobacillosis (foot rot) in lactating cows in many countries. Cefotiofur has been used for treatment of salmonella in calves. At 5 mg/kg q24h IM, it decreased diarrhea and temperature but did not eradicate organism. Cefotiofur sodium has been administered intramammary for treatment of coliform mastitis, but this is an extralabel use. Cefotiofur sodium is used in horses for treatment of streptococcal respiratory infections (registered treatment) and extralabel use for treating other infections such as those caused by gram-negative bacilli, including *Escherichia coli*, *Klebsiella pneumoniae*, and salmonella. Higher doses should be used for nonstreptococcal bacteria in horses. Cefotiofur sodium is registered for a daily subcutaneous injection for treatment of UTIs in dogs, but it has not been evaluated for treatment of other infections.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with

some cephalosporins. For ceftiofur, doses that have exceeded the approved label recommendations have caused bone marrow suppression in dogs. Thrombocytopenia and anemia occurred at doses of 6.6 mg/kg and 11 mg/kg when administered to dogs. High doses have caused diarrhea in horses, but if doses are maintained within the range listed in the dosing section, it has been safe in most horses.

Contraindications and Precautions

Do not administer to animals prone to sensitivity to beta-lactams. Do not administer to animals at high doses.

Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

Instructions for Use

Although dosing information is not available for other species, it has been used safely in dogs, sheep, pigs, horses, and cattle and is expected to be safe for other animals. Ceftiofur sodium is bioequivalent whether administered SQ or IM. In dogs and cats, it has not been evaluated to treat infections other than urinary tract infection in dogs. Higher systemic concentrations may be needed in dogs and cats to treat other infections.

Patient Monitoring and Laboratory Tests

Monitor CBC if high doses are administered for long periods. Susceptibility testing: CLSI guidelines for susceptible bacteria indicate that susceptible bacteria causing respiratory infections in cattle and pigs have minimum inhibitory concentration (MIC) values ≤ 2 mcg/mL. The break point for *Streptococcus* in horses is ≤ 0.25 mcg/mL. (Note that for many human-labeled cephalosporins, the MIC values for susceptibility may be ≤ 8.0 mcg/mL.)

Formulations

Ceftiofur sodium is available in 50 mg/mL vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. After reconstitution, solutions are potent for 7 days if refrigerated and 12 hours at room temperature. If frozen, solutions are stable for 8 weeks. Do not refreeze. Slight discoloration may occur without losing potency.

Small Animal Dosage

Dogs

- UTI: 2.2 to 4.4 mg/kg q24h SQ.

Cats

Dose not established but has been extrapolated from canine dose.

Large Animal Dosage

Horses

- 2.2-4.4 mg/kg q24h IM or 2.2 mg/kg q12h IM for as long as 10 days. Treatment of some gram-negative infections may require doses at the higher range and up to 11 mg/kg/day IM has been given to horses.

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Foals

- 5 mg/kg q12h IV

Cattle

- Bovine respiratory disease (BRD): 1.1-2.2 mg/kg (0.5-1.0 mg/pound) q24h for 3 days IM. Additional doses may be given on days 4 and 5 if necessary. In cattle, these doses also may be administered SQ, which is bioequivalent.

Pigs

- Respiratory infections: 3-5 mg/kg (1.36-2.27 mg/pound) q24h for 3 days IM.

Sheep and Goats

- 1.1-2.2 mg/kg (0.5-1.0 mg/pound) q24h for 3 days IM, SQ. Additional doses may be given on days 4 and 5 if necessary.

Regulatory Information

Cattle withdrawal time: 0 days for milk and 4 days for meat.

Sheep and goat withdrawal time: 0 days for meat.

Pig withdrawal time: 4 days.

Cephalexin

sef-ah-lex 'in

Trade and other names: Keflex and generic brands

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibits synthesis of bacterial cell wall leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cephalexin is a first-generation cephalosporin.

Like other first-generation cephalosporins, it is active against *Streptococcus* and *Staphylococcus* species and some gram-negative bacilli, such as *Pasteurella*, *Escherichia coli*, and *Klebsiella pneumoniae*. However, resistance is common among gram-negative bacteria. It is not active against *Pseudomonas aeruginosa*. *Staphylococcus* spp. resistant to methicillin and oxacillin will be resistant to first-generation cephalosporins.

Indications and Clinical Uses

Like other first-generation cephalosporins, cephalexin is indicated for treating common infections in animals, including UTIs, soft tissue infections, pyoderma and other dermal infections, and pneumonia. Although not approved in the US for animals, at this time it is registered in other countries, and there are published efficacy studies documenting its effectiveness. Efficacy against infections caused by anaerobic bacteria is unpredictable. In horses, half-life is short at only 1.6 hours and oral absorption is only 5%. In dogs, the oral absorption has ranged from 57% to 90%, depending on the study. In dogs the half-life, oral clearance, volume of distribution (V/F), and peak concentration (C_{MAX}) are 2.74 hours, 3.14 mL/kg/min, 0.92 L/kg, and 19.5 mcg/mL, respectively.

Precautionary Information

Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. With oral administration of cephalosporins, vomiting and diarrhea can occur.

Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have a N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone.

Drug Interactions

No drug interactions are reported in animals. However, do not mix with other drugs in a compounded formulation because inactivation may result.

Instructions for Use

Although not approved for veterinary use, trials in dogs show efficacy for treating pyoderma. For cephalexin, use cephalothin to test susceptibility.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 2 mcg/mL for all organisms. Cephalothin is used as a marker to test for sensitivity to cephalexin, cefadroxil, and cephadrine. Cephalexin may cause a false-positive test for urine glucose. The test may be positive with test strips that use either the copper reduction test or an enzymatic reaction.

Formulations

Cephalexin is available in 250- and 500-mg capsules, 250- and 500-mg tablets, 100-mg/mL oral suspension, and 125- and 250-mg/5 mL oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Suspensions should be stored in refrigerator and discarded after 14 days. Cephalexin is compatible with enteral products if used immediately after mixing.

Small Animal Dosage

Dogs

- 10-30 mg/kg q6-12h PO; for pyoderma: 22-35 mg/kg q12h PO.

Cats

- 15-20 mg/kg q12h PO.

Large Animal Dosage

Horses

- 30 mg/kg q8h PO for susceptible gram-positive bacteria (minimum inhibitory concentration ≤ 0.5 mcg/mL).

Regulatory Information

Withdrawal times are not established for animals that produce animals. However, because of relatively short plasma half-life and poor oral absorption, residues should

140 Cetirizine Hydrochloride

not be a risk. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cetirizine Hydrochloride

seh-teer 'ih-zeen hye-droe-klor 'ide

Trade and other names: Zyrtec

Functional classification: Antihistamine

Pharmacology and Mechanism of Action

Antihistamine (H_1 -blocker). Cetirizine is the active metabolite of hydroxyzine. Almost all hydroxyzine in dogs is converted to cetirizine. Cetirizine is similar to other antihistamines—it acts by blocking the histamine type-1 (H_1) receptor and suppressing inflammatory reactions caused by histamine. The H_1 blockers have been used to control pruritus and skin inflammation, rhinorrhea, and airway inflammation. Cetirizine is considered a second-generation antihistamine to distinguish it from other, older antihistamines. The most important difference between cetirizine and older drugs is that it does not cross the blood–brain barrier as readily and produces less sedation. In cats, studies have shown cetirizine to be well absorbed after oral administration with a half-life of 10 hours. In dogs the half-life is approximately 10-11 hours, and in horses it is 5.8 hours. A related drug is levocetirizine (Xyzal), which is the active enantiomer of cetirizine and has two-fold higher activity compared to cetirizine.

Indications and Clinical Uses

Cetirizine is used to treat and prevent allergic reactions in people. It is preferred over older drugs because it has fewer side effects. In dogs and cats it has been considered for pruritus therapy, allergic airway disease, rhinitis, and other allergic conditions. In cats, 1 mg/kg (5 mg/cat) has produced plasma concentrations considered effective. However, it was not effective in decreasing the inflammatory response in cats with hyper-responsive airways (experimentally induced asthma). In dogs, doses of 2 mg/kg suppress histamine response for 8 hours. However, there are no published clinical trials to document efficacy for these conditions.

Precautionary Information

Adverse Reactions and Side Effects

Sedation is not as likely as with other antihistamines. However, with higher doses sedation is still possible. Antimuscarinic effects (atropine-like effects) also are possible, but cetirizine may produce fewer antimuscarinic effects than other antihistamines.

Contraindications and Precautions

Because antimuscarinic effects (atropine-like effects) are possible, do not use in conditions for which anticholinergic drugs may be contraindicated, such as glaucoma, ileus, or cardiac arrhythmias.

Drug Interactions

Do not use with other antimuscarinic drugs.

Instructions for Use

Use of cetirizine has been mostly empirical. There are no clinical studies to document efficacy.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Cetirizine hydrochloride is available in 1-mg/mL oral syrup and 5- and 10-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 2 mg/kg q12h, PO.

Cats

- 1 mg/kg daily, PO.

Large Animal Dosage

Horses

- 0.2-0.4 mg/kg q12h, PO.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Charcoal, Activated

Trade and other names: ActaChar, Charcodote, Liqui-Char, ToxiBan, and generic brands

Functional classification: Antidote

Pharmacology and Mechanism of Action

Adsorbent. It will bind to other drugs and prevent their absorption from the intestine. It may reduce the absorption of a poison by as much as 75%.

Indications and Clinical Uses

Used primarily to adsorb drugs and toxins in intestine to prevent their absorption. Ordinarily, a single dose is administered, but multiple doses will increase clearance of drugs that may undergo enterohepatic circulation.

Precautionary Information

Adverse Reactions and Side Effects

Not absorbed systemically. Safe for oral administration, except that constipation may occur; however, formulations that contain sorbitol may induce diarrhea.

Contraindications and Precautions

Used primarily as treatment for intoxication.

Drug Interactions

Charcoal will adsorb most other drugs administered orally to prevent their absorption.

Instructions for Use

Dosing of activated charcoal has used a ratio of 10/1 (charcoal/toxin) to administer for treatment of intoxication. However, more recent evidence indicates that a ratio >40/1 is more appropriate, which may require higher doses than previously thought. Activated charcoal is effective to treat intoxication if administered up to 4 hours after exposure, but after 4 hours, benefits decrease. Charcoal is available in a variety of forms and usually is used as treatment for poisoning. Many commercial preparations contain sorbitol, which acts as a flavoring agent and promotes intestinal catharsis.

Patient Monitoring and Laboratory Tests

When used as treatment for intoxication, careful monitoring of effects of toxin is necessary because charcoal will not adsorb all of the toxicant.

Formulations

Charcoal is available in oral suspension and granules. Strengths of formulations vary from 15 g/72 mL to 50/240 mL. Many formulations contain sorbitol, which is a sweetener and also can produce an intestinal cathartic effect.

Stability and Storage

Store in a tightly sealed container at room temperature. Do not mix with other compounds because it will adsorb other chemicals.

Small Animal Dosage

Dogs and Cats

- 1-4 g/kg PO (granules) or 6-12 mL/kg (suspension). Administer a single dose shortly after poisoning.

Large Animal Dosage

Large animal use is not reported, but it may be considered for treatment of a poisoning. Consider a dose of 1 g/kg PO (granules) or 6-10 mL/kg (suspension) PO.

Regulatory Information

No residue concerns. Withdrawal time: 0 days.

Chlorambucil

klor-am' byoo-sil

Trade and other names: Leukeran

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Cytotoxic agent. Chlorambucil is a nitrogen mustard and is sometimes used as a substitute for cyclophosphamide. It has a similar action as cyclophosphamide but is one of the slowest-acting of the class of nitrogen mustards.

Indications and Clinical Uses

Chlorambucil is used for treatment of various tumors and immunosuppressive therapy. Although little has been published on the clinical use of chlorambucil, it may be effective in dogs and cats for immune-mediated disease. However, direct comparisons to other immunosuppressive drugs have not been reported. One of the most frequent uses has been for treatment of immune-mediated skin diseases of cats, for which it has been used to treat cats with pemphigus and eosinophilic granuloma complex (EGC). It also has been used to treat inflammatory bowel disease (IBD) in cats.

Precautionary Information

Adverse Reactions and Side Effects

Myelosuppression is possible, although most cats tolerate chlorambucil well. Cystitis does not occur with chlorambucil as with cyclophosphamide. Diarrhea and anorexia may occur in some patients.

Contraindications and Precautions

Cytotoxic, potentially immunosuppressive agent. Do not use in animals with suppressed bone marrow.

Drug Interactions

Chlorambucil will potentiate other immunosuppressive drugs.

Instructions for Use

Chlorambucil may be combined with prednisolone for treatment of immune-mediated disorders.

Patient Monitoring and Laboratory Tests

Monitor CBC in animals during treatment.

Formulations

Chlorambucil is available in a 2-mg tablet.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Chlorambucil undergoes rapid hydrolysis (within 10 minutes) in the presence of water. Hydrolysis occurs most readily at pH >2. Therefore, chlorambucil can decompose rapidly in compounded aqueous formulations, such as those that contain simple syrup and other excipients. Hydrolysis is slower if mixed in alcohol-based solutions. If mixed with alcohol and stored in the freezer, it is stable for 31 days. Exposure to light reduces the drug's stability.

Small Animal Dosage

Dogs

- 2-6 mg/m² q24h initially, then q48h PO. (Equivalent dose is 0.1-0.2 mg/kg.)

Cats

- Immune-mediated disease: 0.1-0.2 mg/kg (approximately ½ tablet) q24h initially, then q48h PO.
- Inflammatory bowel disease: 2 mg per cat, q48-72h, PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Chloramphenicol

klor-am fen'ih-kole

Trade and other names: Chloramphenicol palmitate, Chloromycetin, Chloramphenicol sodium succinate, and generic brands

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Antibacterial drug. Mechanism of action is inhibition of protein synthesis via binding to ribosome. It has a broad spectrum of activity that includes gram-positive cocci, gram-negative bacilli (including *Enterobacteriaceae*), and Rickettsia. Chloramphenicol is usually regarded as a bacteriostatic drug and it is important to maintain drug concentrations above the MIC for as long as possible during the dosing interval. Chloramphenicol is well absorbed orally in most animals, except ruminants. The half-life is approximately 4 hours in dogs and 5 hours in cats but less than 1 hour in horses. After oral administration to foals, however, the half-life is 2.5 hours. The volume of distribution is approximately 1-2 L/kg in most animals. Chloramphenicol sodium succinate is an injectable solution converted to chloramphenicol by hepatic metabolism.

Indications and Clinical Uses

Antibacterial agent used to treat infections caused by a broad spectrum of organisms, including gram-positive cocci, gram-negative bacilli (including *Enterobacteriaceae*), anaerobic bacteria, and *Rickettsia*. Chloramphenicol has been used to treat infections caused by bacteria that are resistant to other common drugs (e.g., methicillin-resistant *Staphylococcus* species). Florfenicol acts via similar mechanism and has been substituted in some animals (see Florfenicol). Chloramphenicol is known for its ability to penetrate lipid membranes and has been used to penetrate tissues with barriers, such as the blood-brain barrier. However, efficacy for treating infections of the CNS has been poor.

Precautionary Information

Adverse Reactions and Side Effects

Bone marrow suppression is possible with high doses or prolonged treatment. This effect is possible in any species with prolonged use, but cats appear particularly susceptible. Bone marrow changes have been observed after 14 days of treatment in cats.

Contraindications and Precautions

Avoid use in pregnant or neonatal animals. Avoid long-term use in cats. Warn animal owners that human exposure to chloramphenicol may pose a risk. Exposure to small doses has caused aplastic anemia in people.

Drug Interactions

Chloramphenicol is a potent microsomal enzyme (cytochrome P450) inhibitor. By inhibiting P450 enzymes it will increase the concentrations of other drugs (e.g., barbiturates) and increase their risk of toxicity. Use cautiously with any other drug that requires metabolism for its clearance.

C

Instructions for Use

Chloramphenicol use is based on susceptibility data. Although rarely available commercially, chloramphenicol palmitate requires active enzymes and should not be administered to fasted (or anorectic) animal.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 4 mcg/mL for streptococci and ≤ 8 mcg/mL for other organisms.

Formulations

Chloramphenicol palmitate is available in a 30-mg/mL oral suspension. Chloramphenicol is available in 250-mg capsules and 100-, 250-, and 500-mg tablets. Chloramphenicol sodium succinate injection, although rarely available, is usually in a concentration of 100 mg/mL. Some forms of chloramphenicol are no longer available in the US.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Chloramphenicol palmitate is insoluble in water. Chloramphenicol is stable at pH of 2-7. Chloramphenicol sodium succinate is stable for 30 days at room temperature and 6 months if frozen.

Small Animal Dosage

Chloramphenicol and Chloramphenicol Palmitate

Dogs

- 40-50 mg/kg q8h PO.

Cats

- 12.5-20 mg/kg q12h PO, (or 50 mg per cat).

Chloramphenicol Sodium Succinate

Dogs

- 40-50 mg/kg q6-8h IV or IM.

Cats

- 12.5-20 mg/cat q12h IV or IM.

Large Animal Dosage

Horses

- 35-50 mg/kg q6-8h PO.

Regulatory Information

It is illegal to administer chloramphenicol to animals that produce food; therefore, there are no withdrawal times established.

Chlorothiazide

klor-oh-thye'ah-zide

Trade and other names: Diuril

Functional classification: Diuretic

Pharmacology and Mechanism of Action

Thiazide diuretic. The thiazide diuretics are used infrequently in veterinary medicine. They include hydrochlorothiazide and chlorothiazide. These drugs are sulfonamide analogs and share similar chemical properties, but the pharmacokinetics have not been very well described in animals. The action of thiazides is to inhibit the Na/Cl cotransporter in the luminal side of the distal tubule. By inhibiting the cotransporter, Na⁺ and Cl⁻ reabsorption is blocked, leading to sodium and water diuresis. Because the action occurs in the distal tubule, these drugs have less of a diuretic effect (less efficacy) than the loop diuretics.

Indications and Clinical Uses

Chlorothiazide use is not common in animals. In people it is used primarily to treat hypertension. In animals it has been used to treat hypercalciuria (increased calcium in the urine that may lead to urinary calculi).

Chlorothiazide inhibits sodium reabsorption in distal renal tubules to produce a more dilute urine.

Because it decreases renal excretion of calcium, it also has been used to prevent uroliths containing calcium. Dosage regimens used are derived either empirically or from extrapolation of the human dose.

Precautionary Information

Adverse Reactions and Side Effects

Chlorothiazide may cause electrolyte imbalance such as hypokalemia.

Contraindications and Precautions

These drugs enhance calcium absorption by decreasing intracellular sodium and enhance the Na⁺/Ca⁺⁺ exchange and decreasing Ca⁺⁺ excretion in urine. They should never be used in hypercalcemia.

Drug Interactions

Avoid administering calcium and vitamin D supplements.

Instructions for Use

Not as effective as high-ceiling diuretics (e.g., furosemide) for producing a diuresis.

Patient Monitoring and Laboratory Tests

Electrolytes should be monitored during chronic therapy.

Formulations

Chlorothiazide is available in 250- and 500-mg tablets, 50-mg/mL oral suspension, and injection vials of 500 mg (with mannitol).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Reconstituted solutions are stable for 24 hours.

Small Animal Dosage

Dogs and Cats

- 20-40 mg/kg q12h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

C

Chlorpheniramine Maleate

klor-fen-eer'ah-meen mal'ee-ate

Trade and other names: Chlortrimeton and Phenetron

Functional classification: Antihistamine

Pharmacology and Mechanism of Action

Antihistamine (H_1 -blocker). Similar to other antihistamines, it acts by blocking the H_1 receptor and suppresses inflammatory reactions caused by histamine. The H_1 -blockers have been used to control pruritus and skin inflammation in dogs and cats. Other commonly used antihistamines include clemastine, chlorpheniramine, diphenhydramine, cetirizine, and hydroxyzine.

Indications and Clinical Uses

Chlorpheniramine is used to prevent allergic reactions and for pruritus therapy in dogs and cats. However, success rates for treatment of pruritus have not been high. In addition to the antihistamine effect for treating allergies, these drugs block the effect of histamine in the vomiting center, vestibular center, and other centers that control vomiting in animals. Use in animals has been primarily derived from empirical use. There is a lack of well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Sedation is the most common side effect. Sedation is the result of inhibition of histamine N-methyltransferase. Sedation may also be attributed to block of other CNS receptors such as those for serotonin, acetylcholine, and alpha-receptors. Antimuscarinic effects (atropine-like effects) also are common, such as dry mouth and decreased GI secretions.

Contraindications and Precautions

Antimuscarinic effects (atropine-like effects) are common. Do not use in conditions for which anticholinergic drugs may be contraindicated, such as glaucoma, ileus, or cardiac arrhythmias.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Chlorpheniramine is included as an ingredient in many OTC cough, cold, and allergy medications.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

148 Chlorpromazine

Formulations

Chlorpheniramine maleate is available in 4- and 8-mg tablets, 2-mg chewable tablets, 2 mg/5-mL syrup, and 10-mg/mL vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Protect from freezing. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 4-8 mg/dog q12h PO; up to a maximum dose of 0.5 mg/kg q12h.

Cats

- 2 mg/cat q12h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Chlorpromazine

klor-proe'mah-zeen

Trade and other names: Thorazine and Largactil

Functional classification: Antiemetic, Phenothiazine

Pharmacology and Mechanism of Action

Phenothiazine tranquilizer/antiemetic. Chlorpromazine is a centrally acting dopamine antagonist. It inhibits action of dopamine as neurotransmitter, which may produce some central-acting effects similar to acepromazine and some antiemetic action.

Indications and Clinical Uses

Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Chlorpromazine is most often used as a centrally acting antiemetic for disorders that produce vomiting via a central-acting mechanism. It is also used for sedation and preanesthetic purposes, although acepromazine has been much more commonly used.

Precautionary Information

Adverse Reactions and Side Effects

Causes sedation. Like acepromazine, it also may cause alpha-adrenergic blockade and vasodilation, but this effect has not been as well documented as for acepromazine. It may produce anticholinergic effects in some animals. Although phenothiazines are reported to decrease the threshold for producing seizures in

some animals, this has not been shown in retrospective studies with acepromazine in animals and has not been reported specifically for chlorpromazine. Like other phenothiazines, it may produce extrapyramidal side effects (involuntary muscle movement) in some individuals. In horses it has produced undesirable side effects, including violent reactions.

Contraindications and Precautions

Use with caution in animals with seizure disorders and animals prone to hypotension. Avoid use in horses.

Drug Interactions

It will potentiate effects from other sedatives.

Instructions for Use

Chlorpromazine is used for vomiting caused by toxins, drugs, or GI disease. Higher doses than listed in dose section have been used with cancer chemotherapy (2 mg/kg q3h SQ).

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Chlorpromazine is available in a 25-mg/mL injection solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Slight discoloration does not affect stability. Some sorption (loss) occurs if stored in polyvinyl chloride (soft plastic) containers.

Small Animal Dosage

All Doses Listed Are a One-Time Injection

Dogs

- 0.5 mg/kg q6-8h IM or SQ.

Cats

- 0.2-0.4 mg/kg q6-8h, up to 0.5 mg/kg, q8h IM or SQ.

Large Animal Dosage

Horses: Avoid use.

Cattle

- 0.22 mg/kg IV or 1.1 mg/kg IM, single dose.

Sheep and Goats

- 0.55 mg/kg IV or 2.2 mg/kg IM, single dose.

Pigs

- 0.5 mg/kg IM, single dose.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Chlortetracycline

klor-tet' rah-sye-kleen

Trade and other names: Anaplasmosis block, Aureomycin soluble powder, Aureomycin tablets, Aureomycin soluble calf tablets, Calf Scour Bolus, Fermycin, and generic brands

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Tetracycline antibacterial drug. Inhibits bacterial protein synthesis by interfering with peptide elongation by ribosome. Chlortetracycline is a bacteriostatic agent with a broad spectrum of activity, which includes gram-positive bacteria and mycoplasma. Most gram-negative bacilli, particularly enteric bacteria (e.g., *E. coli*) of the *Enterobacteriaceae* will be resistant.

Indications and Clinical Uses

Broad-spectrum activity. It is used for routine infections and intracellular pathogens. However, chlortetracycline is poorly absorbed orally and other tetracyclines are preferred for systemic treatment of infections. The most common use for chlortetracycline is as a feed additive to control respiratory and enteric infections in livestock. The clinical use in small animals and horses is rare.

Precautionary Information

Adverse Reactions and Side Effects

Chlortetracycline may bind to bone and developing teeth in young animals. High doses have caused renal injury. Oral administration to horses may produce diarrhea.

Contraindications and Precautions

Avoid use in young animals, except where permitted by label for young pigs or cattle.

Drug Interactions

Chlortetracycline, like other tetracyclines, will bind to other cations orally administered, which will prevent its absorption. Oral absorption will be decreased if it is administered with products with calcium, zinc, aluminum, magnesium, or iron.

Instructions for Use

Chlortetracycline is not administered for systemic use in small animals. Doxycycline has replaced most other tetracyclines for treatment in small animals. Most chlortetracycline used is in powdered form and added to feed or drinking water of livestock.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 2 mcg/mL for streptococci and ≤ 4 for other organisms. Tetracycline is used as a marker to test susceptibility for other drugs in this class such as doxycycline, minocycline, and oxytetracycline.

Formulations

Chlortetracycline is available as a powdered feed additive in 25 g/lb or 64 g/lb. It is also available as an anaplasmosis block in 2.5 g/lb and in 25- and 500-mg tablets. (A range of concentrations exists for premix.)

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with ions that may chelate tetracyclines (calcium, magnesium, iron, aluminum, etc.).

Small Animal Dosage

Dogs and Cats

- 25 mg/kg q6-8h PO.

Large Animal Dosage

Cattle

- Prophylaxis for anaplasmosis: 0.36-0.7 mg/kg/day. (Approximately one block per 10 animals.)
- Tablets: 11 mg/kg q12h for 3-5 days PO.
- Powdered feed additive: 22 mg/kg/day added to water. Actual dose will be affected by feed and water consumption for each animal.

Pigs

- Powdered feed additive: 22 mg/kg/day added to water. Actual dose will be affected by feed and water consumption for each animal.

Regulatory Information

Cattle withdrawal time for meat: Withdrawal times vary from product to product from 1, 2, 5, or 10 days. Most products list a withdrawal time of 1 day for cattle.

Pig withdrawal time for meat: 1-5 days.

Note that for chlortetracycline, withdrawal times may vary considerably from one product to another. One should consult specific product packaging to determine exact withdrawal time.

Chondroitin Sulfate

kon-droy'ten sul'fate

Trade and other names: Cosequin and Glycoflex

Functional classification: Nutritional supplement

Pharmacology and Mechanism of Action

Nutritional supplement for patients with osteoarthritis. According to the manufacturer, and supported by some experimental evidence, chondroitin sulfate provides precursors to stimulate synthesis of articular cartilage and inhibits degradation and improves healing of articular cartilage.

Pharmacokinetic studies have produced conflicting results depending on formulation, species studied, and assay technique. Although some studies have demonstrated adequate oral absorption, there may be limited oral absorption of the intact large molecule. In dogs, oral absorption has been as low as 5%, but in horses absorption as high as 22% or 32% has been reported.

It is usually administered in combination with glucosamine. See Glucosamine section for further details.

Indications and Clinical Uses

Chondroitin sulfate is used primarily for treatment of degenerative joint disease and is usually found in formulations in combination with glucosamine. (See Glucosamine

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for additional details.) Analyses of published clinical studies in dogs have concluded that there is a moderate level of evidence to indicate some benefit in osteoarthritis, but results may be inconsistent among studies. Benefits of treatment in horses with lameness also have been reported from oral administration of chondroitin–glucosamine supplements.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported, although hypersensitivity is possible. Chondroitin is most often administered with glucosamine. See glucosamine for potential adverse effects.

Contraindications and Precautions

No contraindications have been reported.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Doses are based primarily on empiricism and manufacturer's recommendations. There are limited published trials of efficacy or dose titrations available to determine optimal dose. Doses listed are general recommendations and products available may vary.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Because several chondroitin sulfate formulations are available, veterinarians are encouraged to carefully examine product label to ensure proper strength. Veterinary dietary supplements can be highly variable in quality. One product (Cosequin) is available in regular-strength (RS) and double-strength (DS) capsules. RS capsules contain 250 mg glucosamine, 200 mg chondroitin sulfate and mixed glycosaminoglycans, 5 mg manganese, and 33 mg manganese ascorbate. The DS tablets contain double of each of these amounts.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Use the Cosequin RS and DS Strength as a General Guide

Dogs

- 1-2 RS capsules per day.
- 2-4 capsules of DS for large dogs.

Cats

- 1 RS capsule daily.

Large Animal Dosage

Horses: 12 mg/kg glucosamine, 3.8 mg/kg chondroitin sulfate twice daily PO for 4 weeks, then 4 mg/kg glucosamine, 1.3 mg/kg chondroitin sulfate thereafter.

It is common to initiate treatment in horses with a higher dose of 22 mg/kg glucosamine, 8.8 mg/kg chondroitin sulfate, daily PO.

Regulatory Information

Withdrawal times are not established for animals that produce food. Chondroitin sulfate and glucosamine are found naturally and withdrawal times may not be

necessary if these supplements are administered to food animals. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Cimetidine Hydrochloride

syə-met'ih-deen hye-droe-klor'ide

Trade and other names: Tagamet (OTC and prescription)

Functional classification: Antiulcer agent

Pharmacology and Mechanism of Action

Histamine₂ antagonist (H₂ blocker). Stimulation of acid secretion in the stomach requires activation of histamine type 2 receptors, gastrin receptors, and muscarinic receptors. Cimetidine and related H₂ blockers inhibit the action of histamine on the histamine H₂ receptor of parietal cells and inhibit gastric parietal cell gastric acid secretion. Cimetidine increases stomach pH to help heal and prevent gastric and duodenal ulcers.

Indications and Clinical Uses

Cimetidine is used to treat gastric ulcers and gastritis. Although it is often used for animals with vomiting, there are no efficacy data to indicate that it is effective. There also are no efficacy data to support its use for preventing nonsteroidal anti-inflammatory drug (NSAID)-induced bleeding and ulcers. In dogs, clinical efficacy is limited and other drugs (e.g., famotidine, ranitidine, and proton-pump inhibitors) are preferred for ulcer treatment. In horses, cimetidine has been used to prevent or treat GI ulcers. However, the efficacy for these indications has not been proved. For example, studies in horses showed that at 18 g/kg q8h PO, it did not cause healing of ulcers. The poor efficacy may be because of short duration of effect (2-6 hours). In horses, other drugs (e.g., ranitidine, and proton-pump inhibitors) are preferred for ulcer treatment. In calves, cimetidine will increase abomasal pH.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects usually seen only with decreased renal clearance. In people, CNS signs may occur with high doses.

Contraindications and Precautions

Use cautiously with drugs that rely on hepatic metabolism for clearance.

Drug Interactions

Cimetidine is a well-known cytochrome P450 enzyme inhibitor. It may increase concentrations of other drugs used concurrently (e.g., theophylline) because of inhibition of hepatic enzymes. Cimetidine will increase the pH of the stomach, which can inhibit oral absorption of some drugs (e.g., itraconazole and ketoconazole). Cimetidine will inhibit the oral absorption of iron supplements.

Instructions for Use

Efficacy for treating ulcers in animals has not been established. Frequent dosing may be necessary for suppression of stomach acid. Doses are derived from gastric secretory studies in experimental animals.

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Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Cimetidine is available in 100-, 150-, 200-, 300-, 400-, and 800-mg tablets, a 60-mg/mL oral solution, and a 150-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not store injection formulation in refrigerator. Solutions are stable for at least 14 days. Stable if mixed with various enteral products.

Small Animal Dosage

Dogs and Cats

- 10 mg/kg q6-8h IV, IM, or PO.
- Renal failure: 2.5-5 mg/kg q12h IV or PO.

Large Animal Dosage

Horses

- 3 mg/kg diluted in fluid solution and infused IV over 2 minutes, q8h.
- 40-60 mg/kg/day PO. However, oral doses in horses produce inconsistent results.

Calves

- Abomasal ulcers in milk-fed calves: 100 mg/kg q8h PO.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 5

Ciprofloxacin Hydrochloride

sip-roe-floks'ah-sin hye-droe-klor'ide

Trade and other names: Cipro and generic brands

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Fluoroquinolone antibacterial. Acts to inhibit DNA gyrase and cell DNA and RNA synthesis. Bactericidal. Broad antimicrobial activity. Ciprofloxacin is active against gram-negative bacilli, including *Enterobacteriaceae*, and some gram-positive cocci, including *Staphylococcus*. Ciprofloxacin is more active against *Pseudomonas aeruginosa* than other fluoroquinolones, but resistance is possible. Multi-resistant bacteria, including gram-negative bacilli of the *Enterobacteriaceae*, and methicillin-resistant strains of *Staphylococcus*, are likely to be resistant to ciprofloxacin and other fluoroquinolones. Oral absorption of ciprofloxacin has been reported in only a few limited studies. Estimates derived from independent studies in dogs indicate that oral absorption has ranged from a low value of 42% to as high as 74% or 97%, depending on the study. Oral absorption in horses is less than 10% and should not be used orally in horses. In cats oral absorption is low (22%-33%) and

would not be effective for gram-positive bacteria even at 10 mg/kg; but at 10 mg/kg q12h, it was able to reach therapeutic targets against susceptible gram-negative bacteria. Other fluoroquinolones registered for animals have near-complete bioavailability.

Indications and Clinical Uses

Ciprofloxacin, although a human drug, has been used in small animals for treatment of a wide variety of infections, including skin infections, pneumonia, and soft tissue infections. Ciprofloxacin is not registered for animals. However, it can be prescribed by veterinarians, as long as it is not administered to animals that produce food or are intended for food. The administration of ciprofloxacin to animals is considered extralabel and subject to other extralabel restrictions. The variable and potentially low ciprofloxacin oral availability for dogs and cats suggests that doses should be higher than the doses currently used for drugs such as enrofloxacin, marbofloxacin, or orbifloxacin.

Precautionary Information

Adverse Reactions and Side Effects

High concentrations may cause CNS toxicity, especially in animals with renal failure. Ciprofloxacin causes occasional vomiting. Intravenous solution should be given slowly (over 30 minutes). At high doses, it may cause some nausea, vomiting, and diarrhea. Blindness in cats has not been reported for ciprofloxacin. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most susceptible to quinolone-induced arthropathy in the age group of 4 weeks to 28 weeks of age. Large, rapidly growing dogs are the most susceptible. Administration to horses may cause severe enteritis and colic.

Contraindications and Precautions

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures, such as epileptics. It is not recommended to administer ciprofloxacin to horses.

Drug Interactions

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, and calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

Instructions for Use

Doses are based on plasma concentrations needed to achieve sufficient plasma concentration above minimum inhibitory concentration (MIC). Efficacy studies have not been performed in dogs or cats and clinical use is based primarily on anecdotal experience. Injectable ciprofloxacin is available in a human preparation, usually 10 mg/mL (in sterile water) or 2 mg/mL (premixed with 5% dextrose). Dilute the concentrated form to 1-2 mg/mL prior to intravenous use with an intravenous solution and infuse the final solution over 60 minutes. Do not infuse concurrently with other medications (e.g., in a piggyback) because inactivation may occur.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms has not been determined for animals, but for humans is ≤ 1.0 mcg/mL. Most susceptible

156 Cisapride

gram-negative bacteria of the *Enterobacteriaceae* have MIC values less than 0.1 mcg/mL. If ciprofloxacin is used to treat *Pseudomonas aeruginosa*, the in vitro activity can be higher than other veterinary fluoroquinolones. Otherwise, most bacteria that are susceptible to ciprofloxacin are also susceptible to other fluoroquinolones.

Formulations Available

Ciprofloxacin is available in 100-, 250-, 500-, and 750-mg tablets and 2-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Aqueous solutions of 0.5 to 2 mg/mL retain potency up to 14 days when stored. Do not mix with products that contain ions (e.g., iron, aluminum, magnesium, and calcium).

Small Animal Dosage

Dogs

- 20-25 mg/kg q24h PO.
- 10-15 mg/kg q24h IV.

Cats

- 20 mg/kg q24h, PO.
- 10 mg/kg q24h IV.

Large Animal Dosage

No dosing data available. Ciprofloxacin has poor oral absorption in horses (<10%) and is not recommended.

Regulatory Information

There are no withdrawal times established because this drug should not be administered to animals that produce food.

Cisapride

Siss'ah-pride

Trade and other names: Propulsid (Propulsid in Canada), not currently available commercially

Functional classification: Prokinetic agent

Pharmacology and Mechanism of Action

Prokinetic agent. Its mechanism is believed to be as an agonist for the 5-hydroxytryptamine (5-HT₄) receptor on myenteric neurons (5-HT₄ ordinarily stimulates cholinergic transmission in the myenteric neurons). It also acts as an antagonist for the 5-HT₃ receptor. Via this mechanism, or independently, cisapride may enhance release of acetylcholine at the myenteric plexus. Cisapride increases the motility of the stomach, small intestine, and colon. It accelerates the transit of contents in the bowel and intestines.

Indications and Clinical Uses

Cisapride is used to stimulate motility for treating gastric reflux, gastroparesis, ileus, and constipation. The most common uses in animals have been to prevent stomach regurgitation, decrease postoperative ileus, and treat constipation and megacolon in cats. It is not effective to stimulate motility in dogs with megacophagus. Cisapride was removed from the human market and is no longer commercially available.

Compounding pharmacies have made cisapride available to veterinarians in compounded forms (see Formulations section). However, these formulations are not licensed and are unregulated.

Precautionary Information

Adverse Reactions and Side Effects

Adverse cardiac effects have been reported in people and are the cause for discontinuation in human medicine. These cardiac effects have not been reported in animals. High overdoses in dogs (18 mg/kg) have produced abdominal pain, aggression, ataxia, fever, and vomiting. With higher overdoses, diarrhea, ataxia, and central nervous system reactions have been observed.

Contraindications and Precautions

Contraindicated in patients with GI obstruction.

Drug Interactions

Anticholinergic drugs, such as atropine, will diminish the action. Cisapride should not be used with drugs that inhibit metabolism (cytochrome P450 inhibitors) or drugs that inhibit P-glycoprotein. Toxicity may result (see list of drugs in Appendix).

Instructions for Use

Not currently available commercially. Cisapride was discontinued by the manufacturer in July 2000. However, some veterinary pharmacies can fill some orders or prepare compounded formulations for animals. Consult local compounding pharmacist about availability. Doses are based on extrapolation from human doses, experimental studies, and anecdotal evidence. Efficacy studies have not been performed in dogs or cats.

Patient Monitoring and Laboratory Tests

In humans, cardiac effects have been reported (arrhythmias). Monitor ECG in susceptible patients.

Formulations

Cisapride was once available in a 10-mg tablet but has been discontinued by the manufacturer. Formulations used are prepared by compounding from a pure source. To prepare 1 mg/mL injectable solution (follow USP <797> sterile compounding standards), mix 0.104 g of cisapride monohydrate with 20 mL tartaric acid 6% solution. Add sterile water to make up a 100-mL total volume. Keep the solution in the refrigerator, in a sterile vial, protected from light, and labeled with Beyond Use Date of 14 days postcompounding. A 10 mg/mL oral suspension (follow USP <795> compounding standards) has been prepared by mixing 300 mg (0.3 g) of cisapride monohydrate with 15 mL *Ora Plus* and enough *Ora Sweet* added to make a total of volume of 30 mL (*Ora Plus* and *Ora Sweet* are oral formulation suspending agents and vehicles commonly used in commercial pharmacies.)

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Some compounded formulations have been stable for 60 days if the pH is kept neutral. Injectable solution should be used within 14 days.

Small Animal Dosage

Dogs

- 0.1-0.5 mg/kg q8-12h PO, (up to 0.5-1.0 mg/kg).

Cats

- 2.5-5 mg/cat q8-12h PO (up to 1 mg/kg q8h).

Large Animal Dosage

Horses

- 0.1 mg/kg IV. (This formulation is not commercially available, but an intravenous form has been made by combining 40 mg with 1.0 mL of tartaric acid and diluted to obtain a total volume of 10 mL.)

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it poses a risk to humans.

Cisplatin

sis-plah'tin

Trade and other names: Platinol

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Cisplatin acts like a bifunctional alkylator of DNA but forms a reactive carbonium ion, and the cross-linking occurs around the platinum ion instead of an alkyl group. It preferentially binds to the N-7 of guanine and adenine bases. As a result of this reaction, interstrand and intrastrand cross-linking of DNA occurs. The result is inhibition of DNA synthesis. A related drug is carboplatin, which is a second-generation platinum compound used in patients who may not tolerate cisplatin.

Indications and Clinical Uses

Cisplatin is used for treating various solid tumors, including bronchiogenic carcinoma, osteosarcoma, transitional cell carcinoma, and mast cell tumors. It has been shown to be effective for increasing the survival of dogs that have undergone amputations for osteosarcoma.

Precautionary Information

Adverse Reactions and Side Effects

Nephrotoxicity is the most limiting factor to cisplatin therapy. In cats, it causes a dose-related, species-specific, primary pulmonary toxicosis. Vomiting is common in dogs with administration. Transient thrombocytopenia may occur in dogs. Cisplatin has caused potassium wasting and depletion of magnesium.

Contraindications and Precautions

Do not use in cats.

Drug Interactions

Cisplatin may be used with other cancer chemotherapy agents. Do not use with other nephrotoxic drugs.

Instructions for Use

To avoid toxicity, fluid loading before administration using sodium chloride should be performed. Antiemetic agents are often administered before therapy to decrease vomiting. For transitional cell and squamous cell carcinomas, doses used are 40 to 50 mg/m² every 21 to 28 days. For osteosarcoma, it has been used at a dose of 70 mg/m² every 21 days for four treatments.

Patient Monitoring and Laboratory Tests

Monitor renal function in treated animals. Monitor CBC in patients between treatments.

Formulations

Cisplatin is available in a 1-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 60-70 mg/m² q3-4wks IV (administer fluid for diuresis with therapy).

Cats

Do not use in cats.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food.

This drug should not be used in animals intended for food because it is an anticancer agent.

Clarithromycin

klah-rith'roe-mye'sin

Trade and other names: Biaxin and generic brands

Functional classification: Antibiotic

Pharmacology and Mechanism of Action

Macrolide antibiotic, with bacteriostatic activity. It is a substituted 14-carbon macrolide. Clarithromycin was introduced in 1990 as a substitute for erythromycin. Compared to erythromycin it has higher absorption, a longer half-life, and increased intracellular uptake. Site of action is similar to other macrolide antibiotics, which is the 50-S ribosomal subunit in susceptible bacteria. Spectrum includes primarily gram-positive bacteria. Resistance is expected for most gram-negative bacteria. Clarithromycin may have higher activity (lower MIC values) for many bacteria compared to erythromycin or azithromycin. Clarithromycin, like other macrolides, may have anti-inflammatory properties that are independent of the microbiologic effects (e.g., inhibit neutrophil and eosinophil inflammatory reaction). Clarithromycin metabolites may contribute to the activity, but these metabolites are not well-characterized in animals. Clarithromycin is widely

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distributed to intracellular and tissue sites with concentrations in most tissues—including the respiratory tract—exceeding the plasma concentration. In foals, half-life is 4.8-5.4 hours with a volume of distribution of 10.5 L/kg and clearance of 1.27 L/kg/hr. The oral absorption in foals is 57% with a maximum concentration of 0.5-0.9 mcg/mL.

Indications and Clinical Uses

Most common use in people is for treatment of *Helicobacter gastritis* and respiratory infections, where it has retained activity against most respiratory tract pathogens (e.g., *Streptococcus*, mycoplasma, chlamydia). In small animals, clarithromycin has been used for indications such as skin infections and respiratory infections. In foals, clarithromycin has been used for treatment of infections caused by *Rhodococcus equi* (in combination with rifampin) and produced better clinical success than azithromycin.

Precautionary Information

Adverse Reactions and Side Effects

The most common adverse effect from clarithromycin and related drugs is diarrhea and nausea. Many animals may develop soft feces or mild diarrhea. In studies in healthy foals, diarrhea was uncommon from oral doses and was self-limiting. However, if diarrhea becomes severe, treatment should be discontinued.

Contraindications and Precautions

Administer with caution to adult horses, ruminants, rodents, and rabbits because diarrhea and enteritis may develop. Use with caution in pregnant animals.

Drug Interactions

Many macrolide antibiotics are cytochrome P450 enzyme inhibitors and can decrease metabolism of other drugs. For example, in people, it increased digoxin concentrations. However, specific drug interactions of this nature have not been documented in animals.

Instructions for Use

Clarithromycin should be given twice daily to animals because of a short half-life and need for a long time above the minimum inhibitory concentration (MIC).

Patient Monitoring and Laboratory Tests

In absence of a specific value for clarithromycin, use susceptibility for erythromycin to guide use of clarithromycin. Although the CLSI-derived break point for susceptible bacteria is 1 mcg/mL, cures have been observed when treating respiratory pathogens with MIC values as high as 8 mcg/mL, which is attributed to high respiratory concentrations achieved. MIC values for *R. equi* were 0.12 mcg/mL. Organisms resistant to erythromycin and azithromycin will most likely be resistant to clarithromycin.

Formulations

Clarithromycin is available in 250- and 500-mg tablets and 25- and 50-mg/mL oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. 250-mg tablets have been dissolved in water (50 mL) and administered immediately

to foals orally. However, the long-term stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 7.5 mg/kg q12h PO.

Large Animal Dosage

Foals

- 7.5 mg/kg PO q12h PO (often combined with rifampin at 10 mg/kg q12h).

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Clemastine Fumarate

Klem'ass-teen fyoo'mar-ate

Trade and other names: Tavist, and generic brands

Functional classification: Antihistamine

Pharmacology and Mechanism of Action

Antihistamine (H_1 -blocker). Similar to other antihistamines, it acts by blocking the H_1 receptor and suppresses inflammatory reactions caused by histamine. The H_1 blockers have been used to control pruritus and skin inflammation in dogs and cats; however, success rates in dogs have not been high. Commonly used antihistamines include clemastine, chlorpheniramine, diphenhydramine, and hydroxyzine.

Indications and Clinical Uses

Used primarily for treatment of allergy. Some reports have suggested that clemastine is effective for pruritus in dogs. However, the half-life in dogs is short (3.8 hours), and it has rapid clearance. After oral administration the oral absorption is only 3% (20%-70% in humans). At a high dose of 0.5 mg/kg PO, it did not suppress intradermal skin reactions. This evidence suggests that oral administration may not be as effective in dogs as previously thought. Oral absorption studies in horses indicated that it is not absorbed when given orally (bioavailability was only 3%).

Precautionary Information

Adverse Reactions and Side Effects

Sedation is the most common side effect. Sedation is the result of inhibition of histamine N-methyltransferase. Sedation may also be attributed to block of other CNS receptors such as those for serotonin, acetylcholine, and alpha-receptors. Antimuscarinic effects (atropine-like effects) also are possible, such as dry mouth and decreased GI secretions.

Contraindications and Precautions

No contraindications reported for animals.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Clemastine fumarate is used for short-term treatment of pruritus in dogs. It may be more efficacious when combined with other anti-inflammatory drugs. Tavist syrup contains 5.5% alcohol.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Clemastine fumarate is available in 1.34-mg tablets (OTC), 2.64-mg tablets (prescription), and 0.1-mg/mL syrup.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 0.05-0.1 mg/kg q12h PO, up to 0.5-1.5 mg/kg q12h PO.
- Dogs < 10 kg in weight: 1/2 of tablet. (Dose based on q12h treatment and 1.34-mg tablet.)
- Dogs 10-25 kg in weight: 1 tablet. (Dose based on q12h treatment and 1.34-mg tablets.)
- Dogs >25 kg: 1.5 tablets. (Dose based on q12h treatment and 1.34-mg tablets.)
- 0.1 mg/kg IV.

Large Animal Dosage

Horses

- 50 mcg/kg (0.05 mg/kg) q8h IV. It is not absorbed orally in horses.

Regulatory Information

Do not administer to animals that produce food.

RCI Classification: 3

Clenbuterol

klen-byoo'ter-ole

Trade and other names: Ventipulmin

Functional classification: Bronchodilator, beta agonist

Pharmacology and Mechanism of Action

Beta₂-adrenergic agonist (beta₂/beta₁ ratio = 4.0). Bronchodilator. Stimulates beta₂ receptors to relax bronchial smooth muscle. It also may inhibit release of inflammatory mediators, especially from mast cells. Compared to terbutaline, it has lower efficacy because of lower intrinsic activity, and it is only a partial agonist. Clenbuterol differs from other beta agonists because it resists O-sulfate ester conjugation, which produces a longer half-life. It also has better oral absorption (83%) than other beta agonists in horses. In horses, the plasma half-life is 13 hours, but in urine it can be detected for 12 days. In addition to the effects on respiratory smooth muscle, clenbuterol also can produce repartitioning effects, which indicates

that it will stimulate development of more muscle and less fat. Because of this use, it has been abused in humans and used illegally in food-producing animals.

Indications and Clinical Uses

Clenbuterol is indicated for treatment of animals with reversible bronchoconstriction such as horses with recurrent airway obstruction (RAO), formerly called chronic obstructive pulmonary disease (COPD). Studies have demonstrated effects in horses, but there are no reports of use in other species. In horses, it can have repartitioning effects (producing less fat), but it has also decreased exercise capacity and increased rate of fatigue. It should not be used in animals intended for food.

Precautionary Information

Adverse Reactions and Side Effects

Clenbuterol may produce excessive beta-adrenergic stimulation at high doses (tachycardia and tremors). Arrhythmias occur at high doses. Chronic use may have adverse effects on cardiac function in healthy horses.

Contraindications and Precautions

Do not administer to animals intended for food. Veterinarians should be warned that clenbuterol is abused in humans for the purpose of muscle-building and weight loss. Subsequently, high doses in humans may cause cardiac toxicity, such as arrhythmias.

Drug Interactions

Because clenbuterol is a beta agonist, other adrenergic drugs will potentiate the action. In addition, beta-blocking drugs will decrease action. Use with caution with any other drug that may stimulate the heart.

Instructions for Use

Oral administration for horses. Clenbuterol has not been used in small animals. It is prohibited for use in animals intended for food.

Patient Monitoring and Laboratory Tests

Monitor heart rate in animals during treatment. Clenbuterol can be detected in urine for 12 days. Effective plasma concentrations are 500 pg/mL.

Formulations

Clenbuterol is available in 100- and 33-mL bottles of 72.5 mcg/mL syrup.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

No dose has been reported for small animals.

Large Animal Dosage

Horses

- Recurrent airway obstruction: 0.8 mcg/kg (0.008 mg/kg) twice daily PO. If initial dose is not effective, increase dose to two, three, and four times the initial dose, up to 3.2 mcg/kg. Duration of effect is approximately 6-8 hours.

Regulatory Information

There are no withdrawal times established because clenbuterol should not be administered to animals that produce food. In horses, clenbuterol can be detected in urine for 12 days. Although not an approved human drug, it is abused in humans for weight loss and muscle building.

RCI Classification: 3

Clindamycin Hydrochloride

klin-dah-mye'sin hye-droe-klar'ide

Trade and other names: Antirobe, Clindrops, Clindarobe, Clintabs, Clinsol, and generic (veterinary preparations) and Cleocin (human preparations)

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Antibacterial drug of the lincosamide class (similar in action to macrolides). It shares structural, microbiologic activity, and other properties with lincomycin. It inhibits bacterial protein synthesis via inhibition of bacterial ribosome. Clindamycin is bacteriostatic with a spectrum of activity primarily against gram-positive bacteria and anaerobes. Clindamycin, like the macrolide antibiotics, can concentrate in leukocytes and many tissues. Action of clindamycin is primarily against gram-positive organisms such as *Staphylococcus*, *Streptococcus*, and gram-positive rods such as *Corynebacterium*. Clindamycin also is active against mycoplasma and anaerobic organisms, although not all *Bacteroides* species are susceptible. Activity against *Toxoplasma* is controversial. In dogs the volume of distribution (VD) is 2.5 L/kg, the oral absorption is 73%, and the half-life is 4-4.5 hours after a dose of 5.5 mg/kg and 7-10 hours after a dose of 11 mg/kg.

Indications and Clinical Uses

Clindamycin is primarily used for gram-positive or anaerobic bacterial infections involving the skin, respiratory tract, or oral cavity. Resistance with *Staphylococcus* may occur. It is effective for some oral infections and anaerobic infections. It also has been used for *Mycoplasma* infections. Efficacy of clindamycin for treating toxoplasmosis is controversial. Some studies have shown that clindamycin improved clinical signs, but it did not resolve the infection. Another study showed that clindamycin inhibited killing of *Toxoplasma* organisms by leukocytes.

Precautionary Information

Adverse Reactions and Side Effects

Oral clindamycin hydrochloride has been associated with esophageal lesions in cats. Oral liquid product may be unpalatable to cats, possibly because of the high alcohol content (8.6%). High doses have caused vomiting and diarrhea in cats. Clindamycin may alter bacterial population in intestine and cause diarrhea. Enteritis and diarrhea can be particularly serious in horses and ruminants.

Contraindications and Precautions

Do not administer to rodents or rabbits because it may cause diarrhea. Do not administer orally to horses or ruminants because diarrhea, enteritis, and perhaps

death can result. The oral liquid (Antirobe) contains 8.6% ethyl alcohol, which may be unpalatable to cats.

Drug Interactions

Clindamycin injection should not be mixed with other drugs in the same vial, syringe, or IV line.

Instructions for Use

Most doses are based on manufacturer's drug approval data and efficacy trials. Although every-12-hour frequency is recommended most often for dogs, there are studies that demonstrate efficacy when administered at 11 mg/kg every 24 hours for treatment of pyoderma. An injectable formulation is also available (Cleocin), which is clindamycin phosphate. This may be injected either IV or IM. If administering clindamycin IV, it should be diluted and administered by slow infusion (30-60 minutes). Dilution is usually 10:1 in 0.9% saline. It contains benzyl alcohol, and this vehicle has produced toxic reactions in young infants (and perhaps small animals).

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is ≤ 0.25 mcg/mL for streptococci and ≤ 0.5 mcg/mL for other organisms.

Formulations

Clindamycin is available in oral liquid (Aquadrops) 25 mg/mL, 25, 75, 150, and 300 mg capsules, 25, 75, and 150 mg tablets and 150 mg/mL injection (Cleocin).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Protect from freezing. Reconstituted solutions are stable for 2 weeks. Stability of compounded formulations is at least 60 days.

Small Animal Dosage

Dogs

- Staphylococcal infections: 11 mg/kg q12h PO or 22 mg/kg q24h PO. (Label dose for dogs is 5.5-33 mg/kg q12h PO.)
- Refractory infections: Doses up to 33 mg/kg q12h PO.
- Anaerobic infections and periodontal infections: 11-33 mg/kg q12h PO.
- 10 mg/kg q12h IV or IM. (For IV use, it should be diluted and administered by slow infusion.)

Cats

- 5.5 mg/kg q12h or 11 mg/kg q24h PO. (Label dose for cats is 11-33 mg/kg q24h, PO.)
- Refractory infections: Doses up to 33 mg/kg q24h PO.
- Anaerobic infections and periodontal infections: 11-33 mg/kg q24h PO.
- Toxoplasmosis: 12.5 mg/kg, up to 25 mg/kg q12h for 4 weeks PO (see Indications and Clinical Use section).
- 10 mg/kg q12h IV or IM. (For IV use, it should be diluted and administered by slow infusion.)

Large Animal Dosage

Do not administer clindamycin orally to large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Clofazimine

kloe-fah'zih-meen

Trade and other names: Lamprene

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Antimicrobial agent used to treat feline leprosy. It produces a slow bactericidal effect on *Mycobacterium leprae*.

Indications and Clinical Uses

Clofazimine has had limited use in veterinary medicine. Its use is limited to treating infections caused by *Mycobacterium*, such as feline leprosy.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in cats. In people, the most serious adverse effects are gastrointestinal.

Contraindications and Precautions

No contraindications reported for animals.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Doses based on empiricism or extrapolation of human studies.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Clofazimine is available in 50- and 100-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Cats

- 1 mg/kg up to a maximum of 4 mg/kg/day PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Clomipramine Hydrochloride

kloe-mip'rah-meen hye-droe-klor'ide

Trade and other names: Clomicalm (veterinary preparation) and Anafranil (human preparation)

Functional classification: Behavior modification

C

Pharmacology and Mechanism of Action

Tricyclic antidepressant drug (TCA). Used in people to treat anxiety and depression. Action is via inhibition of uptake of serotonin at presynaptic nerve terminals. Beneficial effects may be caused primarily by blocking reuptake of serotonin and modulation of serotonin in areas of the brain that affect anxiety and behavior. Clomipramine has more serotonin-reuptake blocking effects than other TCA drugs. Side effects result from antimuscarinic effects caused by the active metabolite desmethylclomipramine. However, animals produce less of this metabolite than people do.

Indications and Clinical Uses

Like other TCAs, clomipramine is used in animals to treat various behavioral disorders, including obsessive-compulsive disorders (also called canine compulsive disorder) and separation anxiety. In dogs, it has been superior to amitriptyline for treating compulsive disorders; however, it does not appear to be beneficial when used for dominance-related aggression. In cats, with long-term treatment it has been effective for decreasing urine spraying (*J Am Vet Med Assoc*, 226: 378-382, 2005). It was equally effective as fluoxetine for urine spraying in cats, but treated animals returned to urine marking abruptly after drug was discontinued. It has not been effective for psychogenic alopecia in cats.

Precautionary Information

Adverse Reactions and Side Effects

Reported adverse effects include sedation and reduced appetite. Clomipramine has a bitter taste. Other side effects associated with TCAs are antimuscarinic effects (dry mouth, rapid heart rate, and urine retention) and antihistamine effects (sedation). In cats, sedation and weight gain have been observed. For clomipramine, antimuscarinic effects may be caused by an active metabolite. Clomipramine can decrease total T4 and free-T4 thyroid concentrations in dogs, but it may still be within normal reference ranges. Overdoses can produce life-threatening cardiotoxicity. If an overdose occurs, immediately contact a poison control center. In trials performed in cats, no significant adverse effects were observed.

Contraindications and Precautions

Use cautiously in patients with heart disease.

Drug Interactions

Do not use with other behavior-modifying drugs such as serotonin reuptake inhibitors. Do not use with monoamine oxidase inhibitors (MAOIs), such as selegiline or amitraz.

Instructions for Use

When adjusting doses, one may initiate therapy with a low dose and increase gradually. There may be a 2-4 week delay after initiation of therapy before beneficial effects are observed. After achieving a favorable response, the dose can be gradually lowered in some animals. In cats, doses of 1.25 to 2.5 mg per cat have been administered once daily for psychogenic alopecia. In cats, up to 5 mg once a day has been used for urine spraying.

Patient Monitoring and Laboratory Tests

Monitor animal's heart rate and rhythm periodically during treatment. Like other TCAs, clomipramine may decrease total T4 and free-T4 concentrations in dogs.

Formulations

Clomipramine is available in 20-, 40-, and 80-mg tablets (veterinary preparation) and 25-, 50-, and 75-mg capsules (human preparation).

Stability and Storage

Store at room temperature. Protect from moisture. It has been compounded in a tuna-flavored liquid for cats without a decrease in efficacy.

Small Animal Dosage

Dogs

- 1-3 mg/kg/day q12h PO. Start at lower dose and gradually increase. Increases in dose should be made approximately every 14 days until desired effect is observed.

Cats

- 1-5 mg per cat q12-24h PO (0.5 mg/kg per day) and gradually increase.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Clonazepam

kloe-nah'zih-pam

Trade and other names: Klonopin and generic brands

Functional classification: Anticonvulsant

Pharmacology and Mechanism of Action

Benzodiazepine. Action is to enhance inhibitory effects of GABA in the central nervous system. Via GABA effects, it has anticonvulsant action, sedative properties, and effects on some behavioral disorders.

Indications and Clinical Uses

Clonazepam has been used as an anticonvulsant in dogs and cats. As a benzodiazepine, it also is used to treat behavior problems in dogs and cats, particularly those associated with anxiety. Tolerance may develop to the anticonvulsant effects with long-term use.

Precautionary Information

Adverse Reactions and Side Effects

Side effects include sedation and polyphagia. Some animals may experience paradoxical excitement.

Contraindications and Precautions

No contraindications reported for animals.

Drug Interactions

No drug interactions are reported in animals. However, it will potentiate effects from other sedatives and CNS depressants.

C

Instructions for Use

Doses are based primarily on reports from human medicine, empiricism, or experimental studies. No clinical efficacy studies have been performed in dogs or cats. Doses as low as 0.1-0.2 mg/kg have been used in animals susceptible to the higher doses listed in the dosage section.

Patient Monitoring and Laboratory Tests

Samples of plasma or serum may be analyzed for concentrations of benzodiazepines. However, many veterinary laboratories may not have this capability and laboratories that analyze human samples may be nonspecific for benzodiazepines.

Formulations

Clonazepam is available in 0.5-, 1-, and 2-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Clonazepam, like other benzodiazepines, will exhibit adsorption to plastic, especially soft plastic (polyvinyl chloride). Compounded oral products are stable for 60 days.

Small Animal Dosage

Dogs

- 0.5 mg/kg q8-12h PO.

Cats

- 0.1-0.2 mg/kg q12-24h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Schedule IV controlled drug

RCI Classification: 2

Clopidogrel

kloe-pid'oh-grel

Trade and other names: Plavix

Functional classification: Antiplatelet drug

Pharmacology and Mechanism of Action

Clopidogrel is a platelet inhibitor. It is a thienopyridine and inhibits adenosine diphosphate (ADP) receptor-mediated platelet activity. A related drug is ticlopidine. Because this mechanism is different from the aspirin-inhibiting effect on platelets, clopidogrel is more effective than aspirin alone and has been used concurrently with aspirin. Clopidogrel is metabolized to an active metabolite that exerts its antiplatelet effect. In cats, clopidogrel produced antiplatelet effects that persisted for 3 days after discontinuation of the drug. Clopidogrel administration also decreased serotonin release from platelets in cats, which may be important because serotonin release may contribute to clinical signs of thromboemboli in cats. In dogs and horses, oral administration has produced significant inhibitory effects on platelets that are superior to aspirin.

Indications and Clinical Uses

Clopidogrel is used to inhibit platelets in patients that are prone to forming blood clots. In patients with a high risk for thrombi and emboli, clopidogrel will inhibit mechanisms that are not effected by aspirin alone. A similar drug is ticlopidine (Ticlid) which should not be used in cats because it produces adverse reactions. In cats clopidogrel has been recommended to prevent cardiogenic arterial thromboembolism associated with cats with heart disease. In dogs it has been used to prevent embolism caused by heartworm disease and other conditions. In dogs, at a dose of either 0.5 or 1.0 mg/kg, decreased ADP-induced platelet aggregation occurs for 3 days after discontinuation of drug administration in some dogs and longer than 7 days in others. At 2 mg/kg orally, q24h, clopidogrel significantly suppressed platelet activity in horses, which persisted for 6 days after the last dose.

Precautionary Information

Adverse Reactions and Side Effects

Bleeding in susceptible patients. No adverse effects have been identified in cats, but in people pruritus and skin rash have been reported.

Contraindications and Precautions

Do not use in patients that have a high risk of bleeding.

Drug Interactions

Use cautiously with other drugs that may inhibit blood clotting.

Instructions for Use

Administer with, or without, aspirin in patients prone to thrombi and emboli. The dose in cats of 19 mg is approximately one fourth of a human tablet. It is likely that smaller doses are effective, but they have not been evaluated because it is impractical to divide the human 75-mg tablet into fractions smaller than one fourth.

Patient Monitoring and Laboratory Tests

Monitor for bleeding.

Formulations

Clopidogrel is available in 75-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Cats

- 19 mg per cat (1/4 tablet) q24h PO.
(Smaller doses may be effective but have not been evaluated in cats.)

Dogs

- 0.5 or 1 mg/kg q24h, PO.
An oral loading dose may be given at 2-4 mg/kg followed by 1 mg/kg q24h, PO. (In some cases, a higher oral loading dose of 10 mg/kg has been used.)

Large Animal Dosage

Horses

- 2 mg/kg, PO, q24h.

Regulatory Information

Do not administer to animals that produce food.

Cloprostenol Sodium

Kloe pros' te nole

Trade and other names: Estrumate, estroPLAN

Functional classification: Prostaglandin

Pharmacology and Mechanism of Action

Cloprostenol is a synthetic prostaglandin, structurally related to PGF₂-alpha, that produces PGF₂-alpha effects. Synthetic prostaglandins are much more potent than natural prostaglandins, and one should not use these at the same dose as natural prostaglandins. Prostaglandin F₂ analogues have a direct luteolytic action on the corpus leuteum. After injection, cloprostenol causes functional regression of the corpus luteum (Luteolysis). In nonpregnant cycling cattle, this effect will result in starting estrus 2 to 5 days after injection. In pregnant animals, it will terminate pregnancy. In animals with prolonged luteal activity that have pyometra, mummified fetus, or luteal cysts, the luteolysis usually results in resolution of the problem and return to normal cycling.

Indications and Clinical Uses

Cloprostenol has been used in cattle to induce luteolysis (beef and dairy cattle) to manipulate the timing of the estrus cycle to benefit breeding management practices. It also can be used to terminate pregnancy resulting from undesired mating and to treat conditions associated with prolonged luteal function (e.g., pyometra, luteal cysts). Cloprostenol has been used to terminate pregnancy in any animal that forms a corpus luteum. Most reports on successful termination of pregnancy have been performed on cattle, horses, and dogs. In dogs, cloprostenol has been administered in combination with other drugs (e.g., cabergoline [Dostinex] and bromocriptine [Parlodel]) to terminate pregnancy. When used to terminate pregnancy, it has been almost 100% effective. In horses, it has been administered to induce premature labor in the last 2-4 weeks of pregnancy.

Precautionary Information

Adverse Reactions and Side Effects

Induces abortion in pregnant animals. High doses in cattle (50 and 100× dose) have caused discomfort, milk letdown, and some frothing. There are no long-term effects on fertility. Endometritis can occur in some animals after treatment for pyometra. When used to treat pyometra in dogs, panting, vomiting, nausea, and diarrhea can be seen 15-45 minutes after injection. In dogs, for termination of pregnancy, side effects have been mild but may include vomiting, nausea, and panting, occurring shortly after the injection and lasting for approximately 15-20 minutes. To avoid vomiting, it is recommended to wait 8 hours after feeding. Abortion may be followed by 1 week (approximately) of mucoid vulvar discharge. Mammary enlargement and mild milk production may occur in some dogs.

Contraindications and Precautions

Synthetic prostaglandins are much more potent than natural prostaglandins, so observe doses carefully to avoid overdose of the synthetic forms. Handle with caution. Cloprostenol can be absorbed through intact skin, so human exposure should be avoided. It is recommended that all women should avoid handling cloprostenol. Humans with respiratory problems should avoid contact with cloprostenol because it can induce an asthma reaction.

Instructions for Use

Give injections to cattle IM. When cloprostenol is injected in cattle, return to estrus activity usually occurs in 3 to 5 days, at which time animals may be inseminated. In some cases, a second injection may be given 11 days after the first injection (double-injection plan), with estrus occurring at 2-5 days after the second injection. When used to terminate pregnancy in cattle, it can be used any time from day 7 to 5 months after breeding, and the fetus is expelled usually after 4-5 days. In dogs it has been used to terminate pregnancy approximately 30-40 days after breeding. In dogs, when used to terminate pregnancy, it has been used in combination with other drugs (bromocriptine or cabergoline) to allow for a lower dose of 1 mcg/kg, which has fewer side effects. Administer cloprostenol at least 8 hours after feeding to avoid vomiting.

Patient Monitoring and Laboratory Tests

Monitor for continued vulvar discharge after treatment. Measurement of serum progesterone may be used to monitor therapy, especially if termination of abortion is prolonged.

Formulations

Cloprostenol is available in an injectable aqueous solution containing 250 mcg cloprostenol/mL. Dilution in saline is recommended for accurate dosing to dogs.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated, but prior to injection in small animals, it may be diluted with saline solution.

Small Animal Dosage

Dogs (terminate pregnancy):

- 1 to 2.5 mcg/kg once daily SQ, for 4 to 5 days, starting on day 25 after mating. (Side effects are lower with 1 mcg/kg.)

- Starting 35-45 days after mating, administer 1 mcg/kg SQ (after 10-fold dilution in saline) on days 1 and 3 of treatment. It can be administered with cabergoline (Galastop) 5 mcg/kg oral q24h on days 1 through 7 of treatment.
- 1 mcg/kg q48h SQ, administered with bromocriptine. (see Bromocriptine for additional information.)

Large Animal Dosage

Cattle: 2 mL (500 mcg) IM, once, or repeated again 11 days after the first injection.

Horses: (Terminate pregnancy) 2 mL (500 mcg) per horse, IM. In some conditions, repeated injections are administered (e.g., every 12 hours). To induce premature labor in the last 2-4 weeks of pregnancy, administer two doses 30 minutes apart (oxytocin also is used for this indication). For endometritis, 250 mcg (1 mL) IM twice, 12 hours apart, usually combined with oxytocin.

Regulatory Information

To be used only by licensed veterinarians. No withdrawal times are listed on approved label for food animals.

Clorazepate Dipotassium

klor-az'eh-pate dye-poe-tah'see-um

Trade and other names: Tranxene and generic

Functional classification: Anticonvulsant

Pharmacology and Mechanism of Action

Benzodiazepine. Clorazepate is one of the active metabolites of diazepam, producing similar effects as diazepam but longer acting. After oral absorption it is quickly converted to the active drug, referred to as nordiazepam or desmethyldiazepam. Similar to diazepam and other benzodiazepines, its action is to enhance inhibitory effects of GABA in the central nervous system.

Indications and Clinical Uses

Clorazepate is used for antiseizure action, sedation, and treatment of some behavioral disorders. It has been used in dogs and cats when other drugs are not effective. It has been used in refractory epileptics, but tolerance may develop to the anticonvulsant effects with long-term use.

Precautionary Information

Adverse Reactions and Side Effects

Side effects include sedation and polyphagia. Some animals may experience paradoxical excitement. Chronic administration may lead to dependence and a withdrawal syndrome if discontinued.

Contraindications and Precautions

No serious contraindications. In rare individuals, benzodiazepines have caused paradoxical excitement. They may cause fetal abnormalities early in pregnancy, but this has not been reported with veterinary use.

Drug Interactions

No drug interactions are reported in animals. However, it will potentiate effects from other sedatives and CNS depressants.

Instructions for Use

Doses are based primarily on reports from human medicine, empiricism, or experimental studies. Higher doses may be used for short-term treatment of noise phobia. However, for most indications, no clinical efficacy studies have been performed in dogs or cats. Clorazepate tablets degrade quickly in the presence of light, heat, or moisture.

Patient Monitoring and Laboratory Tests

Samples of plasma or serum may be analyzed for concentrations of benzodiazepines. Plasma concentrations in the range of 100-250 ng/mL have been cited as the therapeutic range for people. Other references have cited this range as 150 to 300 ng/mL. However, there are no readily available tests for monitoring in many veterinary laboratories. Laboratories that analyze human samples may have nonspecific tests for benzodiazepines. With these assays, there may be cross-reactivity among benzodiazepine metabolites.

Formulations Available

Clorazepate is available in 3.75-, 7.5-, 11.25-, and 15-mg tablets.

Stability and Storage

Keep in original packaging or store in tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 0.5-2 mg/kg q8-12h PO, and as frequently as 4 hours.

Cats

- 0.2-0.4 mg/kg q12-24h, up to 0.5-2.2 mg/kg, q12h, PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 2

Cloxacillin Sodium

kloks-ah-sill'in soe'dee-um

Trade and other names: Cloxapen, Orbenin, and Tegopen

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Inhibits bacterial cell wall synthesis by binding to penicillin-binding proteins. Cloxacillin is similar in spectrum and activity as amoxicillin, except that it is resistant to the beta-lactamase enzyme produced by *Staphylococcus*. The spectrum is limited to gram-positive bacteria, especially staphylococci. Methicillin-resistant *Staphylococcus* species are resistant to cloxacillin.

Indications and Clinical Uses

The spectrum of cloxacillin includes gram-positive bacilli, including beta-lactamase-producing strains of *Staphylococcus*. Therefore, it has been used to treat

staphylococcal infections in animals, including pyoderma. Because of the availability of other beta-lactam drugs for treating gram-positive infections such as those caused by *Staphylococcus*, cloxacillin is used infrequently in small animals.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects of penicillin-drugs are most commonly caused by drug allergy. This can range from acute anaphylaxis when administered to other signs of allergic reaction when other routes are used. When administered orally (especially with high doses), diarrhea is possible.

Contraindications and Precautions

Use cautiously in animals allergic to penicillin-like drugs.

Drug Interactions

No drug interactions are reported in animals. However, do not mix with other drugs because inactivation may result.

Instructions for Use

Doses based on empiricism or extrapolation from human studies. No clinical efficacy studies available for dogs or cats. Oral absorption is poor; if possible, administer on an empty stomach.

Patient Monitoring and Laboratory Tests

Culture and sensitivity testing: Use oxacillin as a guide for sensitivity testing.

Formulations

Cloxacillin is available in 250- and 500-mg capsules and 25-mg/mL oral solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 20-40 mg/kg q8h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Dairy cows (intramammary use) withdrawal time for milk: 30 days for dry-cow treatment.

Cattle withdrawal time for meat: 10 days for meat and 48 hours for milk for the lactating cow treatment.

Codeine

Koe'deen

Trade and other names: Generic, codeine phosphate, and codeine sulfate

Functional classification: Analgesic, opioid, antitussive

Pharmacology and Mechanism of Action

Opiate agonist, analgesic. Mechanism is similar to morphine, except with approximately 1/10 potency of morphine. Codeine is extensively metabolized. In dogs, oral absorption is low (<5%) but it is rapidly converted to other metabolites that may have analgesic activity, such as glucuronidated forms of codeine. The activity of codeine and perhaps some active metabolites is to bind to mu receptors and kappa-opiate receptors on nerves and inhibit release of neurotransmitters involved with transmission of pain stimuli (such as Substance P). It also may inhibit release of some inflammatory mediators. Central sedative and euphoric effects are related to mu-receptor effects in brain.

Indications and Clinical Uses

Codeine, or codeine with acetaminophen, is indicated for treatment of moderate pain. It also has been used as an antitussive. Despite the widespread use of codeine in humans, the efficacy in animals for its antitussive or analgesic use has not been established. Oral absorption in dogs is low. Because a small portion of codeine is converted to morphine (only 10% in people) and duration of morphine is short in dogs, the clinical effectiveness of codeine in dogs may be questionable.

Precautionary Information

Adverse Reactions and Side Effects

Like all opiates, side effects from codeine are predictable and unavoidable. Side effects include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses.

Contraindications and Precautions

Schedule II controlled substance. Tolerance and dependence occurs with chronic administration. High doses (60-mg tablet with acetaminophen) can cause sedation in dogs. Cats are more susceptible to excitement than other species. Some codeine formulations may contain other ingredients (e.g., acetaminophen) that should not be administered to cats.

Drug Interactions

No drug interactions are reported in animals. However, it will potentiate effects from other sedatives and CNS depressants.

Instructions for Use

Available as codeine phosphate and codeine sulfate oral tablets. Doses listed for analgesia are considered initial doses; individual patients may need higher doses depending on degree of tolerance or pain threshold. When administering acetaminophen-codeine combinations, the high-dose tablet (containing 60-mg codeine) tends to cause sedation in dogs (body weight 20-30 kg) and the lower dose (containing 30 mg) is recommended.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, if necessary, atropine can be administered. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

Formulations

Codeine is available in 15-, 30-, and 60-mg tablets, 5-mg/mL syrup, and 3-mg/mL oral solution. It is also available in formulations with acetaminophen.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Analgesia: 0.5-1 mg/kg q4-6h PO.
- Antitussive: 0.1-0.3 mg/kg q4-6h PO.

Cats

- Analgesia: 0.5 mg/kg q6h PO. Increase dose as needed to control pain.
- Antitussive: 0.1 mg/kg q6h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Drug controlled by DEA. Schedule II; some antitussive forms are Schedule V. RCI Classification: 1

Colchicine

Kol' chih-seen

Trade and other names: Colcryls and generic brands

Functional classification: Anti-inflammatory agent

Pharmacology and Mechanism of Action

Anti-inflammatory agent. It inhibits fibrosis and formation of collagen.

Indications and Clinical Uses

In people, colchicine is used to treat gout. In animals it has been used as an antifibrotic agent to decrease fibrosis and development of hepatic failure (possibly by inhibiting formation of collagen). Anti-inflammatory effects may be caused from inhibition of neutrophil and mononuclear migration. Antifibrotic effects result from blockage of microtubular-mediated transcellular movement of proteins and to inhibit secretion of procollagen molecules into the extracellular matrix. It has also been used in animals to control amyloidosis. In Shar Pei dogs, colchicine has been used to treat a fever syndrome, possibly because of its use in people for treating Mediterranean fever.

Precautionary Information

Adverse Reactions and Side Effects

Most common adverse effects are nausea, abdominal pain, and diarrhea. Colchicine may cause dermatitis in people, but this has not been reported in dogs or cats.

Contraindications and Precautions

Do not administer to pregnant animals.

Drug Interactions

There are no drug interactions reported for small animals.

178 Colony-Stimulating Factors: Sargramostim and Filgrastim

Instructions for Use

Doses based on empiricism. There are no well-controlled efficacy studies in veterinary species.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Colchicine is available in 600-mcg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 0.01-0.03 mg/kg q24h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Colony-Stimulating Factors: Sargramostim and Filgrastim

Trade and other names: Leukine and Neupogen

Functional classification: Hormone

Pharmacology and Mechanism of Action

Stimulates granulocyte development in bone marrow. Two drugs in this class include filgrastim (rG-CSG) and sargramostim (rGM-CSF).

Indications and Clinical Uses

Colony-stimulating factors are used primarily to regenerate blood cells to recover from cancer chemotherapy or other bone marrow-suppressing therapy. Their use is uncommon in animals.

Precautionary Information

Adverse Reactions and Side Effects

Pain at injection site. Edema has been reported in people.

Contraindications and Precautions

There are none identified in small animals.

Drug Interactions

There are no drug interactions reported for small animals.

Instructions for Use

Doses are based on limited experimental information and extrapolations from human experience. To prepare sargramostim, add 1 mL to make up 250 mcg/mL

or 500 mcg/mL vial. Dilute further with 0.9% saline solution to less than 10 mcg/mL for infusion. Do not shake vial to prevent foaming; gently swirl vial to mix contents.

Patient Monitoring and Laboratory Tests

Monitor CBC to assess treatment. Treatment can be discontinued when neutrophils recover.

Formulations

Colony-stimulating factors are available in 300 mcg/mL (Neupogen) and 250 and 500 mcg/mL (Leukine).

Stability and Storage

Store in a tightly sealed container protected from light.

Small Animal Dosage

Dogs and Cats

Sargramostim: 250 mcg/m² (0.25 mg/m²) IV infusion over 2 hours, or SQ.

Filgrastim: 5 mcg/kg (0.005 mg/kg) once daily, SQ, for 2 weeks, or 10 mcg/kg/day.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Corticotropin

kor-tih-koe-troe'pin

Trade and other names: Acthar

Functional classification: Hormone

Pharmacology and Mechanism of Action

Corticotropin (ACTH). Corticotropin is a natural peptide hormone, composed of 39 amino acids. The formulation is prepared into a gel for injection. It stimulates normal synthesis of cortisol and other hormones from adrenal cortex.

Indications and Clinical Uses

ACTH is used for diagnostic purposes to evaluate adrenal gland function. Another closely related synthetic product, cosyntropin, is used for the same purpose. The availability of Acthar gel has been limited, and cosyntropin is often used as a substitute. Compounded formulations may not be equivalent.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects unlikely when used as single injection for diagnostic purposes.

Contraindications and Precautions

Do not administer IV.

Drug Interactions

There are no drug interactions reported for small animals.

Instructions for Use

Doses are established by measuring normal adrenal response in animals. See also Cosyntropin, which is sometimes preferred for clinical use. However, availability and cost of cosyntropin and ACTH are the factors that usually determine which is used in small animals.

Patient Monitoring and Laboratory Tests

Monitor cortisol concentrations. Post-ACTH cortisol response should be as follows:

Dogs 5.5-20.0 mcg/dL; > 20 mcg/dL is consistent with hyperadrenocorticism.

Cats 4.5-15 mcg/dL; > 15 mcg/dL is consistent with hyperadrenocorticism.

Following treatment for hyperadrenocorticism (e.g., treatment with mitotane) response should be 1-5 mcg/dL.

Formulations

ACTH is available in 80 units (International Units)/mL gel.

Stability and Storage

Store in a tightly sealed container protected from light.

Small Animal Dosage

Dogs

- ACTH response test: Collect pre-ACTH sample and inject 2.2 sample and inject 2.2 units (IU)/kg IM. Collect post-ACTH sample post-ACTH sample at 2 hours.

Cats

- ACTH response test: Collect pre-ACTH sample and inject 2.2 units (IU)/kg IM. Collect post-ACTH sample at 1.5 and 2 hours.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No withdrawal times are available. Because clearance is rapid and there is little risk from residues, no withdrawal time is suggested for food animals.

Cosyntropin

koe-sin-troe'pin

Trade and other names: Cortrosyn, Synthetic corticotropin, Tetracosactrin, and Tetracosactide

Functional classification: Hormone

Pharmacology and Mechanism of Action

Cosyntropin is a synthetic form of the peptide hormone corticotropin (ACTH).

It is also known in international formularies as Tetracosactrin or Tetracosactide.

Cosyntropin is an aqueous solution, whereas ACTH is a gel. Therefore cosyntropin

can be administered IV, but ACTH gel cannot. Cosyntropin is also more potent than ACTH. Administration of cosyntropin will stimulate secretion of cortisol from

adrenal glands. Administration of cosyntropin also will stimulate secretion of sex hormones of adrenal origin.

Indications and Clinical Uses

Cosyntropin is used for diagnostic purposes to evaluate adrenal gland function. Maximum peak cortisol secretion occurs at 60-90 minutes. It is used for the same purpose as corticotropin, but in humans it is preferred over corticotropin because it is less allergenic.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects unlikely when used as a single injection for diagnostic purposes. In people, cosyntropin is preferred over ACTH gel because cosyntropin is less allergenic.

Contraindications and Precautions

Maximum dose for dogs should be 250 mcg.

Drug Interactions

There are no drug interactions reported for small animals.

Instructions for Use

Use for diagnostic purposes only; it is not intended for treatment of hypoadrenocorticism. Cosyntropin is preferred to ACTH gel because it is available in a formulation that is easier to use in dogs and cats. In dogs, cosyntropin has been administered at 5 mcg/kg IV or IM and 250 mcg/dog IM. All three protocols produce similar results and IM injection produces similar results as IV injection. Compounded formulations of ACTH may produce similar results at 60 minutes postinjection but may have lower cortisol concentrations at 90 and 120 minutes compared to a proprietary formulation. One may split reconstituted Cortrosyn into aliquots of 50 mcg each (250-mcg vial split into 5 aliquots) or 25 mcg each (250-mcg vial split into 10 aliquots) and frozen in plastic syringes.

Patient Monitoring and Laboratory Tests

Monitor cortisol concentrations. Post-ACTH cortisol response should be as follows:

Dogs: 5.5-20.0 mcg/dL; >20 mcg/dL is consistent with hyperadrenocorticism. More specifically, 5.5-17 mcg/dL normal, 17-25 mcg/dL borderline, 25-30 mcg/dL suggestive, and >30 mcg/dL are highly likely for hyperadrenocorticism.

If monitoring sex hormones of adrenal origin, a sample for analysis should be taken at 60 minutes after injection.

Cats: 4.5-15 mcg/dL; >15 mcg/dL is consistent with hyperadrenocorticism.

Following treatment for hyperadrenocorticism (e.g., treatment with mitotane) response should be 1-5 mcg/dL.

Formulations

Cosyntropin is available in 250-mcg per vial.

Stability and Storage

Once prepared, this formulation can be kept in the refrigerator for 4 months. Frozen cosyntropin can be stored in aliquots. For example, it can be stored in small syringes and frozen at -20°C for up to 6 months. Some compounded formulations are stable and have produced reliable results at the 60-minute sample but may be lower at the 120-minute sample compared to the proprietary preparation.

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Small Animal Dosage

Dogs

- Response test: Collect pre-cosyntropin sample and inject 5 mcg/kg IV or IM and collect post sample at 30 and 60 minutes or one sample at 60 minutes. Maximum dose for dog should be 250 mcg. The following guidelines can be used for dosing: less than 5 kg, 25 mcg; 5-10 kg, 50 mcg; 10-15 kg, 75 mcg; 15-20 kg, 100 mcg; 20-25 kg, 125 mcg; 25-30 kg, 150 mcg; 30-40 kg, 200 mcg; 40-50 kg, 225 mcg; and more than 50 kg, 250 mcg (1 vial).

Cats

- Response test: Collect pre-cosyntropin sample and inject 125 mcg (0.125) IV or IM per cat and collect post sample at 60 and 90 minutes after IV administration or at 30 and 60 minutes after intramuscular administration.

Large Animal Dosage

Horses

Not recommended as a reliable test in horses.

Regulatory Information

No withdrawal times are available. Because clearance is rapid and there is little risk from residues, no withdrawal time is suggested for animals intended for food.

Cyanocobalamin

syeh-ahn-oh-koe-bahl'ah-min

Trade and other names: Cobalamin, Vitamin B₁₂

Functional classification: Vitamin

Pharmacology and Mechanism of Action

Vitamin B₁₂ supplement.

Indications and Clinical Uses

Vitamin B₁₂ has been used to treat some conditions of anemia. Vitamin B₁₂ is used to manage vitamin B deficiencies associated with cobalt deficiency, inadequate intake, or intestinal malabsorption. In patients with exocrine pancreatic insufficiency (EPI) or inflammatory bowel disease, particularly cats, deficiency of cobalamin is common and supplementation is recommended.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are rare, except in high overdoses, because water-soluble vitamins are easily excreted in the urine.

Contraindications and Precautions

No contraindications reported for animals.

Drug Interactions

There are no drug interactions reported for small animals.

Instructions for Use

Not necessary to supplement in animals with well-balanced diets.

Patient Monitoring and Laboratory Tests

Cobalamin concentrations can be measured in most laboratories. Recommended plasma/serum concentrations are as follows: dogs, 252-908 ng/L and cats, 290-1,500 ng/L. Less than 160 ng/mL in cats is clearly deficient. Monitor CBC when used to treat anemia.

Formulations

Cyanocobalamin is available in tablets ranging from 25 to 1000 mcg. Injection formulations range from 1000 to 5000 mcg/mL. Vitamin B complex solutions may contain 10-100 mcg/mL of vitamin B₁₂.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 100-200 mcg/day PO or 250-500 mcg/day IM or SQ.

Cats

- 50-100 mcg/day PO or 250 mcg IM or SQ, weekly. If levels are maintained with once-weekly injections for 6 weeks, increasing the interval to 2 weeks, 4 weeks, and 6 weeks (incrementally) can be attempted.

Large Animal Dosage

Calves and Foals

- 500 mcg once per foal or calf, twice weekly IM or SQ.

Cattle and Horses

- 1000-2000 mcg per horse or cattle, once or twice weekly IM or SQ.

Lambs and Pigs

- 500 mcg once per lamb or pig, twice weekly IM or SQ.

Regulatory Information

No withdrawal times are available. Because clearance is rapid and there is little risk from residues, no withdrawal time is suggested for animals intended for food.

Cyclophosphamide

syə-kloə-foss'fah-mide

Trade and other names: Cytoxan, Neosar, and CTX

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Cytotoxic and anticancer agent. Cyclophosphamide belongs to the group of nitrogen mustards. They are alkylating agents (bifunctional alkylating agents) that alkylate various macromolecules but preferentially alkylate the N-7 of the guanine base of DNA. They are cytotoxic to cancer cells and are toxic to the rapidly dividing cells of the bone marrow. Cyclophosphamide must be metabolized to active

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metabolites for pharmacologic effect, which requires P-450 enzyme activation. The metabolites, hydroxyphosphamide and aldophosphamide, are cytotoxic. Aldophosphamide is converted at the tissue site to phosphoramidate mustard and acrolein. Phosphoramidate mustard is responsible for the antitumor effect, and acrolein is responsible for the cytotoxic action that causes toxicity (e.g., hemorrhagic cystitis). The half-life of the parent drug in dogs is 4-6.5 hours.

Indications and Clinical Uses

Cyclophosphamide is used primarily as adjunct for cancer chemotherapy and as immunosuppressive therapy. Cyclophosphamide is probably the most potent of the nitrogen mustards. It is used in chemotherapy protocols for a variety of tumors, carcinomas, sarcomas, feline lymphoproliferative diseases, mast cell tumor, mammary carcinoma, and especially lymphoproliferative tumors (lymphoma). Cancer protocols such as cyclophosphamide, Oncovin, and prednisone (COP) and cyclophosphamide, hydroxydaunomycin, Oncovin, and prednisone (CHOP) incorporate cyclophosphamide as one of the agents. The other major use of cyclophosphamide is for immunosuppression. Although it has been used for various immune-mediated disorders in animals (immune-mediated hemolytic anemia, pemphigus, systemic lupus erythematosus [SLE]), efficacy has not been reported in controlled studies for these diseases. In one trial it was shown that cyclophosphamide (50 mg/m²) had no benefit over prednisolone alone for treatment of immune-mediated hemolytic anemia (*J Vet Intern Med*, 17: 206-212, 2003).

Precautionary Information

Adverse Reactions and Side Effects

Cyclophosphamide is toxic to the bone marrow in a dose-dependent manner. After a single large bolus dose, the nadir of toxicity occurs in 7-10 days, but the effect is reversible because stem cells are usually unaffected. Recovery usually occurs in 21-28 days. Vomiting and diarrhea may occur in some patients. Sterile, hemorrhagic cystitis is a serious and limiting complication to therapy. It is caused by the toxic effects of metabolites on the bladder epithelium (especially acrolein) that are concentrated and excreted in the urine. Various attempts are used to decrease the injury to the bladder epithelium. Corticosteroids are usually administered with cyclophosphamide to induce polyuria and decrease inflammation of the bladder. The drug mesna (Mesnex, mercaptoethane sulfonate) provides free active thiol groups to bind metabolites of cyclophosphamide in the urine. Furosemide (2.2 mg/kg) administered at the same time as the cyclophosphamide dose may decrease risk of sterile hemorrhagic cystitis. Cats are less susceptible to developing cystitis compared to dogs. Cyclophosphamide may cause hair loss when used in some chemotherapeutic protocols. Dogs most susceptible are those with continuously growing hair (e.g., poodles and Old English sheepdogs). Cats do not tend to lose hair from cyclophosphamide treatment.

Contraindications and Precautions

Bone marrow suppressive and immunosuppressive. Use cautiously in animals at risk for infection. Teratogenic and embryotoxic. Do not use in pregnancy.

Drug Interactions

Use cautiously with other drugs that may cause bone marrow suppression. Although this drug is highly metabolized to active metabolites, it is not known what effect other drugs have on enzyme activity.

Instructions for Use

Cyclophosphamide is usually administered with other drugs (other cancer drugs in cancer protocols or corticosteroids when used for immunosuppressive therapy). Consult specific anticancer protocols for specific regimens. For example, the COAP protocol (COAP is a combination of cyclophosphamide, vincristine, prednisolone, and cytosine arabinoside) uses 50 mg/m² orally, every 48 hours, with vincristine, cytosine arabinoside, and prednisone for 8 weeks, but one CHOP protocol uses 100-150 mg/m² IV on the first day of the protocol, followed by other drugs such as doxorubicin, vincristine, and prednisone. In dogs, the maximum tolerated dose is 500 mg/m² IV (with autologous bone marrow support).

Patient Monitoring and Laboratory Tests

Monitor CBC in animals during treatment. Monitor urinalysis in dogs during treatment.

Formulations

Cyclophosphamide is available in 25 mg/mL injection and 25- and 50-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Tablets are coated and should not be split in order to retain stability. Do not let temperatures exceed 30°C. Subject to hydrolysis in aqueous solutions. Use reconstituted solutions within 24 hours at room temperature and within 6 days if refrigerated, although some refrigerated solutions have been stable for 60 days.

Small Animal Dosage

Dogs

- Anticancer dose: 50 mg/m² (approx. 2.2 mg/kg) q48h or once daily 4 days/week PO. Alternatively, some protocols use 150-300 mg/m² IV and repeat in 21 days.
- Metronomic dose (continuous administration to suppress T-cells): 10 mg/m², q24h, PO (approximately 0.3 mg/kg).
- Immunosuppressive therapy: Dog: 50 mg/m² q48h PO or 2.2 mg/kg once daily for 4 days/week.
- Pulse therapy: 200-250 mg/m² (10 mg/kg), once every 3 weeks.

Cats

- 6.25-12.5 mg/cat once daily 4 days/week.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Cyclosporine, Cyclosporin A

Sye'kloe-spor-een

Trade and other names: Atopica (veterinary preparation), Neoral (human preparation), Sandimmune, Optimune (ophthalmic), Gengraf, and generic brands. In the US it is called cyclosporine; the international name is ciclosporin.

Functional classification: Immunosuppressive drug

Pharmacology and Mechanism of Action

Immunosuppressive drug. Cyclosporine binds to a specific cellular receptor on calcineurin and inhibits the T-cell receptor-activated signal transduction pathway. Particularly important are its effects to suppress interleukin-2 (IL-2) and other cytokines and block proliferation of activated T-lymphocytes. The action of cyclosporine is more specific for T-cells as compared to B-cells. Cyclosporine also inhibits the mitochondrial permeability-transition pores that may attenuate myocardial injury during reperfusion. The half-life of cyclosporine is 8-9 hours (average) in dogs and 8-10 hours (average) in cats. However, there is high variability on both species. Oral absorption is low (20%-30%) and may be affected by food and drug interactions.

Indications and Clinical Uses

Cyclosporine use for keratoconjunctivitis sicca (KCS) is limited to topical administration. Systemic uses (usually oral) for cyclosporine include immune-mediated hemolytic anemia, atopy in dogs, and perianal fistulas. Other diseases have been treated with cyclosporine, such as sebaceous adenitis, idiopathic sterile nodular panniculitis, immune-mediated hemolytic anemia (IMHA), inflammatory bowel disease (IBD), immune-mediated polyarthritis, myasthenia gravis, and aplastic anemia. It has also been used for treatment of granulomatous meningoencephalitis (3-6 mg/kg q12h). In dogs evidence is established for treatment of atopic dermatitis, for which there is similar efficacy as prednisolone. However, there is minimal effectiveness for immune-mediated pemphigus. In dogs, some dermatologists have reported improved efficacy when combined with azathioprine for immune-mediated diseases (e.g., PF). In cats, cyclosporine has shown beneficial effects for treatment of eosinophilic granuloma complex, inflammatory bowel disease, atopic dermatitis (60% effective), stomatitis, and airway disease (feline asthma). In horses it is effective as a localized treatment of anterior uveitis.

Precautionary Information

Adverse Reactions and Side Effects

The most common adverse effect in dogs is GI problems (vomiting, diarrhea, and anorexia). Neurotoxicity has been seen in dogs from high doses, which can be seen as tremors. However, this is uncommon from recommended doses. Although renal injury has been reported with older formulations, it has not been reported from use of current formulations of cyclosporine. High doses (three times clinical dose) have produced skin lesions and gingival proliferation and dose-related vomiting, diarrhea, weight loss, gingivitis, and periodontitis that reversed after discontinuing the drug. Cyclosporine can inhibit pancreatic beta cells, but diabetes has not been reported in pets from clinical use. Gingival

hyperplasia and papillomas have been observed in dogs with chronic use. In cats, secondary infections, tumors, and toxoplasmosis have been reported from its use. Unlike other immunosuppressive drugs, it does not cause myelosuppression. Cyclosporine may induce new hair growth in dogs.

Effect on vaccination: At three times the clinical dose it did not affect the immune response to killed rabies vaccine in dogs, but it failed to increase antibody titers from live parvovirus vaccine.

Contraindications and Precautions

Do not use in pregnancy. Warn animal owners to keep out of reach of children. If used with other drugs, consult Drug Interactions section for possible interference.

Drug Interactions

Cimetidine, erythromycin, fluconazole, or ketoconazole may increase cyclosporine concentrations when used concurrently. Doses of ketoconazole of 2.5 to 10 mg/kg/day in dogs have been shown to substantially decrease the clearance of cyclosporine and reduce the required dose by one half or more. Grapefruit juice also inhibits clearance and will reduce the required dose, although high doses are needed. Food will decrease oral absorption by 15%-22%.

Instructions for Use

Atopica (veterinary) and Neoral (human) are identical formulations, except that sizes of capsules vary. After animals have been treated with initial doses of 5 mg/kg per day and are stable, doses may be adjusted by increasing the interval to once every other day, or every third day, rather than lowering daily dose. Individual doses may be adjusted by monitoring of blood concentrations, but monitoring is not necessary for routine use. Atopica and Neoral oral products are absorbed more predictably than Sandimmune. Atopica and Neoral may produce 50% higher blood concentrations in some patients or reduce the variability in absorption that was associated with the Sandimmune formulations. Feeding may reduce oral absorption in dogs but does not decrease efficacy. Generic formulations are available for humans, but have not been evaluated for bioequivalence to Atopica in dogs. Oral solution can be diluted to make it more palatable. To reduce the dose, some veterinarians have administered ketoconazole or other enzyme-inhibiting compounds concurrently. When used to treat animals for organ transplantation, the doses are generally higher and the blood concentrations maintained at a higher level.

Patient Monitoring and Laboratory Tests

Although routine blood concentration monitoring is not necessary, it may be helpful to identify drug interactions, poor absorption, or poor compliance. When monitoring, collect whole blood in ethylenediaminetetraacetic acid (EDTA; purple-top) tube for submission to laboratory. Suggested trough blood concentration range (whole blood assay) is 300-400 ng/mL, although in some studies, levels as low as 200 ng/mL have been effective. If the assay uses fluorescence polarization immunoassay (FPIA) with a commercially available test system (commonly referred to as the TDx method), the feline measured concentration should be multiplied by 0.5 to arrive at a true value; the canine measured concentration should be multiplied by 0.65 to arrive at a drug value. Cyclosporine does not interfere with intradermal skin testing.

Formulations

Cyclosporine is available in 10-, 25-, 50-, and 100-mg capsules (Atopica) and 25 and 100 microemulsion capsules and 100-mg/mL oral solution (Neoral, for microemulsion), 100-mg/mL oral solution and 25-, 100-mg capsules (Sandimmune), 0.2% ophthalmic ointment (Optimune). Generic human capsules are available, (e.g., Gengraf). The human generic formulations are therapeutically equivalent in people but have not been compared in dogs or cats to Atopica.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not refrigerate, but store at below 30°C. Compounded ophthalmic products are stable at room temperature for 60 days, but do not refrigerate.

Small Animal Dosage

Dogs

- 3-7 mg/kg/day PO. The typical starting dose is 5 mg/kg/day, PO. After induction period, some dogs with atopic dermatitis have been controlled with doses as low as 5 mg/kg every other day to every third day.
- For perianal fistulas and immune-mediated diseases (e.g., IMHA), higher doses and more frequent administration have been used (every 12 hours).
- For immune suppression associated with organ transplantation, doses should be higher (e.g., 3-7 mg/kg q12h PO).

Cats

- 3-5 mg/kg/day PO. Higher doses of 5-10 mg/kg/day PO have been used in many cats every other day.
- For immune suppression associated with organ transplantation, doses should be higher (e.g., 3-5 mg/kg q12h PO).

Large Animal Dosage

Only local administration has been used in horses (ocular). No other dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it may have mutagenic potential.

Cyproheptadine Hydrochloride

Sih'proe-hep'tah-deen hye-droe-klor'ide

Trade and other names: Periactin

Functional classification: Antihistamine

Pharmacology and Mechanism of Action

Phenothiazine with antihistamine and antiserotonin properties. Used as appetite stimulant (probably by altering serotonin activity in appetite center).

Indications and Clinical Uses

A common use of cyproheptadine is to stimulate the appetite in sick animals, especially cats; although, evidence based on controlled studies to demonstrate efficacy is not available. Cyproheptadine is used in some cats for treatment of feline asthma if serotonin is considered a component of the airway inflammation. However, in cats

with hyper-responsive airways, cyproheptadine failed to reduce eosinophilic inflammation (8 mg per cat q12h). It has been used in some instances for treating inappropriate urination (urine spraying) in cats. Cyproheptadine has been used to treat equine pituitary pars intermedia dysfunction (Cushing's syndrome) at 0.6-1.2 mg/kg, but results have been controversial. It is not effective for treatment of canine pituitary-dependent hyperadrenocorticism (Cushing's syndrome). It has been considered as a treatment for animals that have "serotonin syndrome" from antidepressant drugs, although efficacy has not been documented for this use.

Precautionary Information

Adverse Reactions and Side Effects

Stimulates hunger. May cause polyphagia and weight gain. Cyproheptadine also has antihistamine effects, antiserotonin effects, and antimuscarinic effects. In some cats, it has stimulated hyperactivity. In horses, it has been used at high doses without adverse effects.

Contraindications and Precautions

None reported for animals.

Drug Interactions

There are no drug interactions reported for small animals.

Instructions for Use

Clinical studies have not been performed in veterinary medicine. Use is based primarily on empiricism and extrapolation from human results. Syrup contains 5% alcohol.

Patient Monitoring and Laboratory Tests

Monitor weight gain in animals.

Formulations Available

Cyproheptadine is available in 4-mg tablets and 2 mg/5 mL syrup.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze the syrup. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- Antihistamine: 0.5-1.1 mg/kg q8-12h PO, or 2-4 mg/cat PO q12-24h.
- Appetite stimulant: 2 mg/cat PO.
- Feline asthma: 1-2 mg/cat PO q12h.
- Use for inappropriate urination: 2 mg/cat q12h PO, then reduce dose to 1 mg/cat q12h PO.

Large Animal Dosage

Horses

- 0.5 mg/kg q12h PO.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Cytarabine

sye-tare' ah-been

Trade and other names: Cytosar, Ara-C, and Cytosine arabinoside

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Cytarabine (Cytosar) is a compound isolated from a sea sponge. It has also been referred to as cytosine arabinoside and Ara-C. Cytarabine is metabolized to an active drug that inhibits DNA synthesis. It was once thought that its action was via inhibition of the enzyme DNA polymerase, but the exact mechanism of action may not be known. The half-life in dogs is approximately 70 minutes.

Indications and Clinical Uses

Cytarabine has been used for lymphoma and leukemia protocols. The most common use of cytarabine is treatment of lymphoma and myelogenous leukemia. It is usually administered as an intramuscular or subcutaneous injection because it has a short half-life (approximately 20 minutes) when administered IV. It has also been administered to dogs for treatment of granulomatous meningoencephalomyelitis as an alternative to corticosteroids.

Precautionary Information

Adverse Reactions and Side Effects

Cytarabine is bone marrow suppressive and can cause granulocytopenia, especially when delivered via continuous rate infusions. In addition, it may cause nausea and vomiting.

Contraindications and Precautions

Use cautiously in animals administered other bone marrow-suppressing drugs.

Drug Interactions

There are no drug interactions reported for small animals.

Instructions for Use

Cytarabine has been administered to dogs using a variety of protocols (see dosing section), depending on the study published and dependent on clinician preference. There is not strong evidence that one protocol is superior to another. When treating granulomatous meningoencephalomyelitis, dose protocols (either IV or SQ) have used total doses of 200 to 400 mg/m² total dose, divided over 2 days, either as SQ injections twice daily for 2 days, or an IV infusion with the total dose given over 8 hours.

Consult anticancer protocols for precise dosing regimens.

Patient Monitoring and Laboratory Tests

Monitor CBC to assess toxicity.

Formulations

Cytarabine is available in a 100-mg vial for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs (cancer protocols, administered weekly)

- 100-150 mg/m² once daily or 50 mg/m² twice daily for 4 days IV or SQ.
- 600 mg/m², IV or SQ, single dose.
- 300 mg/m² per day as a continuous IV infusion, over 48 hours (600 mg/m² total).

Dogs (granulomatous meningoencephalomyelitis)

- 50 mg/m² twice daily for 2 days and repeated every 3 weeks SQ
- 200 mg/m² infused IV over 16-24 hours. In some patients this dose is repeated on the second day.

Cats

- 100 mg/m² once daily for 2 days.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Dacarbazine

dah-kar'bah-zeen

Trade and other names: DTIC

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Dacarbazine (DTIC) is a monofunctional alkylating agent; thus it effectively blocks RNA synthesis. Its action is cell-cycle nonspecific.

Indications and Clinical Uses

DTIC has been primarily used for malignant melanoma and lymphoreticular neoplasms.

Precautionary Information

Adverse Reactions and Side Effects

Most common adverse effects are leukopenia, nausea, vomiting, and diarrhea.

Contraindications and Precautions

Do not use in cats.

Drug Interactions

There are no drug interactions reported for small animals.

Instructions for Use

Consult anticancer protocol for specific regimens.

Patient Monitoring and Laboratory Tests

Monitor CBC during treatment.

Formulations

DTIC is available in 200-mg vial for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 200 mg/m² for 5 days q3wks IV or 800-1000 mg/m² q3wks IV.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Dalteparin

dahl'tah-pare-in

Trade and other names: Fragmin and LMWH

Functional classification: Anticoagulant

Pharmacology and Mechanism of Action

Low-molecular-weight heparin (LMWH), also known as fragmented heparin. LMWH is characterized by a molecular weight of approximately 5000, compared to conventional heparin (unfractionated, or UFH) with a molecular weight of approximately 15,000. Subsequently, the absorption, clearance, and activity of LMWH differ from UFH. LMWHs produce their effect by binding to antithrombin (AT) and increasing antithrombin III-mediated inhibition of synthesis and activity of coagulation factor Xa. However, LMWH, unlike conventional heparin, produces less inhibition of thrombin (factor IIa). LMWH's activity is described by the Anti-factor Xa/Anti-factor IIa ratio. For dalteparin, the ratio is 2.7:1 (conventional unfractionated heparin ratio is 1:1). In people, LMWHs have several advantages compared to UFH and include greater anti-Xa/IIa activity, more complete and predictable absorption from injection, longer duration, less frequent administration, reduced risk of bleeding, and a more predictable anticoagulant response. However, in dogs and cats, the half-life of LMWH is much shorter than in humans, reducing some of this advantage. In dogs the half-life of dalteparin is approximately 2 hours; in cats it is estimated to be 1.5 hours, which requires much more frequent administration in either species to maintain anti-Xa activity compared to humans. LMWHs used in veterinary medicine include tinzaparin (Innohep), enoxaparin (Lovenox), and dalteparin (Fragmin).

Indications and Clinical Uses

Dalteparin, like other LMWHs, is used to treat hypercoagulability disorders and prevent coagulation disorders such as thromboembolism, venous thrombosis, disseminated intravascular coagulopathy (DIC), and pulmonary thromboembolism. Clinical indications are derived from uses of conventional heparin or extrapolated from human medicine. There have been few clinical studies to examine efficacy of LMWH in animals. Previously published doses extrapolated from humans (100 units/kg q12h, SQ) have been shown *not* to produce adequate and consistent anti-Xa activity in dogs and cats and the doses listed in this entry are needed for therapy.

Precautionary Information

Adverse Reactions and Side Effects

Although better tolerated than regular heparin, bleeding is a risk. LMWHs are associated with a lower incidence of heparin-induced thrombocytopenia in people, but heparin-induced thrombocytopenia from any form of heparin has not been a clinical problem in animals. If excessive anticoagulation and bleeding occur as a result of an overdose, protamine sulfate should be administered to reverse heparin therapy. Protamine dose is 1.0 mg protamine for every 100 U dalteparin administered by slow IV infusion. Protamine complexes with heparin to form a stable, inactive compound.

Contraindications and Precautions

Do not administer IM to prevent hematoma; administer SQ only. LMWH is excreted by renal clearance in animals; therefore, if renal disease is present, the elimination will be prolonged. Rebound hypercoagulability may occur after discontinuation of heparin treatment; therefore, it may be advised to taper the dose slowly when discontinuing treatment.

Drug Interactions

Do not mix with other injectable drugs. Use cautiously in animals that are already receiving other drugs that can interfere with coagulation, such as aspirin and warfarin. Although a specific interaction has not been identified, use cautiously in animals that may be receiving certain chondroprotective compounds such as glycosaminoglycans for treatment of arthritis. Some antibiotics, such as cephalosporins, may inhibit coagulation.

Instructions for Use

Dosing recommendations extrapolated from human medicine are not appropriate for animals. Animal owners should be warned that LMWHs are expensive compared to conventional heparin. When dosing, do not interchange doses on a unit-for-unit basis with other heparins.

Patient Monitoring and Laboratory Tests

Monitoring patients for clinical signs of bleeding problems. When administering LMWH, aPTT and PT clotting times are not reliable indicators of therapy, although prolonged aPTT is a sign of overdosing. Anti-Xa activity is considered the preferred laboratory measure of LMWH activity. Peak anti-Xa activity occurs 2 hours after dosing, and the target range for anti-Xa activity should be 0.5-1.0 U/mL for cats and 0.4-0.8 U/mL for dogs.

Formulations

Dalteparin is available in 2500 units anti-factor Xa (16 mg dalteparin sodium) per 0.2 mL in a single-dose syringe; 5000 units anti-factor Xa (32 mg dalteparin sodium) per 0.2 mL in a single-dose syringe; and 10,000 units anti-factor Xa (64 mg dalteparin sodium) per mL in a 9.5 mL multiple-dose vial.

Stability and Storage

Use multiple-dose vial within 2 weeks of initial penetration. Store in a tightly sealed container protected from light.

Small Animal Dosage

Dogs

- 150 U/kg, q8h, SQ (see monitoring section for dose adjustment).

Cats

- 150 U/kg, q4h, SQ, to 180 U/kg q6h, SQ (see Patient Monitoring and Laboratory Tests section for dose adjustment).

Large Animal Dosage

Horses

- 50 units/kg/day SQ. High-risk patients should receive 100 units/kg/day.

Regulatory Information

Extralabel withdrawal times are not established. However, 24-hour withdrawal times are suggested because this drug has little risk from residues.

Danazol

dan'ah-zole

Trade and other names: Danocrine

Functional classification: Hormone

Pharmacology and Mechanism of Action

Gonadotropin inhibitor. Danazol suppresses luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and estrogen synthesis. Danazol has been used as adjunctive treatment for immune-mediated blood disorders. Its mechanism of action for treating immune-mediated diseases is not understood, but it may interfere with antibody production or the binding of complement or antibody to the platelet or red blood cell. It may also reduce receptors on monocytes for antibodies bound to platelets or red blood cells.

Indications and Clinical Uses

Danazol has hormone effects (antiestrogen) that are used for endometriosis in women. Danazol (Danocrine) also has been used for treating refractory patients with immune-mediated thrombocytopenia and immune-mediated hemolytic anemia. However, available evidence does not show a benefit in dogs when it has been used to treat immune-mediated hemolytic anemia.

Precautionary Information

Adverse Reactions and Side Effects

Danazol's androgenic effects should be considered in treated animals. However, adverse effects have not been reported in animals.

Contraindications and Precautions

It is absolutely contraindicated in pregnancy.

Drug Interactions

It has been used with other drugs in the treatment of immune-mediated diseases without reported interactions.

Instructions for Use

When used to treat autoimmune disease, it is usually used in conjunction with other drugs (e.g., corticosteroids).

Patient Monitoring and Laboratory Tests

Monitor CBC if used for treatment of immune-mediated diseases.

Formulations

Danazol is available in 50-, 100-, and 200-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 5-10 mg/kg q12h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Danazol is an anabolic agent and should not be administered to animals intended for food.

RCI Classification: 4

Danofloxacin Mesylate

dan-oh-floks'ah-sin mess'ih-late

Trade and other names: A180

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Danofloxacin like other fluoroquinolones has activity against a broad spectrum of bacteria, including gram-negative bacilli, especially *Enterobacteriaceae* (*Escherichia coli*, *Klebsiella*, *Salmonella*) and some gram-positive cocci, such as *Staphylococcus*. In particular it has good activity against pathogens in cattle, such as *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni* (formerly *Haemophilus somnus*). In cattle, subcutaneous absorption is high. Half-life is 3-6 hours.

When used to treat bovine respiratory disease (BRD) in cattle at a dose of 6 mg/kg danofloxacin had a half-life of 4.2 hours, a peak concentration of 1.7 mcg/mL, and produced area under the curve (AUC):minimum inhibitory concentration (MIC) ratio >125.

Indications and Clinical Uses

Danofloxacin is indicated for the treatment of BRD caused by *P. multocida*, *M. haemolytica*, and *H. somni* (formerly *H. somnus*). As a fluoroquinolone with a broad spectrum of activity, other organisms are susceptible. However, extralabel use for other diseases in animals intended for food is prohibited. There are no published reports of danofloxacin use in other animals.

Precautionary Information

Adverse Reactions and Side Effects

All fluoroquinolones at high concentrations may cause CNS toxicity.

In safety studies in cattle when high doses were administered it caused lameness, articular cartilage lesions, and CNS problems (tremors, nystagmus, etc.).

Subcutaneous injections may cause tissue irritation. All of the fluoroquinolones have a potential to produce arthropathy in young animals. In field trials, danofloxacin was associated with lameness in some calves. Fluoroquinolones have caused blindness in cats, but this has not been reported in any species from danofloxacin.

Contraindications and Precautions

Do not inject more than 15 mL in one site. Do not use extralabel. Do not use in other species for which safety information is not available. Do not use in animals prone to seizures.

Drug Interactions

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

Instructions for Use

Inject SQ in neck of cattle.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. CLSI break points for sensitive organisms are ≤ 0.25 mcg/mL for cattle respiratory pathogens. Most organisms have minimum inhibitory concentration (MIC) values ≤ 0.06 mcg/mL.

Formulations

Danofloxacin is available in an injectable solution of 180 mg/mL (with 2-pyrrolidone and polyvinyl alcohol).

Stability and Storage

Store below 30°C, protected from light, and protected from freezing. A slight yellow or amber color is acceptable.

Small Animal Dosage**Dogs and Cats**

No small animal dose has been reported.

Large Animal Dosage**Cattle**

- 6 mg/kg (1.5 mL per 100 pounds), once per 48 hours, SQ.

Equine and Swine

No dose has been reported.

Regulatory Information

Do not use in calves intended for veal.

Cattle withdrawal time (for meat): 4 days. Not established for milk because it cannot be used in lactating cattle. It is prohibited to use extralabel.

Dantrolene Sodium

dan'troe-leen soe'dee-um

Trade and other names: Dantrium

Functional classification: Muscle relaxant

Pharmacology and Mechanism of Action

Muscle relaxant. Dantrolene inhibits calcium leakage from sarcoplasmic reticulum. By inhibiting calcium initiation of muscle contraction, it relaxes muscle.

Indications and Clinical Uses

Dantrolene is used as a muscle relaxant. However, in addition to muscle relaxation, it has been used for malignant hyperthermia and it also has been used to relax urethral muscle in cats.

198 Dantrolene Sodium

In horses, it has improved clinical signs associated with exertional rhabdomyolysis (“tying up”).

Precautionary Information

Adverse Reactions and Side Effects

Muscle relaxants can cause weakness in some animals. Use of dantrolene in people has caused hepatitis in some cases.

Contraindications and Precautions

Do not use in animals with hepatic disease. Use with caution in weak or debilitated animals.

Drug Interactions

Do not mix or reconstitute the intravenous solution with acidic solutions because they are incompatible.

Instructions for Use

Give oral doses on an empty stomach. Doses have been primarily extrapolated from experimental studies or extrapolation of human studies. No clinical trials are available in veterinary medicine. To relax the urethra in cats, the most effective dose is 1 mg/kg IV. When administering dantrolene for treatment of malignant hyperthermia in large animals several vials may be needed because of dilute solution in vial.

Patient Monitoring and Laboratory Tests

When used for treatment of malignant hyperthermia, monitor body temperature, acid–base balance, and electrolytes. In people, dantrolene may cause hepatitis and tests of liver injury (e.g., liver enzymes) and/or function are monitored.

Formulations

Dantrolene is available in 100-mg capsules, and 20-mg vial for injection when reconstituted is equal to 0.33 mg/mL injection.

Stability and Storage

When intravenous solution is prepared, it is stable for a short time (6 hours). It may be mixed with solutions such as 5% dextrose and 0.9% sodium chloride. Do not use intravenous solution if cloudiness or precipitation is present in vial. Compounded oral suspensions are stable for 150 days if mixed with acid solutions (e.g., citric acid). Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- Prevention of malignant hyperthermia: 2-3 mg/kg IV.
- Malignant hyperthermia crisis: doses of 2.5-3 mg/kg IV rapid bolus.
- Muscle relaxation: 1-5 mg/kg q8h PO.
- Urethral relaxation: 1-5 mg/kg q8h PO or 0.5-1.0 mg/kg IV.

Cats

- Muscle relaxation: 0.5-2 mg/kg q12h PO.
- Relaxation of urethra: 1-2 mg/kg q8h PO.

Large Animal Dosage

Horses

- 4 mg/kg PO.

Pigs

- Malignant hyperthermia: 1-3 mg/kg IV once.
- Prophylaxis: 5 mg/kg PO.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

D

Dapsone

dap'sone

Trade and other names: Generic brands

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Antimicrobial drug used for treatment of mycobacterium. It may also have some immunosuppressive properties or inhibit function of inflammatory cells.

Indications and Clinical Uses

Although originally used as an antibacterial drug, in veterinary medicine it is used primarily for dermatologic diseases in dogs, especially subcorneal pustular dermatosis and dermatitis herpetiformis. It also has been used for canine pemphigus.

Precautionary Information**Adverse Reactions and Side Effects**

Hepatitis and blood dyscrasias may occur. Because it shares similar properties as a sulfonamide, the same reactions seen with sulfonamides can be seen with dapsone and include anemia, neutropenia, thrombocytopenia, hepatotoxicosis, and skin-drug eruptions. It is toxic to cats and will cause neurotoxicosis and anemia.

Contraindications and Precautions

Do not administer to cats. Do not administer to animals that are sensitive to sulfonamides.

Drug Interactions

Use caution when administering dapsone with trimethoprim/sulfonamide combinations. Trimethoprim may increase blood concentrations of dapsone because it inhibits excretion and potentiates dapsone adverse effects.

Instructions for Use

Doses are derived from extrapolation of human doses or empiricism. No well-controlled clinical studies have been performed in veterinary medicine.

Patient Monitoring and Laboratory Tests

Monitor for signs of hepatic reactions. Monitor CBC occasionally because bone marrow toxicity has occurred in some animals.

Formulations

Dapsone is available in 25- and 100-mg tablets.

200 Deferoxamine Mesylate

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Dapsone may discolor without change in potency. Compounded suspension formulations have been stable for 21 days when mixed with citric acid.

Small Animal Dosage

Dogs

- 1.1 mg/kg q8-12h PO.

Cats

Do not use.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Deferoxamine Mesylate

deh-fer-oks'ah-meen mess'ih-late

Trade and other names: Desferal

Functional classification: Antidote

Pharmacology and Mechanism of Action

Chelating agent with strong affinity for trivalent cations. Because of its ability to bind to and chelate cations, it is used to treat acute iron toxicosis.

Indications and Clinical Uses

Deferoxamine is indicated in cases of severe poisoning, especially iron toxicosis. Deferoxamine also has been used to chelate aluminum and facilitate removal.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. Allergic reactions and hearing problems have occurred in people.

Contraindications and Precautions

No contraindications reported for animals.

Drug Interactions

Deferoxamine will chelate with cations; avoid mixing with cations prior to administration.

Instructions for Use

100 mg of deferoxamine binds 8.5 mg of ferric iron. Contact local poison control center for guidance on dosing after an overdose.

Patient Monitoring and Laboratory Tests

Monitor serum iron concentrations to determine severity of intoxication and success of therapy. Successful therapy is indicated by monitoring urine color (orange-rose color change to urine indicates chelated iron is being eliminated).

Formulations

Deferoxamine is available in a 500-mg vial for injection.

Stability and Storage

Deferoxamine is soluble in water. Stable when stored in solution for 14 days. Store in a tightly sealed container, protected from light, and at room temperature. Do not refrigerate and do not mix solutions with other medications.

Small Animal Dosage

Dogs and Cats

- 10 mg/kg q2h for 2 doses IV or IM, then 10 mg/kg q8h for 24 hours.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. There are no anticipated problems from levels of residues in animals. However, for extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Deracoxib

dare-ah-koks'ib

Trade and other names: Deramaxx

Functional classification: Anti-inflammatory

Pharmacology and Mechanism of Action

Deracoxib is a nonsteroidal anti-inflammatory drug (NSAID). Like other drugs in this class, deracoxib produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the cyclooxygenase (COX) enzyme. The COX enzyme exists in two isoforms called COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations and COX-2 activity is important for some biological effects. Deracoxib, using in vitro assays, is more COX-1 sparing compared to older NSAIDs and is a selective inhibitor of COX-2. The COX-1/COX-2 ratio is high compared to some other drugs registered for dogs. It also is a selective COX-2 inhibitor in cats. It has not been established if the specificity for COX-1 or COX-2 is related to efficacy or safety. Deracoxib has a half-life of 3 hours in dogs at 2-3 mg/kg and 19 hours at 20 mg/kg. It is highly protein bound. Oral absorption is 90% in dogs. Feeding delays absorption but does not diminish overall absorption. In cats the half-life is approximately 8 hours.

Indications and Clinical Uses

Deracoxib is used to decrease pain, inflammation, and fever. It has been used for the acute and chronic treatment of pain and inflammation in dogs. One of the most common uses is osteoarthritis but also has been used for pain associated with

surgery. There has been only limited use of deracoxib in horses, and administration to other large animals has not been reported.

Precautionary Information

Adverse Reactions and Side Effects

GI problems are the most often adverse effects associated with NSAIDs and can include vomiting, diarrhea, nausea, ulcers, and erosions of the GI tract. Gastric and duodenal ulcers have been reported from use of deracoxib in dogs. In field trials with deracoxib, vomiting was the most often reported adverse effect. Renal toxicity, especially in dehydrated animals or animals with preexisting renal disease, has been shown for some NSAIDs. In studies performed in dogs, higher doses (five times the dose) caused azotemia in normal dogs.

Contraindications and Precautions

Dogs and cats with preexisting GI or renal problems may be at a greater risk of adverse effects from NSAIDs. Safety in pregnancy is not known, but adverse effects have not been reported. Safety studies are not available for dogs <4 months of age, pregnant animals, or lactating animals. In cats, use only as a single dose.

Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors.

Instructions for Use

Chewable tablets can be administered with or without food. Long-term studies have not been completed in cats, only single-dose studies have been reported.

Patient Monitoring and Laboratory Tests

Monitor GI signs for evidence of diarrhea, GI bleeding, or ulcers. Because of risk of renal injury, monitor renal parameters (water consumption, BUN, creatinine, and urine-specific gravity) periodically during treatment. Deracoxib does not appear to affect thyroid hormone assays in dogs.

Formulations

Deracoxib is available in 25-, 75-, and 100-mg chewable tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Deracoxib has been mixed in a liquid suspension in water. However, stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Postoperative pain: 3-4 mg/kg once daily as needed for up to 7 days.
Chronic use: 1-2 mg/kg once daily PO.

Cats

- 1 mg/kg single dose, PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals that produce food.

RCI Classification: 4

Desmopressin Acetate

dess-moe-press'in ass'ih-tate

Trade and other names: DDAVP

Functional classification: Hormone

D

Pharmacology and Mechanism of Action

Synthetic peptide similar to antidiuretic hormone (ADH). It produces similar effects as natural ADH and is used to treat diabetes insipidus (DI) in animals. This action is related to stimulation of permeability to water to increase water reabsorption in the distal renal tubule. The difference between DDAVP and natural ADH is that DDAVP is longer acting and produces fewer vasoconstriction effects. In addition to the hormone effects, in humans administration of DDAVP results in a twofold to fivefold increase in the plasma von Willebrand factor. It may induce a 50% increase in von Willebrand factor in some animals but not as consistently as when administered to people.

Indications and Clinical Uses

Desmopressin is used as replacement therapy for patients with DI and also has been used for treatment of patients with mild to moderate von Willebrand's disease prior to surgery or other procedure that may cause bleeding. However, the response in von Willebrand-deficient dogs is not as consistent or as great as in people.

Precautionary Information

Adverse Reactions and Side Effects

No side effects reported. In people, it has rarely caused thrombotic events.

Contraindications and Precautions

There are no specific contraindications.

Drug Interactions

Administration of urea and fludrocortisone will increase the antidiuretic effects.

Instructions for Use

Desmopressin is used only for central forms of DI. Duration of effect is variable (8-20 hours) but typically has a duration of 8-12 hours. It is ineffective for treatment of nephrogenic diabetes insipidus or polyuria from other causes. Intranasal product has been administered as eye drops in dogs. Onset of effect is within 1 hour. Oral tablets are available for humans, but the effects in dogs have not been reported.

Patient Monitoring and Laboratory Tests

Monitor water intake and urinalysis to assess therapy. Desmopressin may be used as a test for DI in animals. To perform this test, administer 2 mcg/kg SQ or IV or 20 mcg intranasally or in the eye. This should be followed by monitoring of urine concentration and the animal's body weight. Increase in urine concentrating ability may indicate a diagnosis of DI.

204 Desoxycorticosterone Pivalate

Formulations

Desmopressin is available in a 4-mcg/mL injection, acetate nasal solution 100-mcg/mL (0.01%) metered spray, and 0.1- and 0.2-mg tablets (scored).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

- DI: 2-4 drops (2 mcg) q12-24h intranasal or in eye. Alternatively, 0.5-2 mcg/dog q12-24h IV or SQ.
- 0.05-0.1 mg q12h PO or as needed. The oral dose may be increased to 0.1-0.2 mg/kg as needed.
- von Willebrand's disease treatment: 1 mcg/kg (0.01 mL/kg), administered SQ, or diluted in 20 mL of saline and administered over 10 min IV.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established. However, this drug has rapid clearance, with little risk from residues; therefore, a short withdrawal time is suggested for food animals.

Desoxycorticosterone Pivalate

dess-oks-ih-kor-tik-oh-steer'one piv'ah-late

Trade and other names: Percorten-V, DOCP, and DOCA pivalate

Functional classification: Corticosteroid

Pharmacology and Mechanism of Action

Mineralocorticoid with no glucocorticoid activity. Desoxycorticosterone mimics the effects of aldosterone by retaining sodium. The pivalate formulation is absorbed slowly and produces a long-lasting effect from a single administration.

Indications and Clinical Uses

Desoxycorticosterone is used for adrenocortico insufficiency (hypoadrenocorticism). Some dogs also may require concurrent glucocorticosteroid therapy when it is used to treat insufficiency.

Precautionary Information

Adverse Reactions and Side Effects

Excessive mineralocorticoid effects are possible with high doses. Signs of iatrogenic hyperadrenocorticism are not expected with this drug.

Contraindications and Precautions

Do not use in pregnant animals. It must be used cautiously in patients with congestive heart failure or renal disease.

Drug Interactions

Aldosterone antagonists (spironolactone) will blunt the effect.

Instructions for Use

Initial dose based on average response in clinical patients, but individual doses may be based on monitoring electrolytes in patients. The actual interval between doses may range from 14 to 35 days.

Patient Monitoring and Laboratory Tests

Monitor serum sodium and potassium.

Formulations

Desoxycorticosterone is available in 25-mg/mL suspension for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 1.5-2.2 mg/kg q25 days IM. Adjust dose by monitoring electrolytes.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established. However because of low risk of residues, no withdrawal times are suggested.

RCI Classification: 4

Detomidine Hydrochloride

deh-toe'mih-deen hye-droe-klor'ide

Trade and other names: Dormosedan, Dormosedan Gel

Functional classification: Alpha₂ Analgesic

Pharmacology and Mechanism of Action

Alpha₂ adrenergic agonist. Alpha₂ agonists decrease release of neurotransmitters from the neuron. The proposed mechanism whereby they decrease transmission is via binding to presynaptic alpha₂ receptors (negative feedback receptors). The result is decreased sympathetic outflow, analgesia, sedation, and anesthesia. Detomidine gel is absorbed from the oral mucous membrane with bioavailability in horses of 22%. Other drugs in this class include xylazine, dexmedetomidine, medetomidine, romifidine, and clonidine.

Indications and Clinical Uses

Detomidine is used primarily as a sedative, anesthetic adjunct, and analgesic. It is used in horses more often than in other species. When used to treat pain from colic in horses, the duration of effect is approximately 3 hours (20 or 40 mcg/kg). Detomidine also has been administered for epidural analgesia. For pain, detomidine appears to be more potent and longer acting than xylazine. Detomidine in the gel form (Dormosedan Gel) for horses is administered orally to produce mucosal absorption. It is indicated for producing minor standing sedation to facilitate minor procedures (shoeing, clipping, trimming) or calming a fractious horse. Onset of action is 40 minutes and duration is 90-180 minutes.

Precautionary Information

Adverse Reactions and Side Effects

At typical doses, sedation, ataxia, swaying, sweating, and bradycardia are common. Cardiac depression, AV block, and hypotension are possible with high doses. In some horses, hyperresponsiveness to stimuli occurs. Diuresis occurs as a consequence of the hyperglycemia produced by α_2 agonists such as detomidine. Yohimbine (0.11 mg/kg) can be used to reverse effects of α_2 agonists such as detomidine. In small animals, atipamezole also can be used to reverse effects from detomidine.

Contraindications and Precautions

Concurrent use of detomidine with sulfonamides IV can lead to cardiac arrhythmias. Xylazine causes problems in pregnant animals, and this also should be considered for other α_2 agonists. Use cautiously in animals that are pregnant because it may induce labor. In addition, it may decrease oxygen delivery to a fetus in late gestation. Detomidine gel can be absorbed across the skin, and from eye and mouth contact in humans. If there is accidental exposure, immediately rinse with soap and water. Contact a physician if there are other concerns.

Drug Interactions

Other drugs that depress the heart may increase risk for arrhythmias.

Instructions for Use

It is used primarily for horses, and although not approved for small animals, dosages are listed below. Atropine (0.01 to 0.02 mg/kg) has been used to prevent bradycardia but is not necessary for routine use. It may be administered with other anesthetics, analgesics, sedatives including butorphanol, and benzodiazepines.

Patient Monitoring and Laboratory Tests

Monitor heart rate and, if possible, the ECG during treatment with this class of drugs. If available, blood pressure monitoring may be indicated in some patients.

Formulations

Detomidine is available in a 10-mg/mL injection. Oral gel is 7.6 mg/mL in a 3 mL syringe.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 5 mcg/kg IV, or 10-20 mcg/kg IM.

Cats

- Oral (transmucosal): 0.5 mg/kg. Administer with ketamine (10 mg/kg) by spraying into cats mouth.

Large Animal Dosage

Horses (*Dose of 10-20 mcg/kg is equivalent to 5-10 mg per horse*)

- Sedation: 20-40 mcg/kg (0.02-0.04 mg/kg) IV or IM. Lower doses of 10-20 mcg/kg are sometimes used in practice initially, then repeated as needed.

For example, doses of 10 mcg/kg (0.01 mg/kg) will produce slightly less ataxia and sedation. Doses as low as 5 mcg/kg have been used in draft horses.

- Analgesia: 20 mcg/kg (0.02 mg/kg) IV or IM. Duration of analgesia may be longer if a dose of 40 mcg/kg is used.
- Constant rate infusion: 10 mcg/kg bolus IV, followed by 0.5 mcg/kg/min for 15 min, then progressively decreasing the rate as needed to 0.1 mcg/kg/min.
- Oral mucosal: 40 mcg/kg (approximately 2.5 mL to a 1,000 pound horse) administered sublingual.

Cattle

- 2-10 mcg/kg (0.002-0.1 mg/kg) IV or 5-40 mcg/kg (0.005-0.04 mg/kg) IM.

Regulatory Information

Cattle withdrawal times (extralabel): 3 days meat; 72 hours milk.

RCI Classification: 3

Dexamethasone

deks-ah-meth'ah-sone

Trade and other names: Azium solution in polyethylene glycol, Dexaject, Dex-A-Vet, Decadron, Dexasone, Voren suspension, and generic brands

Functional classification: Corticosteroid

Pharmacology and Mechanism of Action

Corticosteroid. Anti-inflammatory and immunosuppressive effects of dexamethasone are approximately 30 times more potent than cortisol. Anti-inflammatory effects are complex but primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. Use is for treatment of inflammatory and immune-mediated disease. This dexamethasone solution differs from dexamethasone sodium phosphate in that the sodium phosphate form is water-soluble and appropriate for intravenous administration. Dexamethasone solution is in a polyethylene glycol vehicle that should not be administered rapidly IV. Dexamethasone-21-isonicotinate is a suspension registered for IM use.

Indications and Clinical Uses

Dexamethasone is used for treatment of inflammatory and immune-mediated disease. The use of dexamethasone at high doses for treatment of shock is controversial. Most recent evidence does not support administration of dexamethasone for this use. Dexamethasone is also used as a diagnostic test of adrenal function. Large animal uses include induction of parturition (cattle) and treatment of inflammatory conditions. In cattle, corticosteroids also have been used in the treatment of ketosis. In horses, dexamethasone has been used to treat recurrent airway obstruction (RAO).

Precautionary Information

Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic-pituitary-adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and

immunosuppression. Secondary infections can occur as a result of immunosuppression and include infections from Demodex, toxoplasmosis, fungal infections, and UTIs. High-dose glucocorticoids in animals with neurologic disease can lead to excitotoxic cell death and oxidative injury via increased excitatory amino acids. In horses, dexamethasone adverse effects include risk of laminitis, although this effect is controversial and not supported by strong evidence.

Contraindications and Precautions

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously in animals with diabetes or renal failure and in pregnant animals. Intravenous injections should be done slowly because formulations contain polyethylene glycol, which can cause reactions from rapid intravenous injection (hemolysis, hypotension, and collapse). Do not administer dexamethasone-21-isonicotinate IV (IM use only).

Drug Interactions

Administration of corticosteroids with nonsteroidal anti-inflammatory drugs (NSAIDs) will increase the risk of GI injury. pH is 7-8.5. Do not mix with acidifying solutions. Otherwise, it is compatible with most intravenous fluid solutions.

Instructions for Use

Dosing schedules are based on the condition treated. Anti-inflammatory effects occur at doses of 0.1-0.2 mg/kg, and immunosuppressive effects occur at 0.2-0.5 mg/kg. Dexamethasone is used to test for hyperadrenocorticism. For the low-dose dexamethasone suppression test: dogs 0.01 mg/kg (or 0.015 mg/kg in some references) IV and cats 0.1 mg/kg IV; collect sample at 0, 4, and 8 hours. For high-dose dexamethasone suppression test: dogs 0.1 mg/kg (or 1.0 mg/kg in some references) and cats: 1.0 mg/kg.

Patient Monitoring and Laboratory Tests

For the low-dose and high-dose dexamethasone suppression tests, administer either 0.01 or 0.1 mg/kg and collect cortisol sample at 0, 4, and 8 hours after administration. The normal cortisol concentration after suppression test should be <30-40 nmol/L (1.1-1.3 mcg/dL). For the dexamethasone suppression test for horses, administer 0.04 mg/kg IM and collect postcortisol sample 24 hours later. Normal suppression in horses is <1 mcg/dL.

Formulations

Dexamethasone is available in a 2-mg/mL solution, which contains 500 mg polyethylene glycol; 0.25-, 0.5-, 0.75-, 1-, 1.5-, 2-, 4-, and 6-mg tablets; 0.1- and 1-mg/mL oral solution; and 10 mg per 15 g powder. Dexamethasone-21-isonicotinate suspension is 1 mg/mL.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Dexamethasone formulated in various oral mixtures to enhance flavoring was stable for 26 weeks at room temperature or refrigerated. Dexamethasone sodium phosphate is freely soluble in water, but dexamethasone solution (in polyethylene glycol) is practically insoluble in water.

Small Animal Dosage

Dogs and Cats

- Anti-inflammatory: 0.07-0.15 mg/kg q12-24h IV, IM, or PO.
- Pulse dose: 0.5 mg/kg PO, for 4 consecutive days, then repeated every 28 days.
- Low-dose dexamethasone suppression test: 0.01 mg/kg IV (dog) and 0.1 mg/kg IV (cat).
- High-dose dexamethasone suppression test: 0.1 mg/kg IV (dog) and 1.0 mg/kg IV (cat).
- Dexamethasone-21-isonicotinate: 0.03-0.05 mg/kg IM.

Large Animal Dosage

Cattle and Horses

- 0.04-0.15 mg/kg per day IV or IM. Some product labeling lists a total dose of 5-20 mg/animal, which corresponds to 0.01 to 0.04 mg/kg/day. However, for some conditions, higher doses may be needed.
- Horses, treatment of recurrent airway obstruction: 0.05-0.1 mg/kg IV or IM, q24h, or 0.165 mg/kg PO, q24h, usually for 2-3 days, but oral treatment has been continued for 7 days, then tapered half the dose for another 7 days.
- Induction of parturition (cattle): 0.05 mg/kg (25 mg/animal) as a single dose during the last week or 2 weeks of pregnancy. A dose of prostaglandin PG-F₂ alpha may be administered concurrently (0.5 mg/animal).
- Dexamethasone-21-isonicotinate: 0.01-0.04 mg/kg IM.

Sheep

- Induction of parturition: 0.15 mg/kg/day IM for 1-5 days during the last week of gestation.

Regulatory Information

Dexamethasone is approved for use in cattle, but withdrawal times are not established. Although withdrawal times are not listed on the label, at least 96 hours should be used for milk and 4-8 days for meat. Allow at least 3 weeks to eliminate residues from kidney and liver and 6 weeks to deplete drug from intramuscular injection site.

RCI Classification: 4

Dexamethasone Sodium Phosphate

Trade and other names: Sodium phosphate: Dexaject SP, Dexavet, and Dexasone. Decadron and generic brand tablets

Functional classification: Corticosteroid

Pharmacology and Mechanism of Action

Corticosteroid. Anti-inflammatory and immunosuppressive effects are approximately 30 times more potent than cortisol. Anti-inflammatory effects are complex but primarily occur via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. The difference among formulations is that dexamethasone sodium phosphate is a water-soluble formulation that can be injected intravenously. Dexamethasone solution is in a polyethylene glycol vehicle that should not be administered rapidly IV. Half-life in plasma for dexamethasone ranges from 3 to 6 hours, but duration of action is 36-48 hours.

Indications and Clinical Uses

Use of dexamethasone is for treatment of inflammatory and immune-mediated disease. The use of dexamethasone at high doses for treatment of shock is controversial. Most recent evidence does not support administration of dexamethasone for this use. Large animal uses include induction of parturition (cattle) and treatment of inflammatory conditions. In cattle, corticosteroids also have been used in the treatment of ketosis.

Precautionary Information

Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic-pituitary-adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include Demodex, toxoplasmosis, fungal infections, and UTIs. In horses, additional adverse effects include risk of laminitis.

Contraindications and Precautions

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously, or not at all, in animals receiving nonsteroidal anti-inflammatory drugs (NSAIDs) because these drugs administered concurrently will increase the risk of GI ulceration. Use cautiously in animals with diabetes or renal failure and in pregnant animals.

Drug Interactions

Administration of corticosteroids with NSAIDs will increase the risk of GI injury.

Instructions for Use

Dosing schedules are based on desired effect. Anti-inflammatory effects are seen at doses of 0.1-0.2 mg/kg, and immunosuppressive effects are seen at 0.2-0.5 mg/kg. Dexamethasone is used for testing hyperadrenocorticism. For the low-dose dexamethasone suppression test (for dogs) use 0.01 mg/kg (or 0.015 mg/kg in some references) IV and 0.1 mg/kg IV (for cats). For the high-dose dexamethasone suppression test in dogs use 0.1 mg/kg (or 1.0 mg/kg in some references) and in cats use 1.0 mg/kg. For the test in horses, administer 40 mcg/kg.

Patient Monitoring and Laboratory Tests

Monitor CBC periodically during treatment to assess effects. For monitoring a low-dose dexamethasone suppression test collect samples at 4 and 8 hours after dexamethasone. A normal suppression test should be cortisol <30-40 nmol/L (1.1-1.4 mcg/dL). For dexamethasone suppression in horses, collect samples at 17 and 19 hours. Normal horses should have cortisol <1.0 mcg/dL.

Formulations

Sodium phosphate solution is available as 4 mg/mL, equivalent to 3 mg/mL of dexamethasone base.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Dexamethasone sodium phosphate in other aqueous solutions have been stable for 28 days. Dexamethasone sodium phosphate is freely soluble in water, but dexamethasone solution (in polyethylene glycol) is practically insoluble in water. If

dexamethasone sodium phosphate is mixed with 5% dextrose solution or saline, it is stable for 24 hours.

Small Animal Dosage

Dogs and Cats

- Anti-inflammatory: 0.07-0.15 mg/kg q12-24h IV or IM.
- Shock, spinal injury (efficacy in question): 2.2-4.4 mg/kg IV.
- Low-dose dexamethasone suppression test: 0.01 mg/kg or 0.015 mg/kg IV (for dogs) and 0.1 mg/kg IV (for cats) and collect sample at 0, 4, and 8 hours.
- High-dose dexamethasone suppression test: 0.1 mg/kg or 1.0 mg/kg IV (for dogs) and 1.0 mg/kg IV (for cats).

Large Animal Dosage

Cattle and Horses

- Treatment of inflammation: 0.04-0.15 mg/kg/day IV or IM.
- Ketosis (cattle): 0.01 to 0.04 mg/kg IV or IM.
- Induction of parturition (cattle): 0.05 mg/kg (25 mg per animal) as a single dose during the last week or 2 weeks of pregnancy. A dose of prostaglandin PG-F₂ alpha may be administered concurrently (0.5 mg/animal).
- Dexamethasone suppression test in horses: 40 mcg/kg and collect samples at 17 and 19 hours.

Sheep

- Induction of parturition: 0.15 mg/kg/day IM for 1-5 days during the last week of gestation.

Regulatory Information

Although withdrawal times are not established, at least 96 hours is required for milk and 4-8 days for meat. However, at least 3 weeks are required to eliminate residues from kidney and liver and 6 weeks for intramuscular injection site.

Dexmedetomidine Hydrochloride

dex-meh-deh-toe'mih-deen hye-droe-klor'ide

Trade and other names: Dexdomitor

Functional classification: Analgesic, alpha₂ agonist

Pharmacology and Mechanism of Action

Alpha₂-adrenergic agonist. Alpha₂ agonists decrease release of neurotransmitters from the neuron. Dexmedetomidine and medetomidine (Domitor) are very similar in activity. Medetomidine is a racemic mixture containing 50% dexmedetomidine 50% levomedetomidine. Dexmedetomidine is the active enantiomer of the mixture (D-isomer); therefore (on a mg/mg basis) dexmedetomidine is twice the potency of medetomidine but with the same pharmacological activity and equivalent analgesic and sedative effects. The proposed mechanism whereby they decrease transmission is via binding to presynaptic alpha₂ receptors (negative feedback receptors). The result is decreased sympathetic outflow, analgesia, sedation, and anesthesia. Other drugs in this class include medetomidine, xylazine, detomidine, romifidine, and clonidine. Receptor-binding studies indicate that alpha₂/alpha₁-adrenergic receptor selectivity is more than 1000 times that of xylazine.

Indications and Clinical Uses

Dexmedetomidine, like other α_2 agonists, is used as a sedative, anesthetic adjunct, and analgesia. It is approved for use in both dogs and cats. It can be administered to facilitate examinations, diagnostic procedures, treatments, ear and teeth cleaning, and minor surgery. It has been used to sedate animals for intradermal skin testing without affecting results. In cats the peak effects are observed in 15-60 minutes, and the recovery occurs by 180 minutes. It has similar clinical effects as medetomidine and can be used for similar indications. It can be administered in combination with ketamine, butorphanol, or opiate agonists for sedation and short-term surgical procedures (see Instructions for Use). Dexmedetomidine is well absorbed across membranes and has produced similar effects in cats after oral transmucosal (buccal) administration compared to IM injection.

Precautionary Information

Adverse Reactions and Side Effects

In small animals, vomiting is the most common acute effect. Vomiting is more common in cats than dogs. α_2 agonists decrease sympathetic output. Cardiovascular depression may occur. Like medetomidine, dexmedetomidine can produce an initial bradycardia and hypertension. An initial increase in blood pressure may be followed by a decrease in blood pressure caused by decreased sympathetic tone. Lower respiratory rate and body temperature occur in animals during dexmedetomidine sedation. Transient arrhythmias may occur in some animals. Paradoxical excitement may occur in some animals, and animals with high anxiety levels may not respond predictably to α_2 agonists. If adverse reactions are observed, reverse with atipamezole (Antisedan). Yohimbine also can reverse medetomidine.

Contraindications and Precautions

Use cautiously in animals with heart disease. Use may be contraindicated in older animals with preexisting cardiac disease. Use cautiously in animals with respiratory, liver, or kidney disease. Do not use in animals with signs of shock. Xylazine causes problems in pregnant animals, and this also should be considered for other α_2 agonists. Use cautiously in animals that are pregnant because it may induce labor. In addition, it may decrease oxygen delivery to fetus in late gestation. Dexmedetomidine can be absorbed through intact human skin; therefore, avoid human exposure.

Drug Interactions

Do not use with other drugs that may cause cardiac depression. Do not mix in vial or syringe with other anesthetics. Reverse with atipamezole at a dose of 25-300 mcg/kg IM. Use with opioid analgesic drugs will greatly enhance the CNS depression. Consider lowering doses if administered with opioids. Anticholinergic drugs (e.g., atropine) may be given in moderate doses *prior* to drug administration to prevent bradycardia induced by α_2 agonists, but it is not routinely needed and may prolong initial hypertension. However, administration *simultaneously* with α_2 agonists is not recommended.

Instructions for Use

Dexmedetomidine, medetomidine, and detomidine are more specific for the α_2 receptor than xylazine. They may be used for sedation, analgesia, and minor surgical procedures. It is recommended to withhold food for several hours prior to

administration of alpha₂ agonists to minimize vomiting. Lower doses are often administered for cases when less sedation is needed or when combined with other drugs. Dexmedetomidine can be used with other anesthetics such as propofol, thiopental, opiates, benzodiazepines, and inhalent gas anesthetics. However, lower doses (as much as 40%-60%) of other drugs are anticipated when used with dexmedetomidine. When administered at a dose of 10 mcg/kg to cats, in combination with butorphanol or ketamine there was adequate sedation without significant cardiovascular effects. In dogs and cats, reverse with atipamezole at a dose of 25-300 mcg/kg (equal to volume of dexmedetomidine used) IM.

Patient Monitoring and Laboratory Tests

Monitor vital signs during anesthesia. Monitor heart rate, blood pressure, and ECG during anesthesia. Alpha₂ agonists will increase blood glucose because of effects on insulin secretion.

Formulations

Dexmedetomidine is available in vials containing 0.5 mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 125 mcg/m² IM for preanesthetic, minor sedation, and analgesia (range is 9 mcg/kg for small dogs to 3 mcg/kg for large dogs).
- 375 mg/m² IV or 500 mg/m² IM for deeper sedation, analgesia, and minor surgical procedures (IV dose range is 28 mcg/kg for small dogs to 9 mcg/kg for large dogs; IM dose range is 40 mcg/kg for small dogs to 12 mcg/kg for large dogs).
- Lower doses are used for short-term sedation and analgesia or when combined with other analgesic or anesthetic agents.

Cats

- 40 mcg/kg (0.04 mg/kg) IM (0.35 mL for 4 kg cat). Oral transmucosal administration at this dose produces equivalent effects as IM injection. Reverse with atipamezole 0.2 mg/kg IM.
- Lower doses (e.g., 10 mcg/kg) have been used for short-term sedation and analgesia or when combined with other agents.

Large Animal Dosage

No doses have been established for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. The withdrawal time for xylazine in food animals is 4 days for meat and 24 hours for milk. A minimum of those withdrawal periods should be used for dexmedetomidine. For additional extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Dextran

deks'tran

Trade and other names: Dextran 70 and Gentran-70**Functional classification:** Fluid replacement

Pharmacology and Mechanism of Action

Synthetic colloid used for volume expansion. Dextrans are glucose polymers and are available as low molecular weight (Dextran 40) and high molecular weight (Dextran 70). Dextran 70 is the most often used. The colloids such as dextrans are large-molecular-weight molecules that remain in the vasculature because of their large size. Therefore, they increase colloid osmotic pressure within the vasculature to prevent intravascular fluid loss and inhibit tissue edema. Other colloids used are hetastarch and pentastarch.

Indications and Clinical Uses

Dextran is a high-molecular-weight compound administered IV to maintain intravascular volume. It is used for acute treatment of hypovolemia and shock. Duration of effect is approximately 24 hours.

Precautionary Information

Adverse Reactions and Side Effects

There is only limited use in veterinary medicine, and adverse effects have not been reported. In people, coagulopathies are possible because of decreased platelet function and antithrombotic effects. Acute renal failure has occurred, and anaphylactic shock also has occurred in people.

Contraindications and Precautions

Do not use in animals that are prone to bleeding problems. Dextrans can interfere with cross-matching of blood for transfusion. Cats are more susceptible to fluid overload than dogs, and lower doses must be used in cats.

Drug Interactions

Compatible with most intravenous fluid solutions, including 0.9% saline solution and 5% dextrose solution.

Instructions for Use

Used primarily in critical care situations. Delivered slowly via constant rate infusion (60-90 minutes). In emergency use, bolus doses of 20 mL/kg can be administered more rapidly.

Patient Monitoring and Laboratory Tests

Monitor patient's cardiopulmonary status carefully during administration. Dextrans can interfere with cross-matching of blood.

Formulations

Dextran is available in 250-, 500-, and 1000-mL solution for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 10-20 mL/kg/day IV to effect, usually administered over 30-60 minutes.

Cats

- 5-10 mL/kg/day IV, over 30-60 minutes.

Large Animal Dosage

Horses and Cattle

- 10 mL/kg/day IV.

Regulatory Information

Withdrawal times are not established. However, this drug presents little risk from residues; therefore, a short withdrawal time is suggested for animals intended for food.

Dextromethorphan

deks-troe-meth-or'fan

Trade and other names: Benlyn and others

Functional classification: Antitussive

Pharmacology and Mechanism of Action

Centrally acting antitussive drug. Dextromethorphan shares similar chemical structure to opiates but does not affect opiate receptors and appears to directly affect cough receptor. Dextromethorphan is the d-isomer of levorphan (the l-isomer, levorphan, is an opiate with addictive properties, but the d-isomer does not). Dextromethorphan produces mild analgesia and modulates pain via its ability to act as an n-methyl D-aspartate (NMDA) antagonist, but this is unrelated to the antitussive action.

Indications and Clinical Uses

Dextromethorphan has been used for suppression of nonproductive cough. However, its efficacy for reducing cough has been questioned because of a lack of proof. Dextromethorphan also has been used as an adjunct for treating pain because of NMDA antagonism. Pharmacokinetic studies in dogs indicated that dextromethorphan does not attain effective concentrations after oral administration. Even after intravenous administration, concentrations of the parent drug and active metabolite persisted for only a short time after dosing. Therefore, routine use in dogs is not recommended until more data are available to establish safe and effective doses. Data have not been reported for the pharmacokinetics in cats or any other species.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects not reported in veterinary medicine. High overdose may cause sedation. After administration to dogs, dextromethorphan produced adverse effects seen as vomiting after oral doses and CNS reactions after intravenous

administration. Some preparations contain alcohol, which can be unpalatable in small animals, especially cats.

Contraindications and Precautions

There are no contraindications identified for animals. However, pet owners should be cautioned that many OTC preparations contain other drugs that may produce significant side effects. For example, some combinations also contain acetaminophen, which can be toxic to cats. Some preparations also contain a decongestant, such as pseudoephedrine, which can cause excitement and other side effects.

Drug Interactions

There are no direct interactions identified for dogs. However, interactions are possible when used with other drugs that may interfere with cytochrome P-450 metabolism.

Instructions for Use

Many OTC preparations may contain other ingredients (e.g., antihistamines, decongestants, ibuprofen, and acetaminophen). Adverse effects from each of these ingredients, such as toxic reactions caused by acetaminophen, CNS excitement from decongestants, and GI toxicity from ibuprofen, can occur in animals.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Dextromethorphan is available in syrup, capsules, and tablets in many OTC products. There are many preparations available without a prescription in liquid and tablet form. OTC formulations may vary in concentration but typically contain 2, 5, 10, or 15 mg/mL and in 15-20-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 0.5-2 mg/kg q6-8h PO (however, use is not recommended because efficacy at these doses has not been shown).

Large Animal Dosage

No dosing information available. It has little value for treating large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Dextrose Solution

deks'trose

Trade and other names: D5W

Functional classification: Fluid replacement

Pharmacology and Mechanism of Action

Dextrose is a sugar added to fluid solutions. It is isotonic as delivered. Five percent dextrose contains 50 g of dextrose per liter. The pH of this solution is 3.5-6.5. Alternatively, 50% dextrose solution can be added to intravenous fluids to supplement dextrose. For example, 100 mL of 50% dextrose added to 1000 mL supplies 5% dextrose.

Indications and Clinical Uses

Five percent dextrose is an isotonic fluid solution used for intravenous administration. Dextrose is considered only for short-term use because it is deficient in electrolytes. After the glucose is metabolized, the water is rapidly distributed out of the vascular space. For emergency treatment of hypoglycemia or to supplement fluids, a 50% dextrose solution (500 mg/mL) is used. Dextrose may be administered in a 50% solution to treat periparturient cows with ketosis and hepatic lipidosis or to support anorexic or recumbent cows.

Precautionary Information

Adverse Reactions and Side Effects

High doses can produce pulmonary edema.

Contraindications and Precautions

Use cautiously in animals with low electrolyte concentrations. Five percent dextrose solution is not a suitable maintenance solution because it does not provide electrolytes. It should not be considered as a replacement solution or a source of energy requirements; it supplies only 170 kcal/L. When aggressive treatment is used with 50% dextrose, it may cause rapid decrease in plasma phosphorous and potassium (intracellular shift).

Drug Interactions

No interactions. Five percent dextrose solution is compatible with fluids and most intravenous drugs.

Instructions for Use

Dextrose is a commonly used fluid solution administered via constant rate infusion. However, it is not a maintenance solution. Dextrose 50% solution can also be added to fluids to supply dextrose. For example, 50 mL of 50% dextrose is added to 1000 mL fluids to achieve a final 2.5% solution.

Patient Monitoring and Laboratory Tests

Monitor patient's hydration status and evidence of pulmonary edema during infusion. Monitor acid-base status.

Formulations

Fluid solution for intravenous administration is 5% dextrose, which contains 5 g of glucose per 100 mL (50 g/L). 50% dextrose contains 500 mg/mL (50 g/100 mL).

Stability and Storage

Store in a tightly sealed container at room temperature.

Small Animal Dosage

Dogs and Cats

- 5% dextrose solution: 40-50 mL/kg q24h IV.
- In emergency hypoglycemic crisis: 1 mL 50% dextrose solution IV diluted with saline.

Large Animal Dosage

Calves, Cattle, and Horses

- 5% dextrose solution: 45 mL/kg q24h IV.
- Cows: 0.1-0.2 gm/kg/hr IV of Dextrose 50% solution for 5 days to treat hepatic lipidosis and ketosis.

Regulatory Information

Withdrawal times are not established. However, this drug presents little risk from residues; therefore, no withdrawal time is suggested for animals intended for food.

Diazepam

dye-ay'zeh-pam

Trade and other names: Valium and generic brands

Functional classification: Anticonvulsant

Pharmacology and Mechanism of Action

Benzodiazepine. Central acting CNS depressant. Mechanism of action appears to be via potentiation of GABA-receptor-mediated effects in CNS because it binds to the GABA binding site. Diazepam is metabolized to desmethyldiazepam (nordiazepam) and oxazepam. These metabolites also have some centrally acting benzodiazepine effects. In dogs, the intravenous half-life of diazepam is short (<1 hour), but active metabolites are produced. In cats, the intravenous half-life is approximately 5 hours.

Indications and Clinical Uses

Diazepam is used for sedation, anesthetic adjunct, anticonvulsant, and behavioral disorders. Although it is used as a muscle relaxant, its efficacy for this use is not established. In cats, diazepam has been administered IV for short-term stimulation of appetite. In cats, oral administration has been effective for decreasing urine spraying, but relapses are common when the drug is discontinued. Diazepam is usually administered orally or IV. However, it has been shown to be absorbed adequately in dogs from rectal administration and intranasal administration (41% absorption from nasal spray in dogs).

Precautionary Information

Adverse Reactions and Side Effects

Sedation is the most common side effect. In dogs, ataxia and increased appetite can be observed. Diazepam may cause paradoxical excitement and agitation in dogs. In cats, idiopathic fatal hepatic necrosis has been reported. Chronic administration may lead to dependence and a withdrawal syndrome if

discontinued. Administration IM or SQ can be painful and irritating. Intravenous injection can cause phlebitis.

Contraindications and Precautions

Diazepam is highly dependent on liver blood flow for metabolism. Do not administer to patients with impaired liver function. Long-term use in cats should be avoided because of risk of liver toxicity. Its use for ivermectin-induced CNS intoxication is controversial.

Drug Interactions

Diazepam is highly lipophilic and will bind to (adsorb) soft plastic containers, infusion, sets, and fluid bags. Storage of diazepam in such containers is not recommended. Diazepam is not soluble in aqueous solutions. Admixing with aqueous solutions or fluids can result in precipitation.

Instructions for Use

Clearance in dogs is many times faster than in people (half-life in dogs less than 1 hour), requiring frequent administration. For treatment of status epilepticus, diazepam may be administered IV, intranasal, or rectally. Avoid IM administration because of pain from injection and unpredictable absorption.

Patient Monitoring and Laboratory Tests

Plasma concentrations in the range of 100-250 ng/mL have been cited as the therapeutic range for people. Other references have cited this range as 150 to 300 ng/mL. Although plasma or serum may be analyzed for concentrations of benzodiazepines, there are no readily available tests for monitoring in many veterinary laboratories. Laboratories that analyze human samples may have nonspecific tests for benzodiazepines. With these assays, there may be cross-reactivity among diazepam and the metabolites desmethyldiazepam and oxazepam.

Formulations

Diazepam is available in 2-, 5-, and 10-mg tablets and 5 mg/mL solution for injection.

Stability and Storage

Do not store in soft plastic (PVC) containers or fluid bags. Significant adsorption occurs to soft plastic. However, it is compatible with hard plastic, such as syringes. Do not expose to light. Compounded formulations, especially those prepared for transdermal application, may not be stable. Diazepam is practically insoluble in water but is soluble in alcohol and propylene glycol. Diazepam undergoes hydrolysis in water. Diazepam prepared as an oral suspension (1 mg/mL) in various vehicles (pH 4.2) was stable for 60 days.

Small Animal Dosage

Dogs and Cats

- Preanesthetic: 0.5 mg/kg IV.
- Status epilepticus: 0.5 mg/kg IV, 0.5-1 mg/kg sprayed intranasal, or 1 mg/kg rectal; repeat if necessary.
- Constant rate infusion (CRI): 15 mcg/kg/min (1 mg/kg/hr), which can be decreased by 50% in some animals if excessive side effects are observed.
- Appetite stimulant (cats): 0.2 mg/kg IV.
- Behavior treatment (cats): 1-4 mg/cat q12-24h PO.
- Behavior treatment (dogs): 0.5-2 mg/kg q4-6h, PO.

220 Dichlorphenamide

Large Animal Dosage

Cattle, Sheep, and Goats

- 0.02-0.08 mg/kg IV, up to 0.5 mg/kg slowly IV. Dose according to desired effect. Cows may be recumbent after 0.5 mg/kg. Do not administer IM.

Horses

- Seizures: 0.1-0.4 mg/kg IV (start with 50-100 mg per horse). CRI for foals: 1-3 mg per hour.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Schedule IV controlled drug

RCI Classification: 2

Dichlorphenamide

dye-klor-fen'ah-mide

Trade and other names: Daranide

Functional classification: Diuretic

Pharmacology and Mechanism of Action

Carbonic anhydrase inhibitor. Diuretic. Dichlorphenamide, like other carbonic anhydrase inhibitors, produces a diuresis by inhibiting the reabsorption of bicarbonate in proximal renal tubules via enzyme inhibition. This action results in loss of bicarbonate in the urine and a diuresis. The action of carbonic anhydrase inhibitors results in significant urine loss of bicarbonate, alkaline urine, and water loss.

Indications and Clinical Uses

Dichlorphenamide is rarely used as a diuretic any longer. There are more potent and effective diuretic drugs available such as the loop diuretics (furosemide). Dichlorphenamide, like other carbonic anhydrase inhibitors, is used primarily to reduce intraocular pressure in animals with glaucoma. Methazolamide is used more often than dichlorphenamide or acetazolamide for this purpose, and other treatment regimens are used more often than carbonic anhydrase inhibitors. Dichlorphenamide, like other carbonic anhydrase inhibitors, is sometimes used to produce a more alkaline urine for management of some urinary calculi.

Precautionary Information

Adverse Reactions and Side Effects

With prolonged use it will deplete bicarbonate if not replenished. Sulfonamide derivative. Some animals sensitive to sulfonamides may be sensitive to dichlorphenamide. Hypokalemia may occur in some patients. Severe metabolic acidosis is rare.

Contraindications and Precautions

Use cautiously in animals sensitive to sulfonamides.

Drug Interactions

Dichlorphenamide will produce alkaline urine, which may affect clearance of some drugs. Alkaline urine may potentiate the effects of some antibacterial drugs (e.g., macrolides and quinolones).

Instructions for Use

Dichlorphenamide is not used as diuretic but is most commonly used to treat glaucoma or produce alkaline urine. It has been combined with other antiglaucoma agents.

Patient Monitoring and Laboratory Tests

Monitor ocular pressure for glaucoma treatment. Monitor serum potassium and acid–base status during treatment.

Formulations

Dichlorphenamide is no longer commercially available. However older forms were available in 50-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 3-5 mg/kg q8-12h PO.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Dichlorvos

dye'klor-vos

Trade and other names: Task, Dichlorovos, Atgard, DDVP, Verdisol, and Equigard

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic drug. Kills parasites by anticholinesterase action.

Indications and Clinical Uses

Dichlorvos is used primarily to treat intestinal parasites. Parasites that may be treated include *Toxocara canis* and *Toxascaris leonina* (roundworms), *Ancylostoma caninum*, *Uncinaria stenocephala* (hookworms), and *Trichuris vulpis* (whipworms). However, efficacy against *T. vulpis* may be erratic. In horses, it may be used for the removal and control of bots (*Gastrophilus intestinalis*, *G. nasalis*), large strongyles (*Strongylus vulgaris*, *S. equinus*, *S. edentatus*), small strongyles (of the genera *Cyathostomum*,

222 Dichlorvos

Cylicocercus, *Cylicodontophorus*, *Triodontophorus*, *Poteriostomum*), pinworms (*Oxyuris equi*), and large roundworm (*Parascaris equorum*). In pigs, it is used to treat and control of mature, immature, and/or fourth-stage larvae of the whipworm (*Trichuris suis*), nodular worm (*Oesophagostomum* sp.), large roundworm (*Ascaris suum*), and the thick stomach worm (*Ascarops strongylina*).

Precautionary Information

Adverse Reactions and Side Effects

Overdoses can cause organophosphate intoxication (treat with pralidoxime chloride and atropine). Signs of toxicity include salivation, diarrhea, difficulty breathing, and muscle twitching.

Contraindications and Precautions

Do not use in patients with heartworms. Do not administer within 2 days of administration of a cholinesterase-inhibiting drug. Use a split-dosage schedule in animals that are old, heavily parasitized, anemic, or otherwise debilitated. Do not use in young foals, kittens, or puppies. Its use may exacerbate clinical signs in animals with respiratory disease, such as bronchitis and obstructive pulmonary disease. Do not allow birds access to feed containing this preparation or to fecal excrement from treated animals.

Drug Interactions

Do not use with other anticholinesterase drugs. Do not use with other antifilarial agents, muscle relaxants, CNS depressants, or tranquilizers.

Instructions for Use

Administer in about one third of the regular canned dog food ration or in ground meat. Dogs may be treated with any combination of capsules and/or pellets so that the animal receives a single dose. One half of the single recommended dosage may be given, and the other half may be administered 8 to 24 hours later. For horses, administer in the grain portion of the ration. It may be administered at one half of the single recommended dosage and repeated 8 to 12 hours later for treatment of old, emaciated, or debilitated subjects or those reluctant to consume medicated feed. Split the dose if heavy parasitism may cause concern over mechanical blockage of the intestinal tract.

Patient Monitoring and Laboratory Tests

Monitor for parasites as part of a regular parasite control program.

Formulations

Dichlorvos is available in 10- and 25-mg tablets. Manufacture of equine formulations has been discontinued.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 26.4-33 mg/kg once PO.

Cats

- 11 mg/kg once PO.

Large Animal Dosage

Pigs

- 11.2-21.6 mg/kg once PO. For pregnant sows, mix into a gestation feed to provide 1000 mg/head daily during last 30 days of gestation, mixed at a rate of 334-500 g/ton of feed. For other pigs, mix at 334 per ton of feed and feed as sole ration for 2 consecutive days (rate of 8.4 pounds of feed per head until the medicated feed has been consumed).

Horses

- 31-41 mg/kg once PO.

Regulatory Information

Do not administer to horses intended for food.

For other animals, no regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Diclazuril

dih-klaz'yoor-il

Trade and other names: Clincox

Functional classification: Antiprotozoal

Pharmacology and Mechanism of Action

Coccidiostat. Diclazuril is a triazinone antiprotozoal that is effective for treating infections caused by *Isospora* spp., *Toxoplasma gondii*, and *Eimeria* spp. and has been used for treating coccidiosis. It also has been used in horses to treat equine protozoal myeloencephalitis (EPM) caused by *Sarcocystis neurona*. Toltrazuril sulfone (ponazuril) is an active metabolite found in serum and cerebrospinal fluid (CSF) of treated horses. Because of the availability of a commercial formulation of ponazuril (Marquis), it is preferred over diclazuril by many veterinarians for treating infections in horses.

Indications and Clinical Uses

Dosage information for diclazuril has been based on approved indications, experimental studies, pharmacokinetic data, and limited clinical experience. Diclazuril has been replaced by ponazuril for treating most cases of EPM in horses.

Precautionary Information

Adverse Reactions and Side Effects

No specific adverse effects have been reported.

Contraindications and Precautions

No contraindications have been reported.

Drug Interactions

No drug interactions have been reported.

Instructions for Use

Administer orally to horses.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Diclaruzil is available as a feed additive for poultry in other countries and has been imported into the United States with permission from the FDA.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

No dosing information has been reported for small animals.

Large Animal Dosage**Horses**

- Treatment of EPM: 2.5 mg/kg q12h PO for a minimum of 21 days.

Regulatory Information

Do not administer to horses intended for food. For other animals, no regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888 USFARAD (1-888-873-2723).

Dicloxacillin Sodium

dye-kloks-ah-sill'in soe'dee-um

Trade and other names: Dynapen and generic

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Dicloxacillin is a beta-lactam antibiotic—a semisynthetic derivative of penicillin. It resembles ampicillin in activity except it has greater stability against staphylococcal beta-lactamase. Like other antibiotics in this class, it inhibits bacterial cell wall synthesis by binding to penicillin-binding proteins and weakening the cell wall. The spectrum is limited to gram-positive bacteria, especially staphylococci.

Indications and Clinical Uses

Dicloxacin has a relatively narrow spectrum of activity. Like cloxacillin and oxacillin, the spectrum of dicloxacillin includes gram-positive bacilli, including beta-lactamase-producing strains of *Staphylococcus*. Therefore, it has been used to treat staphylococcal infections in animals, including pyoderma. It is not active against methicillin-resistant *Staphylococcus*. Because of availability of other drugs for small animals to treat this spectrum of bacteria, dicloxacillin is not used commonly. Because it is an oral drug with limited absorption in large animals, its use is limited to small animal oral administration.

Precautionary Information**Adverse Reactions and Side Effects**

Adverse effects of penicillin drugs are most commonly caused by drug allergy. This can range from acute anaphylaxis when administered to other signs of

allergic reaction when other routes are used. When administered orally (especially with high doses), diarrhea is possible.

Contraindications and Precautions

Use cautiously in animals allergic to penicillin-like drugs.

Drug Interactions

There are no specific drug interactions. Dicloxacillin is absorbed better on an empty stomach in dogs.

D

Instructions for Use

No clinical efficacy studies available for dogs or cats. In dogs, oral absorption is low and may not be suitable for therapy. Administer if possible on an empty stomach.

Patient Monitoring and Laboratory Tests

Use oxacillin as a guide for sensitivity testing. Break points for oxacillin apply to dicloxacillin.

Formulations

Dicloxacillin is available in 125-, 250-, and 500-mg capsules and 12.5-mg/mL oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with other drugs. Reconstituted oral suspension is stable for 14 days refrigerated. Compounded formulations, especially aqueous formulations, may not be stable.

Small Animal Dosage

Dogs and Cats

- 11-55 mg/kg q8h PO.

Large Animal Dosage

No dose has been reported for large animals. Oral absorption is low.

Regulatory Information

No regulatory information is available. Because oral absorption is expected to be minimal, when using systemically to food animals, apply similar withdrawal times as for ampicillin. Alternatively, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Diethylcarbamazine Citrate

dye-eth-il-kar-bam'eh-zeen sih'trate

Trade and other names: Caricide, Filaribits, and Nemacide

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Heartworm preventative and anthelmintic. Produces neuromuscular blockade in parasite through inhibition of neurotransmitter that causes paralysis of worms.

Indications and Clinical Uses

Caricide tablets and some other brands used for heartworm prevention have been voluntarily withdrawn from the sponsor. Because of the availability of other heartworm preventatives, the use of diethylcarbamazine has diminished significantly. Diethylcarbamazine has been used to prevent infection caused by heartworms in dogs. It is administered regularly during heartworm season in endemic areas. It is not effective to treat heartworms once infection is established. Other uses of diethylcarbamazine include control of ascarids infections (*Toxocara canis* and *Toxascaris leonina*) and as an aid in treatment of ascarid infections at higher doses (55 to 110 mg/kg). In cats, diethylcarbamazine has been used to treat ascarid worm infections (55-110 mg/kg).

Precautionary Information

Adverse Reactions and Side Effects

Overdoses cause vomiting. If administered to an animal with positive microfilaria, reactions, including pulmonary reactions, are possible. This drug is a piperazine derivative, which is a class of antiparasitic drugs considered generally safe in animals.

Contraindications and Precautions

Dogs with established heartworm infections caused by *Dirofilaria immitis* should not receive diethylcarbamazine until they have been treated with an adulticide to kill the adult heartworms followed by appropriate microfilaricidal treatment. Reactions can occur in animals with positive microfilaria. However, there are no breed sensitivities or other specific contraindications.

Drug Interactions

No specific drug interactions are reported.

Instructions for Use

Specific protocols for heartworm administration may be based on the region of country because the time (season) required for heartworm prevention depends on the duration of active mosquitoes during the year. Although diethylcarbamazine is effective to prevent heartworms, it requires almost continual daily treatment for efficacy. Two or three doses should not be missed. Occasionally some animals vomit immediately after dosing. Administration with food sometimes decreases this reaction. If diethylcarbamazine treatment has been interrupted, the American Heartworm Society recommends switching chemoprophylaxis to macrocyclic lactones (ivermectin and related drugs).

Patient Monitoring and Laboratory Tests

Monitor heartworm status of patient. It is important to test for microfilaria in animals before prescribing. Manufacturers recommend that animals that are currently receiving diethylcarbamazine be checked for microfilaria every 6 months. Reactions can occur in animals with positive microfilaria.

Formulations

Although some brands have been withdrawn by the sponsor, some availability of other diethylcarbamazine tablets may vary with manufacturer and brand name. Not every brand name is available in the sizes listed. Both plain and chewable tablets have been available. Tablet sizes include 30, 45, 50, 60, 100, 120, 150, 180, 200, 300, and 400 mg. Syrup has been available as 60 mg/mL.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Heartworm prophylaxis: 6.6 mg/kg q24h PO.
- Treatment of ascarids: 55-110 mg/kg PO, as a single treatment (110 mg/kg dose may be divided into twice per day).

Cats

- Ascarid treatment: 55-110 mg/kg PO. When treating Ascarid parasites, consider repeating treatment in 10-20 days to remove immature worms.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available.

For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Diethylstilbestrol

dye-eth-il-stil-bess'trole

Trade and other names: DES and generic brands

Functional classification: Hormone

Pharmacology and Mechanism of Action

Diethylstilbestrol, known as DES, is a synthetic drug with estrogen effects. It differs from steroid compounds because it does not have a steroid ring. It is used for estrogen replacement in animals. When used to treat urinary incontinence, the action of DES is believed to increase sensitivity of alpha receptors in the urinary sphincter to restore continence.

Indications and Clinical Uses

DES is most commonly used to treat estrogen-responsive incontinence in dogs. Phenylpropanolamine (PPA) has been used in dogs when DES therapy is no longer effective. Conjugated estrogens (e.g., Premarin at 20 mcg/kg twice weekly) have been used in some dogs when DES is unavailable. Estriol also has been used in some dogs to treat incontinence. DES also has been used to induce abortion in dogs. Commercial forms of DES are no longer available, but it is available through some compounding pharmacies.

Precautionary Information

Adverse Reactions and Side Effects

Side effects may occur that are caused by excess estrogen. Estrogen therapy may increase risk of pyometra and estrogen-sensitive tumors. Although bone marrow depression (particularly anemia) has been reported from administration of other

estrogens in dogs and has been cited as a potential risk, it is a rare complication of DES therapy.

Contraindications and Precautions

DES has been associated with development of cancer, and human exposure should be minimized as much as possible (the use is prohibited in food animals). Although not reported as a significant clinical problem with DES, problems with anemia have occurred with administration of high doses of estrogens to animals.

Drug Interactions

No significant drug interactions have been reported for animals. However, in people, administration of estrogens increases thyroid-binding globulin and may decrease the active form of thyroid hormone (T4) in patients receiving thyroid supplementation.

Instructions for Use

Doses listed are for treating urinary incontinence and vary depending on response. Titrate dose to individual patient's response. Although used to induce abortion, it was not efficacious in one study that administered 75 mcg/kg.

Patient Monitoring and Laboratory Tests

Monitor CBC to detect signs of bone marrow toxicity. Monitor T4 levels if patients are hypothyroid and receiving supplementation.

Formulations

DES has been available in 1- and 5-mg tablets and 50-mg/mL injection. DES is no longer marketed commercially in the US, but it is available from compounding pharmacists.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been reported. However, compounded tablets are available from compounding pharmacies, and anecdotal information indicates that they are effective.

Small Animal Dosage

Dogs

- 0.1-1 mg/dog q24h PO. Size of dose is proportional to size of dog. Continue daily dose for 5 days, then reduce frequency of administration to 2 or 3 times per week.

Cats

- 0.05-0.1 mg/cat q24h PO.

Large Animal Dosage

No dose is available for large animals. Use in animals intended for food is prohibited.

Regulatory Information

It is prohibited to administer DES to animals that produce food.

Difloxacin Hydrochloride

dye-floks'ah-sin hye-droe-klor'ide

Trade and other names: Dicural

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Fluoroquinolone antibacterial drug. Acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. Bactericidal with broad spectrum of activity. Antibacterial activity includes *Escherichia coli*, *Klebsiella* spp., *Pasteurella* spp., and other gram-negative bacilli. Activity against *Pseudomonas aeruginosa* is less than for other gram-negative bacilli. Activity against gram-positive cocci includes *Staphylococcus*, *Streptococcus* and *Enterococcus* are more resistant. In horses, it has an oral half-life of 10.8 hours and bioavailability of 68%.

Indications and Clinical Uses

Difloxacin, like other fluoroquinolones, is used for a variety of infections including skin infections, wound infections, and pneumonia. Unlike other fluoroquinolones, difloxacin does not have high renal clearance. Urine concentrations may not be sufficient for some UTIs.

Precautionary Information

Adverse Reactions and Side Effects

High concentrations may cause CNS toxicity, especially in animals with renal failure. Difloxacin may cause some nausea, vomiting, and diarrhea at high doses. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4 weeks to 28 weeks of age. Large, rapidly growing dogs are the most susceptible. Safety in cats has not been reported. It has not been reported if there is a potential to cause retinal ocular injury in cats.

Contraindications and Precautions

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures, such as epileptics. Avoid use in cats unless safety has been established.

Drug Interactions

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, or calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

Instructions for Use

Dose range can be used to adjust dose depending on severity of infection and susceptibility of bacteria. Bacteria with low minimum inhibitory concentration (MIC) values can be treated with a low dose; susceptible bacteria with higher MIC values should be treated with a higher dose. Difloxacin is primarily eliminated in feces rather than urine (urine is less than 5% of clearance). Sarafloxacin is an active desmethyl metabolite but produced in low amounts. Oral absorption in horses is low and should only be used for bacteria with MIC less than 0.12 mcg/mL.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms is ≤ 0.5 mcg/mL for canine pathogens. Other fluoroquinolones may be used in some cases to estimate susceptibility to this fluoroquinolone. However, if ciprofloxacin is used to test susceptibility to *Pseudomonas aeruginosa*, ciprofloxacin may be several times more active than other fluoroquinolones.

Formulations

Difloxacin is available in 11.4-, 45.4-, and 136-mg tablets. (In some countries, 5% injectable is available.)

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated but has been mixed with simple syrup (100 mg/mL) for horses.

Small Animal Dosage

Dogs

- 5-10 mg/kg q24h PO.

Cats

No dosing information for cats is available. There is no safety information available.

Large Animal Dosage

Horses: 5 mg/kg PO, q24h.

Regulatory Information

Do not administer to animals intended for food.

Digitoxin

dih-jih-toks'in

Trade and other names: Digimerck (European)

Functional classification: Cardiac inotropic agent

Pharmacology and Mechanism of Action

Cardiac inotropic agent. Digitoxin increases cardiac contractility and decreases heart rate. The mechanism is via inactivation of cardiac muscle sodium-potassium ATPase and increased intracellular accumulation of calcium, triggering calcium release from the sarcoplasmic reticulum. In addition, neuroendocrine effects include sensitization of baroreceptors, which decreases heart rate. Beneficial effects for heart failure may be via these neuroendocrine effects.

Indications and Clinical Uses

Digitoxin is indicated in patients with myocardial failure and to control the rate of supraventricular tachycardias. Digitoxin formulation availability for treating patients is limited. Digitoxin is no longer be obtained in the US. Subsequently, most of the digitoxin use has been replaced by digoxin. Digoxin is an active metabolite of digitoxin and may be used instead of digitoxin.

Precautionary Information

Adverse Reactions and Side Effects

Digitalis glycosides have narrow therapeutic index. Digitoxin may cause a variety of arrhythmias in patients (e.g., AV block and ventricular tachycardia). It frequently causes vomiting, anorexia, and diarrhea. Digitoxin has adverse effects potentiated by hypokalemia, reduced by hyperkalemia.

Contraindications and Precautions

Do not administer to animals with AV block or at risk for other serious arrhythmias. Do not administer to animals with potassium electrolyte abnormalities.

Drug Interactions

High potassium will diminish clinical effect; low potassium will enhance effect and toxicity. Quinidine may increase plasma concentrations. Calcium-channel blocking drugs and beta blockers may potentiate action on AV node conduction.

Instructions for Use

Use of digitoxin has diminished in recent years in favor of digoxin. If available, it may be used with other cardiac drugs.

Patient Monitoring and Laboratory Tests

Monitor serum digoxin concentrations in patients to determine optimum therapy. When monitoring, collect blood samples 2-6 hours after dosing. The therapeutic range is 10-30 ng/mL.

Formulations

Digitoxin was once available in 0.05- and 0.1-mg tablets. (It is no longer available and must be obtained from European sources).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 0.02-0.03 mg/kg q8h PO.

Large Animal Dosage

Cattle

- 50-60 mcg/kg q6h IV.

Regulatory Information

Do not administer to cattle intended for food.

RCI Classification: 4

Digoxin

dih-joks'in

Trade and other names: Lanoxin and Cardoxin

Functional classification: Cardiac inotropic agent

Pharmacology and Mechanism of Action

Cardiac inotropic agent. Digoxin increases cardiac contractility and decreases heart rate. The mechanism is via inactivation of cardiac muscle sodium–potassium ATPase and increased intracellular availability of calcium, triggering calcium release from sarcoplasmic reticulum. In addition, neuroendocrine effects include sensitization of baroreceptors, which decreases heart rate by increasing vagal tone. Beneficial cardiac effects may be caused by decreased heart rate and suppression of the AV node to inhibit re-entrant cardiac arrhythmias via these neuroendocrine effects.

Indications and Clinical Uses

Digoxin is used in heart failure for inotropic effect and decreased heart rate in dogs, cats, and occasionally other animals. It is used in supraventricular arrhythmias to decrease ventricular response to atrial stimulation via suppression of the AV node. Digoxin may be used with other drugs for heart failure such as angiotensin-converting enzyme (ACE) inhibitors (e.g., enalapril), diuretics (furosemide), and vasodilators.

Precautionary Information

Adverse Reactions and Side Effects

Digitalis glycosides such as digoxin have a narrow therapeutic index. They may cause a variety of arrhythmias in patients (e.g., AV and ventricular tachycardia) and may produce delayed after depolarization-induced arrhythmias. Digoxin frequently causes vomiting, anorexia, and diarrhea. Digoxin adverse effects are potentiated by hypokalemia and reduced by hyperkalemia.

Contraindications and Precautions

Some breeds of dogs (Doberman pinscher) and cats are more sensitive to adverse effects.

Drug Interactions

High potassium will diminish clinical effect; low potassium will enhance effect and toxicity. Digoxin is a substrate for p-glycoprotein and many drugs are capable of increasing digoxin concentrations, including quinidine, aspirin, clarithromycin (and other macrolides), and chloramphenicol (see Appendix for list of p-glycoprotein inhibitors). Administration of phenobarbital chronically may decrease digoxin concentrations by increasing clearance. Calcium-channel blockers and beta blockers will potentiate action on AV node conduction, increasing the risk of AV block. Digoxin is absorbed better in an acid stomach, and proton pump inhibitors or H₂ blockers may reduce oral absorption.

Instructions for Use

When dosing, calculate dose on lean body weight. Doses should be 10% less for elixir because of increased absorption. When used to treat atrial fibrillation in dogs, combined with diltiazem, it may produce greater reduction in ventricular rate than either drug alone.

Patient Monitoring and Laboratory Tests

Monitor patients carefully. Monitor serum digoxin concentrations in patients to determine optimum therapy. Therapeutic range is 0.8-1.5 ng/mL 8-10 hours after a dose. Some cardiologists recommend concentrations of 0.9-1.0 ng/mL and below for treating heart failure and to reduce heart rate to 140-160 bpm. Adverse effects are common at concentration above 3.5 ng/mL, but in some sensitive patients, this

may be as low as 2.5 ng/mL. Patients may be monitored with ECG to detect digoxin-induced arrhythmias.

Formulations

Digoxin is available in 0.0625-, 0.125-, and 0.25-mg tablets and 0.05- and 0.15-mg/mL elixir.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is not stable if mixed with low pH solutions (pH <3). Do not compound oral tablets with other medications.

Small Animal Dosage

Dogs

- 0.0025-0.005 mg/kg q12h, PO (dose used by most cardiologists).
- Alternatively, doses have varied based on dog's body weight: dogs < 20 kg: 0.005-0.01 mg/kg q12h and if >20 kg: 0.22 mg/m² q12h PO (subtract 10% for elixir).
- Rapid digitalization: 0.0055-0.011 mg/kg q1h IV to effect.
- Atrial fibrillation: 0.005 mg/kg q12h, PO (may be combined with diltiazem at 3 mg/kg q12h PO).

Cats

- 0.008-0.01 mg/kg q48h PO. (Approximately 1/4 of a 0.125 mg tablet/cat).

Large Animal Dosage

Cattle

- 22 mcg/kg (0.022 mg/kg) IV loading dose, followed by 0.86 mcg/kg/hr IV or multiple doses of 3.4 mcg/kg q4h. Plasma concentrations to monitor are similar as for other animals.

Horses

- 2 mcg/kg (0.002 mg/kg) IV, q12h.
- 15 mcg/kg (0.015 mg/kg) q12h PO.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 4

Dihydroxycholesterol

dye-hye-droe-tak-iss'ter-ole

Trade and other names

Functional classification: Vitamin

Pharmacology and Mechanism of Action

Vitamin D analogue. Vitamin D promotes absorption and utilization of calcium.

Indications and Clinical Uses

Dihydroxycholesterol is used as treatment of hypocalcemia, especially hypoparathyroidism associated with thyroidectomy. The most common use is for replacement in cats that have had thyroidectomy for treatment of hyperthyroidism.

234 Diltiazem Hydrochloride

Calcitriol is another drug that is used to regulate calcium concentrations in animals (see Calcitriol).

Precautionary Information

Adverse Reactions and Side Effects

Overdose may cause hypercalcemia.

Contraindications and Precautions

Avoid use in pregnant animals because it may cause fetal abnormalities.

Drug Interactions

No specific drug interactions are reported for animals. However, use cautiously with high doses of preparations containing calcium. Use with caution with thiazide diuretics.

Instructions for Use

Doses for individual patients should be adjusted by monitoring serum calcium concentrations.

Patient Monitoring and Laboratory Tests

Monitor serum calcium concentration.

Formulations

No formulations are currently available in the US. It can only be obtained from some compounding pharmacies. Older formulations consisted of 0.125-mg capsules; 0.5-mg/mL oral liquid (20% alcohol); and 125-, 200-, and 400-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dog and Cats

- 0.01 mg/kg/day PO.
- Acute treatment: 0.02 mg/kg initially, then 0.01-0.02 mg/kg q24-48h PO thereafter. The dose should be adjusted on the basis of measuring calcium concentrations. Effective doses can range from 0.1 to 0.3 mg/kg.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Diltiazem Hydrochloride

dil-tye'ah-zem hye-droe-klor'ide

Trade and other names: Cardizem and Dilacor

Functional classification: Calcium-channel blocker

Pharmacology and Mechanism of Action

Calcium-channel blocking drug. Diltiazem blocks calcium entry into cells via blockade of voltage-dependent slow calcium channel. Via this action, it produces

vasodilation, negative chronotropic effects, and negative inotropic effects. However, the action on cardiac tissue (SA node and AV node) predominates over other effects. Half-life in dogs is approximately 3 hours (range 2.5-4 hrs), and it is shorter in horses (1.5 hrs).

Indications and Clinical Uses

Diltiazem is used primarily for control of supraventricular arrhythmias, systemic hypertension, and hypertrophic cardiomyopathy. It also is used for atrial flutter, AV nodal re-entry arrhythmias, and other forms of tachycardia. Diltiazem is more effective on heart tissues (AV node and SA node) than on blood vessels. It should not be used as a primary treatment of hypertension and to produce vasodilation; one of the dihydropyridines calcium-channel blocking drugs (e.g., amlodipine) is preferred. In cats it is considered one of the drugs of choice for treatment of feline hypertrophic cardiomyopathy (HCM). In dogs, diltiazem has been used to treat acute renal failure. It may improve renal perfusion by decreasing renal vasoconstriction and improving renal perfusion. In horses, diltiazem may be effective for atrial fibrillation. However, treated horses had variable results, and some developed hypotension and sinus arrest. Transdermal administration of diltiazem has not been shown to be effective in cats.

Precautionary Information

Adverse Reactions and Side Effects

Hypotension, myocardial depression, bradycardia, and AV block are the most important adverse effects. If acute hypotension occurs, treat with aggressive fluid therapy and administration of calcium gluconate or calcium chloride. It may cause anorexia in some patients. High doses in cats have caused vomiting. When cats were administered 60 mg of Dilacor XR it produced lethargy, GI disturbances, and weight loss in 36% of cats.

Contraindications and Precautions

Do not inject rapidly when administering IV. Do not administer to patients with hypotension.

Drug Interactions

Calcium-channel blocking drugs have been associated with drug interactions in people by interfering with drug metabolism. These interactions have not been documented in veterinary patients but are possible because of similar mechanisms. Therefore, use with caution when administering other drugs that may be p-glycoprotein (efflux protein produced by MDR gene) substrates. (See Appendix.) Do not mix intravenous solutions with furosemide.

Instructions for Use

Diltiazem is preferred over verapamil in patients with heart failure because of less myocardial depression. When used to treat atrial fibrillation in dogs, combined with digoxin it may produce greater reduction in ventricular rate than either drug alone. See detailed instructions for cats in Small Animal Dosage section.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during treatment. Monitor blood pressure with acute treatment for atrial fibrillation. If blood concentrations are monitored, to produce a reduction in heart rate 80-290 ng/mL are necessary in people and 60-120 ng/mL in dogs.

Formulations

Diltiazem is available in 30-, 60-, 90-, and 120-mg tablets; 60-, 90-, 120-, 180-, 240-, and 300-mg extended release capsules; and in a 5-mg/mL injection solution.

Dilacor XR has three or four tablets in one unit.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Extended-release tablets are difficult to manipulate for pet owners. Compounded transdermal formulations may not be stable. Compounded oral formulations, prepared with various sugars and flavorings, were stable for 50-60 days. Injectable solution may be mixed with intravenous fluids but should be discarded after 24 hours. Do not freeze.

Small Animal Dosage

Dogs

- 0.5-1.5 mg/kg q8h PO. For atrial fibrillation 5 mg/kg q12h, PO and a combination of diltiazem (3 mg/kg q12h PO) plus digoxin (0.005 mg/kg q12h, PO) has been used.
- Atrial fibrillation: 0.05-0.25 mg/kg IV administered q5min to effect.
- Supraventricular tachycardia: 0.25 mg/kg over 2 min IV (repeat if necessary). First, inject 0.25 mg/kg, then wait 20 minutes for response before repeating. Constant rate infusion (CRI): 0.15-0.25 mg/kg IV over 2 minutes, then 1-8 mcg/kg/min.
- Acute renal failure: 0.2 mg/kg IV (slowly), followed by 3-5 mcg/kg/min constant rate infusion.

Cats

- 1.75-2.4 mg/kg q8h PO. Most common dose in cats with immediate-release formulations is 10 mg per cat, q8h, PO, with frequency reduced to q12h in some cats.
- Dilacor XR or Cardizem CD: 10 mg/kg once daily PO. Extended-release tablets can be more difficult to use in cats compared to other tablets but have been used at 30 or 60 mg per cat (see below).

Tablets are difficult to break for use in cats. Note that “XR,” “SR,” and “CD” all refer to slow-release formulations. Dilacor XR-240 mg contains four 60-mg tablets. XR-180 contains three 60-mg tablets. Slow- and extended-release tablets are not recommended for routine use in cats because they produce inconsistent plasma concentrations that may result in ineffective treatment in some and adverse effects in others. Based on available information for cats, use either Dilacor XR 30 or Dilacor XR 60. The dose of 30 mg per cat of Dilacor XR (extended-release tablets) produced fewer adverse effects than 60 mg per cat.

Large Animal Dosage

Horses

- 0.125 mg/kg IV over at least 2 minutes. Repeat every 10 minutes, as needed, or until total dose of 1.1 mg/kg. Doses as high as 1-2 mg/kg have been used in research animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Dimenhydrinate

dye-men-hye'drih-nate

Trade and other names: Dramamine (Gravol in Canada)

Functional classification: Antihistamine

D

Pharmacology and Mechanism of Action

Antihistamine (H_1 -blocker). Diphenhydramine is the active moiety of dimenhydrinate.

Similar to other antihistamines, it acts by blocking the H_1 receptor and suppresses inflammatory reactions caused by histamine. The H_1 blockers have been used to control pruritus and skin inflammation in dogs and cats; however, success rates in dogs have not been high. Commonly used antihistamines include clemastine, chlorpheniramine, diphenhydramine, and hydroxyzine. Dimenhydrinate is converted to active diphenhydramine. Dimenhydrinate also has central-acting antiemetic properties, possibly by acting on the vomiting center or via the chemoreceptor-trigger zone (CRTZ).

Indications and Clinical Uses

Dimenhydrinate is used to prevent allergic reactions and for pruritus therapy in dogs and cats. However, success rates for treatment of pruritus have not been high. In addition to the antihistamine effect for treating allergies, dimenhydrinate, like other antihistamines, acts as an antiemetic via the drug effects on the centers that control vomiting in animals. Antihistamines used as antiemetics are administered for motion sickness, vomiting induced by chemotherapy, and GI disease that stimulates vomiting.

Precautionary Information

Adverse Reactions and Side Effects

Sedation is the most common side effect. Sedation is the result of inhibition of histamine N-methyltransferase. Sedation may also be attributed to the block of other CNS receptors such as those for serotonin, acetylcholine, and alpha-receptors. Antimuscarinic effects (atropine-like effects) also are common, including dry mouth and decreased GI secretions.

Contraindications and Precautions

Antimuscarinic effects (atropine-like effects) are common. Do not use in conditions for which anticholinergic drugs may be contraindicated, such as glaucoma, ileus, or cardiac arrhythmias.

Drug Interactions

No drug interactions are reported. However, use with other sedatives and tranquilizers may increase sedation.

Instructions for Use

Like other antihistamines, there have been no clinical studies on the use of dimenhydrinate. It is primarily used empirically for treatment of vomiting and to prevent allergic reactions.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Dimenhydrinate is available in 50-mg tablets and 50-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 4-8 mg/kg q8h PO, IM, or IV.

Cats

- 12.5 mg/cat q8h IV, IM, or PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Dimercaprol

dye-mer-cap'role

Trade and other names: British anti-lewisite (BAL) in oil

Functional classification: Antidote

Pharmacology and Mechanism of Action

Chelating agent. Dimercaprol is also known as BAL. It is a dithiol chelating agent for chelating with heavy metals. It binds to arsenic, lead, and mercury to treat toxicosis.

Indications and Clinical Uses

Used to treat lead, gold, mercury, and arsenic toxicity. There are two formulations: dimercaptopropane-1-sulfonic acid (DMPS) and meso-2,3-dimercaptosuccinic acid. Because these are not readily available, they may be compounded from a bulk source.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are not reported in veterinary medicine. In people, sterile abscesses occur at the injection site. High doses have caused seizures, drowsiness, and vomiting.

Contraindications and Precautions

Dimercaprol is used only to treat intoxications.

Drug Interactions

There are no drug interactions reported.

Instructions for Use

Use as soon as possible after intoxicant exposure. Alkalinization of urine will increase toxin removal. For lead intoxication, dimercaprol may be used with edetate calcium.

Patient Monitoring and Laboratory Tests

Heavy metal concentrations can be measured to assess treatment.

Formulations

Dimercaprol is available in an injection that must be prepared by compounding.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- 4 mg/kg q4h IM.

Large Animal Dosage

- 4 mg/kg q4h IM.

Regulatory Information

Withdrawal time: 5 days for milk and meat (extralabel use).

Dimethyl Sulfoxide (DMSO)

di-meth-il sulf-oks'ide

Trade and other names: DMSO and Domoso

Functional classification: Anti-inflammatory

Pharmacology and Mechanism of Action

DMSO is a solvent that is a byproduct of the paper-making process. It is highly hygroscopic (water absorbing). It readily displaces water and will penetrate cell membranes, skin, and mucosa easily. It produces anti-inflammatory, antifungal, and antibacterial properties. The clinical anti-inflammatory action of DMSO is uncertain. It may produce anti-inflammatory or protective effects on cell membranes via its ability to scavenge oxygen-derived free radicals. In horses, at a dose of 1 g/kg, the half-life is 8.6 hours. Twenty-six percent of the administered dose was excreted in the urine. In dogs, the half-life is 36 hours.

Indications and Clinical Uses

DMSO is administered topically and systemically (IV) for treatment of various inflammatory conditions. It is popular in horses for treatment of laminitis, arthritis, pneumonia, intestinal ischemia, synovitis, and nervous system injuries. Despite popular use, there are no published reports of efficacy for clinical use, and evidence to support use as an anti-inflammatory agent in treatment of clinical disease is primarily anecdotal. There is no evidence to support use to protect ischemic reperfusion injury in the equine intestine, to treat laminitis, or to improve neurologic disease. It does not promote drug penetration across the blood-brain barrier.

Precautionary Information

Adverse Reactions and Side Effects

DMSO is irritating to skin and mucosal membranes. It is hygroscopic and also induces release of histamine in skin. Long-term use has produced ocular lens changes in laboratory animals. Concentrated DMSO, when administered IV, will cause significant hemolysis. Intravenous use also has been associated with hemoglobinemia, acute colic, diarrhea, myositis, muscle tremors, and collapse. These reactions are more likely at doses of 2 g/kg or greater. DMSO produces a strong odor when administered.

Contraindications and Precautions

Although many veterinarians administer it systemically, DMSO is not approved for this use. It may enhance transdermal absorption of toxicants and contaminants on the skin. Do not administer IV at concentrations >10% or at doses >1 g/kg. Do not administer concentrated solution systemically.

Drug Interactions

DMSO is a strong solvent. It will dissolve other compounds. It may act as a penetration enhancer and increase transmembrane penetration of other compounds.

Instructions for Use

Dilute prior to use to 10% for intravenous infusion. Doses vary widely among veterinarians. Dose listed of 1 g/kg is common, but ranges of 0.2 to 4 g/kg have been cited in the literature for horses.

Patient Monitoring and Laboratory Tests

Monitor CBC during use.

Formulations

DMSO is available in a solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with other compounds, unless it is done immediately prior to administration.

Small Animal Dosage

Dogs and Cats

- 1 g/kg IV slowly. Do not administer solutions stronger than 10%.

Large Animal Dosage

Horses and Cattle

- 1 g/kg IV slowly. Dilute prior to use. Do not administer concentrations >10%. For most conditions, administration is every 12 hours.

Regulatory Information

Not approved for use in animals intended for food. No withdrawal times are available.

RCI Classification: 5

Dinoprost Tromethamine

dye'noe-prahst troe-meth'ah-meen

Trade and other names: Lutalyse, Prostin F₂ alpha, ProstaMate, Prostaglandin F₂ alpha, and PGF₂ alpha

Functional classification: Prostaglandin

D

Pharmacology and Mechanism of Action

Dinoprost is a prostaglandin (PGF₂ alpha) that induces luteolysis. Prostaglandin F₂ and its analogs have a direct luteolytic action on the corpus luteum. After injection, it will produce a functional regression of the corpus luteum (Luteolysis). In nonpregnant cycling cattle, this effect will result in starting estrus 2 to 5 days after injection. In pregnant animals, it will terminate pregnancy. In animals with prolonged luteal activity that have pyometra, mummified fetus, or luteal cysts, the luteolysis usually results in resolution of the problem and return to normal cycling.

Indications and Clinical Uses

Dinoprost is used for estrus synchronization in cattle and horses by causing luteolysis. In horses and cattle it is used to control timing of estrus in estrus-cycling females and in clinically anestrous females that have a corpus luteum. In pigs, dinoprost is used to induce parturition when given within 3 days of farrowing. In dogs, dinoprost has been used to treat open pyometra. In cattle, dinoprost has been used for treatment of chronic endometritis.

In large animals, dinoprost is used to induce abortion in the first 100 days of gestation, but use for inducing abortion in small animals has been questioned.

Precautionary Information

Adverse Reactions and Side Effects

Prostaglandin F₂ alpha causes increased smooth muscle tone, resulting in diarrhea, abdominal discomfort, bronchoconstriction, and increase in blood pressure. In small animals, other side effects include vomiting. Induction of abortion may cause retained placenta.

Contraindications and Precautions

Do not administer IV. Dinoprost induces abortion in pregnant animals. Use caution when handling this drug by veterinarians, animal owners, and technical help. It should not be handled by pregnant women. Absorption through intact human skin is possible. People with respiratory problems also should not handle dinoprost.

Drug Interactions

According to the label, dinoprost should not be used with nonsteroidal anti-inflammatory drugs (NSAIDs) because these drugs inhibit synthesis of prostaglandins. However, NSAIDs should not affect concentrations of PGF₂ alpha administered by this product. When using oxytocin concurrently, it should be used cautiously because there is a risk of uterine rupture.

Instructions for Use

Use in treating pyometra should be monitored carefully. If pyometra is not open, severe consequences may result. When used in cattle, after a single injection, cattle should be bred at the usual time relative to estrus. When administering two injections, cattle can be bred after the second injection either at the usual time relative to detected estrus or at about 80 hours after the second injection. Estrus is expected to occur 1 to 5 days after injection if a corpus luteum was present. Cattle that do not become pregnant will be expected to return to estrus in about 18 to 24 days. When used in cattle to induce abortion, it should be used only during the first 100 days of gestation. Cattle that abort will abort within 35 days after injection.

In pigs, administer within 3 days of predicted farrowing for parturition induction. Farrowing should start in approximately 30 hours.

Patient Monitoring and Laboratory Tests

When used for estrus synchronization, monitor for signs of estrus. Animals should be bred at usual time relative to estrus.

Formulations

Dinoprost is available in a 5-mg/mL solution for intramuscular injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Pyometra: 0.1-0.2 mg/kg, once daily for 5 days SQ.
- Terminate pregnancy: 0.025-0.05 mg (25-50 mcg)/kg q12h IM.

Cats

- Pyometra: 0.1-0.25 mg/kg, once daily for 5 days SQ.
- Terminate pregnancy: 0.5-1 mg/kg IM for 2 injections.

Large Animal Dosage

Cattle

- Terminate pregnancy: 25-mg total dose, administered once IM.
- Estrus synchronization: 25 mg (5 mL) IM once or twice at 10-12-day intervals.
- Pyometra: 25 mg administered once IM.

Horses

- Estrus synchronization: 1 mg/100 pounds (1 mg/45 kg) or 1-2 mL administered once IM. Mares should return to estrus within 2-4 days and ovulate 8-12 days after treatment.

Pigs

- Induction of parturition: 10 mg (2 mL) administered once IM. Parturition occurs within 30 hours.

Regulatory Information

Do not administer to horses intended for food.

To be used in beef cattle and nonlactating dairy cows only.

Diphenhydramine Hydrochloride

dye-fen-hye'drah-meen hye-droe-klor'ide

Trade and other names: Benadryl

Functional classification: Antihistamine

Pharmacology and Mechanism of Action

Antihistamine (H_1 blocker). Diphenhydramine is the active moiety of dimenhydrinate (Dramamine). Similar to other antihistamines, it acts by blocking the H_1 receptor (H_1) and suppresses inflammatory reactions caused by histamine. Commonly used antihistamines include clemastine, chlorpheniramine, diphenhydramine, and hydroxyzine.

Indications and Clinical Uses

Diphenhydramine, like other antihistamines, is used to prevent allergic reactions and for pruritus therapy in dogs and cats. However, success rates for treatment of pruritus have not been high. In addition to the antihistamine effect for treating allergies, these drugs block the effect of histamine in the vomiting center, vestibular center, and other centers that control vomiting in animals.

Precautionary Information

Adverse Reactions and Side Effects

Sedation is the most common side effect. Sedation is the result of inhibition of histamine N-methyltransferase. Sedation may also be attributed to block of other CNS receptors such as those for serotonin, acetylcholine, and alpha-receptors. Antimuscarinic effects (atropine-like effects) also are common, including dry mouth and decreased GI secretions. Excitement has been observed in cats and in other animals at high doses.

Contraindications and Precautions

Antimuscarinic effects (atropine-like effects) are common. Do not use in conditions for which anticholinergic drugs may be contraindicated, such as glaucoma, ileus, or cardiac arrhythmias.

Drug Interactions

There are no specific drug interactions. However because of anticholinergic (atropine-like) effects, it may counteract drugs that are administered for a parasympathomimetic action (e.g., drugs used to stimulate intestinal motility).

Instructions for Use

Antihistamine used primarily for allergic disease in animals. These drugs also can be used to treat or prevent vomiting in animals. Clinical studies documenting efficacy have been limited. Most use is empirical with doses extrapolated from human use.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Diphenhydramine is available OTC in a 2.5-mg/mL elixir, 25- and 50-mg capsules and tablets, and 50-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Protect from freezing.

Small Animal Dosage

Dogs

- 2.2 mg/kg q8-12h PO, IM, or SQ.
For large dogs this is equivalent to an oral dose of 25 or 50 mg per dog.

Cats

- 2-4 mg/kg q6-8h PO.
- 1 mg/kg q8h IV or IM.

Large Animal Dosage

- 0.5-1 mg/kg as a single dose, as needed, IM.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Diphenoxylate

dye-fen-oks'ih-late

Trade and other names: Lomotil

Functional classification: Antidiarrheal

Pharmacology and Mechanism of Action

Opiate agonist. Binds to mu-opiate receptors in intestine and stimulates smooth muscle segmentation in intestine, decreases peristalsis, and enhances fluid and electrolyte absorption.

Indications and Clinical Uses

Diphenoxylate is used for acute treatment of nonspecific diarrhea. It has primarily a local effect. Loperamide (Imodium) has a similar action and has become more popular for this indication. An additional use, not often used in veterinary medicine, is as an antitussive.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in veterinary medicine. Diphenoxylate is poorly absorbed systemically and produces few systemic side effects. Excessive use can cause constipation.

Contraindications and Precautions

Do not use in patients with diarrhea caused by infectious causes. Opiates should not be used for chronic treatment of diarrhea.

Drug Interactions

There are no specific drug interactions reported. However, use cautiously with other opiates and other drugs that may cause constipation (e.g., antimuscarinic drugs).

Instructions for Use

Doses are based primarily on empiricism or extrapolation of human dose. Clinical studies have not been performed in animals. Diphenoxylate contains atropine, but the dose is not high enough for significant systemic effects.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Diphenoxylate is available in 2.5-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 0.1-0.2 mg/kg q8-12h PO.
Antitussive doses have been as high as 0.5 mg/kg q12h, PO.

Cats

- 0.05-0.1 mg/kg q12h PO.

Large Animal Dosage

No use in large animals is reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). Schedule V controlled drug.

RCI Classification: 4

Dipyridamole

dye-peer-id'ah-mole

Trade and other names: Persantine

Functional classification: Anticoagulant

Pharmacology and Mechanism of Action

Platelet inhibitor. Mechanism of action is attributed to increased levels of cyclic AMP in platelet, which decreases platelet activation.

Indications and Clinical Uses

In people dipyridamole has been used to prevent thromboembolism and hypercoagulable states. However, use of dipyridamole has been infrequent in animals. It may be indicated in clinical conditions in which platelet inhibition is desired. It is indicated primarily to prevent thromboembolism. It is more common to administer other platelet inhibitors such as clopidogrel, with and without aspirin.

Precautionary Information**Adverse Reactions and Side Effects**

Adverse effects have not been reported in animals. However, bleeding problems are expected in animals prone to coagulopathies or receiving other anticoagulants.

Contraindications and Precautions

Do not use in animals with bleeding problems.

Drug Interactions

Aspirin may potentiate effects.

Instructions for Use

Dipyridamole is used primarily in people to prevent thromboembolism. Use in animals has not been reported. When used in people, it is combined with other antithrombotic agents (e.g., warfarin).

Patient Monitoring and Laboratory Tests

It may be necessary to monitor bleeding times in some animals.

Formulations

Dipyridamole is available in 25-, 50-, and 75-mg tablets and 5-mg/mL injection. It is also available combined with aspirin as 200 mg dipyridamole plus 25 mg aspirin (Aggrenox).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Compounded oral formulations have been stable for 60 days.

Small Animal Dosage**Dogs and Cats**

- 4-10 mg/kg q24h PO.

Large Animal Dosage

No use in large animals is reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Dirlotapide

Dir-loe' ta-pyed

Trade and other names: Slentrol

Functional classification: Obesity medication

Pharmacology and Mechanism of Action

Dirlotapide is used to produce weight loss in dogs. It is related to another medication used for obesity in dogs, mitratapide (Yarvitan), which is approved in Europe. Dirlotapide is an inhibitor of the microsomal triglyceride transfer protein (MTP). The inhibition is selective, and the liver form of MTP is not affected in

dogs. Inhibition of this enzyme reduces the ability of intestinal enterocytes to process triglycerides by preventing uptake of lipids into cholemicrons. As a result, there is decreased fat absorption and increased fecal fat. The accumulation of these triglycerides in the intestinal cells sends a signal (satiety messenger) to the central nervous system to suppress the appetite. In dogs the effect on the intestinal cells reduces the uptake of dietary lipids, in association with decreased postprandial serum triglycerides, phospholipids, and cholesterol. The weight loss is attributed to the reduced appetite, rather than impaired processing of dietary lipids. It does not produce a direct centrally acting effect. Bioavailability of oral dirlotapide is variable but in the range of 20%-40%, with a volume of distribution (VD) of 1.3 L/kg. It is highly protein bound. Administration with food increases absorption. The plasma half-life is variable (1.2-11 hours). The effects on the intestinal cells and appetite appear to be local (intestinal) rather than attributed to plasma levels because similar weight reduction effects are not observed when dirlotapide is administered by injection.

Indications and Clinical Uses

Dirlotapide is used in the management of obesity in dogs. During the treatment protocol, there is a consistent weight loss (approximately 3% per month) that is primarily fat tissue, not lean tissue. Overall, during the entire treatment period it may result in weight loss of 18%-22% of body weight, but response can vary among individual dogs. Dirlotapide should not be used without instituting the proper protocol as outlined by the sponsor. It should be used in an overall weight management program, which also includes appropriate dietary changes. Before using to treat overweight or obesity, rule out other diseases such as hypothyroidism or hyperadrenocorticism.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are proportional to dose. Decreased appetite occurs as a mode of action of the drug. Vomiting may also occur as a common effect related to the drug's mechanism of action. Nausea and diarrhea also may occur. None of these signs are necessarily cause to stop the medication and may resolve with time. However, if vomiting and nausea persist, evaluation and adjustment of dose may be necessary. Changes in liver enzymes also are expected. There may be increases in ALT and AST liver enzymes associated with treatment. However, if there are high increases in ALT, or marked elevation in other values (AST, GGT, Alk Phos, or total bilirubin), treatment should be stopped and the patient reassessed. There may be decreased absorption of fat-soluble vitamins A and E. The reduced absorption of these vitamins has not been clinically significant.

Contraindications and Precautions

Do not administer to cats. Do not use in dogs with concurrent liver disease or dogs on long-term corticosteroid therapy. Humans should not take this drug. Safety in pregnancy has not been established.

Drug Interactions

No drug interactions have been reported. It has been safely administered with NSAIDs and ACE inhibitors.

Instructions for Use

Feed a complete diet when using this medication. There is a specific protocol (see dosing section) that must be followed for proper use of this drug. Protocol follows an initial weight loss phase, usually 4 weeks, an adjustment phase of variable duration, followed by a weight management phase of 12 weeks. The entire protocol may comprise 26 weeks. If reductions in diet are not maintained and diet is not restricted, animals may regain weight following cessation of treatment. To avoid rebound weight gain, continue feeding the maintenance diet amount identified during the post-treatment phase. Dirlotapide may be given directly in the mouth or with food. The appetite suppression is less in dogs that are fed a low-fat diet.

Patient Monitoring and Laboratory Tests

Monitor patient's weight. Monitor blood chemistry profile for changes in liver enzymes and reduced albumin and electrolytes.

Formulations

Dirlotapide is available in a 5-mg/mL solution in MCT oil.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Once opened it has a shelf-life of 3 months. Do not refrigerate.

Small Animal Dosage

Dogs

- Initial dose is 0.05 mg/kg (0.01 mL/kg), then increased to 0.1 mg/kg (0.02 mL/kg) at 14 days. Thereafter, the dose is adjusted monthly on the basis of weight loss in each individual dog. The maximum dose is 1.0 mg/kg (0.2 mL/kg).

Cats

Do not use in cats.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food.

Disopyramide

dye-soe-peer'ah-mide

Trade and other names: Norpace (Rhythmotan in Canada)

Functional classification: Antiarrhythmic agent

Pharmacology and Mechanism of Action

Antiarrhythmic agent of Class I. Disopyramide blocks inward sodium channel and depresses myocardial electrophysiologic conduction rate.

Indications and Clinical Uses

Disopyramide is used for control of ventricular arrhythmias. Its use in veterinary medicine is not as common as for other drugs. Studies of efficacy in animals have not been reported.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. High doses may cause cardiac arrhythmias.

Contraindications and Precautions

At high doses, it may induce arrhythmias in some patients.

Drug Interactions

No drug interactions are reported for animals. Use cautiously with other drugs that may affect the cardiac rhythm.

Instructions for Use

Disopyramide is not commonly used in veterinary medicine because of its short half-life in dogs. Other antiarrhythmic drugs are preferred.

Patient Monitoring and Laboratory Tests

Monitor ECG in treated animals. This drug can be proarrhythmogenic.

Formulations

Disopyramide is available in 100- and 150-mg capsules and 10-mg/mL injection (Canada only).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Compounded oral formulations have been stable for 30 days.

Small Animal Dosage

Dogs

- 6-15 mg/kg q8h PO.

Cats

No dose established.

Large Animal Dosage

No use in large animals is reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Dithiazanine Iodide

dye-thye-az'ah-noon eye'oe-dide

Trade and other names: Dizan

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Microfilaricidal drug for dogs. It is also active against hookworms, roundworms, and whipworms.

Indications and Clinical Uses

Dithiazanine is used to eliminate heartworm microfilaria in dogs. It also has been used to treat some intestinal parasites. The filaricidal activity of the macrocyclic

250 Dithiazanine Iodide

lactones (ivermectin and related drugs) has replaced drugs such as dithiazanine. Instead of using dithiazanine for microfilaricidal treatment, the American Heartworm Society recommends the use of macrocyclic lactones.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are rare. Vomiting is reported in some dogs. Dithiazanine causes discoloration of feces.

Contraindications and Precautions

Do not use in animals with reduced renal function. Do not administer to heartworm-positive dogs until 6 weeks after adulticide therapy has been given.

Drug Interactions

No specific drug interactions have been reported.

Instructions for Use

Administer with food. If powder is used, mix with food as top dressing. Before other drugs were available, this was the only microfilaricidal agent for dogs. However, with improved availability and efficacy of other drugs such as the macrocyclic lactones, the use has diminished significantly.

Patient Monitoring and Laboratory Tests

Monitor heartworm status after a course of therapy by checking for microfilaria.

Formulations

Dithiazanine is rarely available in commercial tablets any longer. Older formulations included 10-, 50-, 100-, and 200-mg tablets and 200-mg/TB powder.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Heartworm: 6.6-11 mg/kg q24h for 7-10 days PO.
- Roundworms: 22 mg/kg once daily for 3-5 days PO.
- Hookworms: 22 mg/kg once daily for 7 days PO.
- Whipworms: 22 mg/kg once daily for 10-12 days PO.

Cats

No dose has been reported.

Large Animal Dosage

No use in large animals has been reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Dobutamine Hydrochloride

doe-byoo'tah-meen hye-droe-klor'ide

Trade and other names: Dobutrex

Functional classification: Cardiac inotropic agent

D

Pharmacology and Mechanism of Action

Adrenergic agonist. Dobutamine is a racemic mixture (R and S isomers) that has both beta₁- and beta₂-adrenergic activity. However, its clinical effects are caused by the relative cardioselective agonist activity on beta₁ receptors. There are both agonist and antagonist effects on alpha-receptors, the clinical effects of which are uncertain. The primary advantage of dobutamine is that it produces positive inotropic effects without excessive tachycardia. The lack of tachycardia distinguishes it from other sympathomimetic agents. At appropriate infusion rates, dobutamine can improve contractility without increasing heart rates. Dobutamine has a short half-life in animals (2-3 minutes). Therefore, it must be given via constant intravenous infusion and has a short onset of activity.

Indications and Clinical Uses

Dobutamine is used primarily for the acute treatment of heart failure. It produces an inotropic effect without increasing heart rates. Short treatment regimens (e.g., 48 hours) can have a residual positive effect in some animals.

Precautionary Information

Adverse Reactions and Side Effects

Dobutamine may cause tachycardia and ventricular arrhythmias at high doses or in sensitive individuals. If tachycardia or arrhythmias are detected, stop infusion rate and resume at a lower rate.

Contraindications and Precautions

Do not use in animals with ventricular arrhythmias.

Drug Interactions

Do not mix with alkaline solutions, such as those containing bicarbonate. Do not infuse in intravenous line with heparin, cephalosporins, or penicillins. Otherwise, it is compatible with most fluid solutions. Do not administer to animals receiving monoamine oxidase inhibitors (MAOIs; e.g., selegiline).

Instructions for Use

Dobutamine has a rapid elimination half-life (minutes) and therefore must be administered via carefully monitored constant rate infusion (CRI). Dose rates (infusion rate) can be adjusted by monitoring patient response. In dogs, doses as low as 2 mcg/kg/min have improved cardiac output.

Patient Monitoring and Laboratory Tests

Monitor heart rate and ECG during treatment. Cardiac arrhythmias are possible during infusions, especially at high doses.

Formulations

Dobutamine is available in a 250-mg/20 mL (12.5 mg/mL) vial for injection.

Stability and Storage

Usually dilute in 5% dextrose solution (e.g., 250 mg in 1 L 5% dextrose). A slight pink tinge to the solution can occur without loss of potency; however, do not use if color turns brown.

Small Animal Dosage

Dogs

- 5-20 mcg/kg/min IV infusion. Generally start with low dose and titrate upward.

Cats

- 2 mcg/kg/min IV infusion.

Large Animal Dosage

Horses

- 5-10 mcg/kg/min (0.005-0.01 mg/kg/min) IV infusion. Observe for increases in heart rate and ventricular arrhythmias. Adjust dose as needed based on patient response and heart rate.

Regulatory Information

No regulatory information is available. Because of a short half-life, no risk of residue is anticipated in food animals.

RCI Classification: 3

Docusate

dok'yoo-sate

Trade and other names: Docusate calcium: Surfak and Doxidan, Docusate sodium: DSS, Colace, and Doxan, and generic brands

Functional classification: Laxative

Pharmacology and Mechanism of Action

Docusate sodium and docusate calcium are stool softeners. They act as surfactants to help increase water penetration into feces. They act to decrease surface tension to allow more water to accumulate in the stool.

Indications and Clinical Uses

Docusate is indicated for medical conditions in which softened feces are desirable, such as after intestinal or anal surgery, to help pass hardened feces and when administering drugs that slow intestinal transit (e.g., opiates). Docusate is indicated for treatment of constipation.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects reported in animals. In people, high doses have caused abdominal discomfort.

Contraindications and Precautions

Some formulations of docusate calcium and docusate sodium products have contained the stimulant cathartic phenolphthalein, which should be used cautiously in cats. Examine label of products to ensure absence of phenolphthalein.

Drug Interactions

No specific drug interactions are reported for animals.

Instructions for Use

Doses are based on extrapolations from humans or empiricism. No clinical studies reported for animals.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Docusate calcium is available as 60-mg tablets and 240-mg capsules.

Docusate sodium is available as 50- and 100-mg capsules and 10-mg/mL liquid.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage**Dogs**

- Docusate calcium: 50-100 mg/dog q12-24h PO.
- Docusate sodium: 50-200 mg/dog q8-12h PO.

Cats

- Docusate calcium: 50 mg/cat q12-24h PO.
- Docusate sodium: 50 mg/cat q12-24h PO.

Large Animal Dosage

- Docusate sodium: 10 mg/kg/day PO.

Regulatory Information

No regulatory information is available for animals intended for food. Because docusate has primarily a local acting effect in the intestine, there is a minimal risk of residues in animals intended for food.

Dolasetron Mesylate

doe-lah'seh-tron mess'ih-late (also, dahl-AH-set-rahn)

Trade and other names: Anzemet

Functional classification: Antiemetic

Pharmacology and Mechanism of Action

Antiemetic drug from the class of drugs called serotonin antagonists. These drugs act by inhibiting serotonin (5-HT, type 3) receptors. During chemotherapy, there may be 5-HT released from injury to the GI tract, which stimulates vomiting centrally. The emetic response induced by serotonin is inhibited by this class of drugs. In people, dolasetron is completely metabolized to hydrodolasetron (active), which is presumably the same active metabolite for dogs and cats. Serotonin antagonists used for antiemetic therapy include granisetron, ondansetron, dolasetron, and tropisetron.

Indications and Clinical Uses

Like other serotonin antagonists, dolasetron is used primarily for its antiemetic effects during chemotherapy, for which they generally have been superior to other drugs in efficacy. These drugs also may be used to control vomiting from surgery (postoperative nausea and vomiting).

Precautionary Information

Adverse Reactions and Side Effects

Dolasetron adverse effects have not been reported in animals. These drugs have little affinity for other 5-HT receptors. Some effects may be indistinguishable from concurrent cancer drugs.

Contraindications and Precautions

There are no important contraindications identified in animals.

Drug Interactions

No drug interactions are reported. However, dolasetron is subject to effects from cytochrome P450 inducers and inhibitors. (See Appendix.)

Instructions for Use

Dolasetron has been used infrequently in veterinary medicine because of its expense. Doses are derived from anecdotal experience or extrapolation from human studies and no clinical studies are reported from animal studies. These drugs are more effective if used to prevent vomiting (administered prior to a chemotherapeutic agent) rather than to treat ongoing vomiting. This class of drugs may be combined with corticosteroids (e.g., dexamethasone) to enhance the antiemetic action.

Patient Monitoring and Laboratory Tests

Monitor GI signs in vomiting patient.

Formulations

Dolasetron is available in 50- and 100-mg tablets and 20-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It may be added to fluid solutions (compatible in most IV fluid solutions), but do not mix with other intravenous drugs. Do not use injection after 24 hours when added to fluids. Oral formulations have been added to fruit juice up to 2 hours at room temperature without loss of stability.

Small Animal Dosage

Dogs and Cats

- Prevention of nausea and vomiting: 0.6 mg/kg, q12-24h, IV, SQ, or PO.
- Treating vomiting and nausea: 1 mg/kg once daily IV or PO.

Large Animal Dosage

No dose has been reported.

Regulatory Information

Use in animals intended for food is negligible. No regulatory information is available.

Domperidone

dahm-pare'ih-done

Trade and other names: Motilium and Equidone

Functional classification: Prokinetic agent

Pharmacology and Mechanism of Action

Domperidone is a motility modifier with actions similar to metoclopramide, although it is chemically unrelated. A difference between metoclopramide and domperidone is that the latter does not cross the blood–brain barrier. Therefore, adverse CNS effects are not as much of a problem with domperidone. Domperidone stimulates motility of the upper GI tract, probably through dopaminergic effects or by increasing acetylcholine effects. The action of domperidone is to inhibit dopamine receptors and enhance action of acetylcholine in GI tract.

Indications and Clinical Uses

Domperidone has been used to treat gastroparesis and treatment of vomiting. In horses, domperidone has been used to treat fescue toxicosis and periparturient agalactia. Fescue toxicosis is caused by a fungus that produces a toxin, which causes reproductive problems in horses. The action of domperidone to increase lactation is through the stimulation of prolactin.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects that are seen with metoclopramide are not as common with domperidone because it does not cross the blood–brain barrier as readily as metoclopramide. It causes a transient increase in aldosterone and prolactin secretion. It has also caused a transient increase in plasma ACTH, which could exacerbate equine Cushing's syndrome.

Contraindications and Precautions

Do not use in patients with GI obstruction.

Drug Interactions

Acidity is needed for oral administration. Do not administer with stomach antacids such as omeprazole, cimetidine, or antacids.

Instructions for Use

Domperidone has questionable efficacy as a prokinetic agent (for treatment of ileus) in animals. A formulation has been available as an investigational drug for use in horses in the US for treatment of agalactia and fescue toxicosis.

Patient Monitoring and Laboratory Tests

No specific monitoring is required, but clinical monitoring of GI motility is important.

Formulations

Domperidone is not available in US at this time for small animal use. In Canada, it is available as 10-mg tablets. Formulation used in horses is oral gel at 11% (110 mg/mL), which is not FDA approved but has been available from some sources.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Doses for small animals have not been established, but 2-5 mg per dog or cat q8-12h PO has been used.

Large Animal Dosage

Horses

- Use in horses for fescue toxicity and agalactia.
- Equidone oral gel (11%): 10 days prior to foaling at 1.1 mg/kg daily PO, starting 10 days before the scheduled foaling date. (This dose is equivalent to 5 mL per 500 kg or 5 mL per adult horse daily PO of the 11% oral gel.) Continue until foaling. If there is not adequate milk production after foaling, continue for 5 additional days.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Dopamine Hydrochloride

doe'pah-meen hye-droe-klor'ide

Trade and other names: Intropin

Functional classification: Cardiac inotropic agent

Pharmacology and Mechanism of Action

Adrenergic and dopamine agonist. Dopamine is a neurotransmitter and an immediate precursor to norepinephrine. At low doses it stimulates the dopamine (DA₁) receptors, at moderate doses it stimulates the adrenergic receptors, and at high doses it acts as an alpha₁-receptor agonist (producing vasoconstriction). At doses that stimulate DA₁ receptors, it increases c-AMP in smooth muscle cells and causes relaxation and vasodilation. It has been administered to stimulate the heart and to increase urine flow (see below for explanation of renal effects).

Indications and Clinical Uses

Dopamine is used therapeutically to stimulate myocardium via action on cardiac beta₁-receptors. Dopamine infusions will increase both blood pressure and cardiac output. These effects are caused by stimulating cardiac contractility and heart rate by acting as an agonist for beta₁-adrenergic receptors. In addition, dopamine increases the release of norepinephrine from nerve terminals (dopamine is a precursor for norepinephrine). It produces a greater chronotropic effect than dobutamine. It has been proposed that dopamine dilates renal arterioles, increases renal blood flow, and increases the glomerular filtration rate. This effect is proposed to occur via activation of renal dopamine-1 (DA₁) receptors. Because of this proposed effect, in the past it has been used for acute renal failure. However, recent evaluation has raised doubts about the clinical effectiveness of dopamine for treatment of acute renal failure. Cats do not have as many DA₁ receptors as other animals; therefore, it has not been

effective in cats to produce diuresis. In addition, evaluation in people and other animals has not produced desired effects.

Precautionary Information

Adverse Reactions and Side Effects

Dopamine may cause tachycardia and ventricular arrhythmias at high doses or in sensitive individuals.

Contraindications and Precautions

Dopamine is unstable in alkaline fluids.

Drug Interactions

Do not mix with alkaline solutions. Otherwise, it is compatible with most fluid solutions.

Instructions for Use

Dopamine has a rapid elimination half-life (minutes) and therefore must be administered via carefully monitored constant rate infusion (CRI). Because the actions of dopamine are dose dependent, the rate administered is adjusted to reach the desired clinical effect. Dopamine has been administered at doses of 2-10 mcg/kg/min for the acute management of heart failure and cardiogenic shock. When preparing intravenous solutions, one may admix 200-400 mg of dopamine with 250-500 mL of fluid. Dopamine is unstable in alkaline fluid solutions, such as those containing bicarbonate.

Low dose (vasodilation, D₁ receptor): 0.5-2 mcg/kg/min; medium dose (cardiac stimulating, beta₁-receptor): 2-10 mcg/kg/min; and high dose (vasoconstriction, alpha-receptors): >10 mcg/kg/min.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm while administering dopamine.

Formulations

Dopamine is available in 40, 80, and 160 mg/mL for IV injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It may be added to fluids such as 5% dextrose, saline, and lactated Ringer's solution. It is stable for 24 hours after dilution. Do not use if solution turns a brown or purple color.

Small Animal Dosage

Dogs and Cats

- 2-10 mcg/kg/min IV infusion. Dose rate is dependent on desired effects.

Large Animal Dosage

Horses and Cattle

- 1-5 mcg/kg/min IV infusion.

Regulatory Information

No regulatory information is available. Because of a short half-life, no risk of residue is anticipated in food animals.

RCI Classification: 2

Doramectin

dore-ah-mek'tin

Trade and other names: Dectomax

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic drug. Avermectins (ivermectin-like drugs) and milbemycins (milbemycin, doramectin, and moxidectin) are macrocyclic lactones and share similarities, including mechanism of action. These drugs are neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in parasites. Paralysis and death of the parasite is caused by increased permeability to chloride ions and hyperpolarization of nerve cells. These drugs also potentiate other chloride channels, including ones gated by GABA. Mammals ordinarily are not affected, because they lack glutamate-gated chloride channels, and there is a lower affinity for other mammalian chloride channels. Because these drugs ordinarily do not penetrate the blood-brain barrier, GABA-gated channels in the CNS of mammals are not affected. Therefore, it produces longer and more sustained plasma concentrations. It is effective against nematodes and arthropods but has no effect on flukes or tapeworms.

Indications and Clinical Uses

Doramectin is used for treatment or prevention of GI parasite (nematode) infections in livestock, lice infestation, lungworm infection, and treatment of scabies. There are reports of a single injection (200-300 mcg/kg) used in cats for treatment of notoedric mange (infections from the mite *Notoedres cati*).

Precautionary Information

Adverse Reactions and Side Effects

Toxicity may occur at high doses and in breeds in which ivermectin-like drugs cross the blood-brain barrier. Sensitive breeds include collies, Australian shepherds, Shetland sheepdogs, and old English sheepdogs. Toxicity is neurotoxic, and signs include depression, ataxia, impaired vision, coma, and death. Sensitivity to ivermectin-like drugs may be because of mutation in the blood-brain barrier (p-glycoprotein deficiency). Treatment of hypodermal larvae in cattle may elicit reactions in tissues from dead larvae. These drugs are safe for pregnant animals. No adverse effects were seen in cats treated with doses as high as 345 mcg/kg.

Contraindications and Precautions

Doramectin is only approved in cattle. Certain breeds of dogs (Shetland sheepdogs and Collie-type breeds) are more sensitive to adverse effects than other breeds.

Drug Interactions

Use cautiously with drugs that may inhibit p-glycoprotein at the blood-brain barrier (see Appendix).

Instructions for Use

Doses vary depending on use. In cattle, for treatment of hypodermal larvae, treatment should begin at the end of fly season. Administration to cattle should use a 16- or 18-gauge needle for subcutaneous administration. For intramuscular

injection, use a 1.5-inch needle and inject in the neck muscle. When administering the topical form, remove mud and manure from hide. If it rains within 2 hours of administration, decreased efficacy may occur.

Patient Monitoring and Laboratory Tests

Monitor for microfilaremia prior to administration in small animals.

Formulations

Doramectin is available in a 1% (10 mg/mL) injection and a 5-mg/mL (0.5%) topical transdermal solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Demodex treatment: 600 mcg/kg/wk for 5-23 weeks SQ.

Cats

- Mite infection: 200-270 mcg/kg once SQ.
- 0.1 mL of 1% solution given once SQ.

Large Animal Dosage

Cattle

- 200 mcg/kg (0.2 mg/kg) or 1 mL per 50 kg (110 pounds), single injection, IM or SQ.
- Transdermal solution: Give 500 mcg (0.5 mg) per kg or 1 mL per 10 kg (4.5 pounds) as a single dose along the animal's back, along the midline.

Pigs

- 300 mcg/kg (0.3 mg/kg) or 1 mL per 34 kg (75 pounds), single injection, IM.

Regulatory Information

Cattle withdrawal time (meat): 35 days.

Pig withdrawal time (meat): 24 days.

Do not administer to lactating dairy cattle.

Do not administer to female dairy cattle older than 20 months of age.

Cattle transdermal solution withdrawal time (meat): 45 days. Do not administer to lactating dairy cattle; do not administer within 2 months of calving.

Doripenem

dor-i-pen'em

Trade and other names: Doribax

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Beta-lactam antibiotic of the carbapenems class with broad spectrum of activity.

Action on cell wall is similar to other beta-lactams, which is to bind penicillin-binding proteins (PBP) that weaken or interfere with cell wall formation. In *Escherichia coli* and *Pseudomonas aeruginosa*, doripenem binds to PBP 2, which is

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involved in the maintenance of cell shape, and to PBPs 3 and 4. Carbapenems have a broad spectrum of activity and are among the most active of all antibiotics. Doripenem has similar activity as imipenem and meropenem to include gram-negative bacilli, including *Enterobacteriaceae* and *Pseudomonas aeruginosa*. It is slightly more active against *Pseudomonas aeruginosa*. It also is active against most gram-positive bacteria, except methicillin-resistant strains of *Staphylococcus*. It is not active against *Enterococcus*.

Indications and Clinical Uses

Doripenem is indicated primarily for resistant infections caused by bacteria resistant to other drugs. It is especially valuable for treating resistant infections caused by *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*. Doripenem is not used in veterinary medicine as commonly as meropenem or imipenem.

Precautionary Information

Adverse Reactions and Side Effects

Carbapenems pose similar risks as other beta-lactam antibiotics, but adverse effects are rare. Doripenem does not cause seizures as frequently as imipenem.

Contraindications and Precautions

Some slight yellowish discoloration may occur after reconstitution. Slight discoloration will not affect potency. However, a darker amber or brown discoloration may indicate oxidation and loss of potency.

Drug Interactions

Do not mix in vial or syringe with other antibiotics or with solutions containing other drugs.

Instructions for Use

Doses in animals have been based on pharmacokinetic studies rather than efficacy trials. To prepare intravenous injection mix 500-mg vial with 10 mL of sterile water for injection or sodium chloride 0.9% injection, gently shaking vial to form a suspension (concentration, 50 mg/mL). Withdraw suspension and add to infusion bag containing normal saline 100 mL or dextrose 5%, gently shaking until clear (concentration, 4.5 mg/mL). To prepare 250-mg dose, mix with 10 mL of sterile water for injection or sodium chloride 0.9% injection, gently shaking vial to form a suspension (concentration, 50 mg/mL). Withdraw suspension and add to infusion bag containing normal saline 100 mL or dextrose 5%, gently shaking until clear (concentration, 4.5 mg/mL). Remove 55 mL of this solution from bag and discard. Infuse remaining solution (concentration, 4.5 mg/mL).

Patient Monitoring and Laboratory Tests

Susceptibility testing: Use susceptibility to imipenem to guide testing for doripenem. Enteric gram-negative bacteria usually have MIC values less than 0.5 mcg/mL. *Pseudomonas aeruginosa* usually have MIC values less than 2.0 mcg/mL.

Formulations

Doripenem is available in a 500-mg vial for injection.

Stability and Storage

Store vial at 59°F to 86°F. Constituted suspension in vial may be stored for 1 hour prior to dilution in infusion bag. Infusion solution prepared in saline may be stored at room temperature for 8 hours (includes infusion time) or under refrigeration for

24 hours (includes infusion time). Infusion solution prepared in dextrose 5% may be stored at room temperature for 4 hours (includes infusion time) or under refrigeration for 24 hours.

Small Animal Dosage

Dogs and Cats

- 8 mg/kg q8h, IV. Infuse over 30 minutes to 1 hour.

Large Animal Dosage

No large animal doses have been reported. However, doses similar to the range used in small animals are suggested for foals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Doxapram Hydrochloride

doks'ah-pram hye-droe-klor'idē

Trade and other names: Dopram, Respiram

Functional classification: Respiratory stimulant

Pharmacology and Mechanism of Action

Respiratory stimulation of doxapram results from direct stimulation of the medullary respiratory center and activation of the aortic and carotid body chemoreceptors to improve sensitivity to carbon dioxide. These receptors are sensitive to changes in CO₂, which in turn stimulate the respiratory center. Doxapram is used primarily in emergency during anesthesia or to decrease the respiratory depressant effects of certain drugs (e.g., opiates, barbiturates). An important use in veterinary medicine is stimulation of respiration in young horses. The half-life is short (2 hours), but the duration of action is only 5-10 minutes after IV administration.

Indications and Clinical Uses

Doxapram may stimulate respiration in dogs, cats, and horses, during and after general anesthesia. It has been used to stimulate respiration on newborn animals following dystocia or cesarean section surgery. Doxapram will increase ventilation (tidal volume, respiratory rate) and reduce acidosis. In horses, doxapram will cause cardiac stimulation and respiratory stimulation. There have been reports that administration to neonates may increase their suckling activity shortly after birth and subsequently decrease the incidence of failure of passive transfer of immunoglobulins. The primary use of doxapram in horses is for the treatment of respiratory acidosis in foals caused by hypoxic-ischemic encephalopathy (perinatal asphyxia or neonatal maladjustment syndrome) in neonatal foals. Administration to foals has restored normal ventilation, improved blood pH, PaO₂, and respiratory rate in neonatal foals in a dose-dependent manner. Doxapram also has been used in dogs to assist in the diagnosis of laryngeal paralysis.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. Central nervous stimulation and excitement are possible with high doses or rapid infusions.

Contraindications and Precautions

Do not use in animals with cardiac or respiratory arrest. Do not use with positive pressure ventilation

Drug Interactions

Use with theophylline or aminophylline may increase CNS excitement.

Instructions for Use

Doxapram has a rapid onset of effect (usually occurs in 20-40 seconds with peak effect at 1-2 minutes) and a short duration of action. The duration of effect varies from 5 to 12 minutes. Treatment guidelines have been developed primarily for foals. Single-dose injections may be administered, followed by constant rate infusions.

Patient Monitoring and Laboratory Tests

Monitor patient's heart and respiratory rate.

Formulations

Doxapram is available in a 20-mg/mL solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. The pH is 3.5 to 5 for intravenous administration, which may affect compatibility with other drugs. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

- 5-10 mg/kg IV.
- Neonate: 1-5 mg SQ, sublingual, or via umbilical vein.

Large Animal Dosage

Foals: initial IV dose of 0.5 mg/kg, followed by a constant rate infusion of 0.03 to 0.08 mg/kg/min for 20 minutes; or initiate treatment with 0.05-0.08 mg/kg/min constant rate infusion and continue for 8-12 hours.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Doxepin

doks'eh-pin

Trade and other names: Sinequan

Functional classification: Behavior-modifying drug, tricyclic

Pharmacology and Mechanism of Action

Tricyclic antidepressant (TCA). For treatment of depression, this class of drugs is thought to act by increasing synaptic concentrations of norepinephrine and serotonin (5-HT) in the CNS. Doxepin is only a moderate to weak inhibitor of the reuptake of these neurotransmitters. Doxepin also has antihistamine (H₁) properties.

Indications and Clinical Uses

Doxepin has been used to treat anxiety disorders and dermatologic conditions in dogs and cats. Some use for dermatitis is related to the drug's antihistamine properties. Although it has been used for treating pruritus and dermatitis in small animals, it has not been effective for treating atopic dermatitis in dogs. Doxepin has been used to treat lick granuloma in dogs.

Precautionary Information

Adverse Reactions and Side Effects

Tricyclic antidepressants have some antimuscarinic effects that may increase heart rate, cause xerostomia, and affect the GI tract. Some sedation is possible with doxepin.

Contraindications and Precautions

As with other tricyclic antidepressants, do not administer with other antidepressant drugs. Use cautiously in patients with glaucoma. Use cautiously in patients with seizure disorders.

Drug Interactions

Doxepin may increase sedative effects from antihistamines. Do not administer with monoamine oxidase inhibitors (MAOIs).

Instructions for Use

Doxepin has primarily been administered to treat pruritus in dogs. The efficacy for this use has been disappointing.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Doxepin is available in 10-, 25-, 50-, 75-, 100-, and 150-mg capsules. Generic and Sinequan are available in a 10-mg/mL oral solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Oral formulations can be mixed with various flavorings, juices, and foods without loss of stability.

Small Animal Dosage

Dogs

- 1-5 mg/kg q12h PO. Start with low dose (for example 0.5 to 1 mg/kg) and gradually increase.
- Lick granuloma: 0.5-1 mg/kg q12h PO. (For comparison, antipruritic dose for people is 10 to 25 mg/person once to three times per day and increased as needed.)

Cats

- 0.5-1 mg/kg q12-24h. Start with low dose initially.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Doxorubicin Hydrochloride

doks-oh-roo'bih-sin hye-droe-klar'ide

Trade and other names: Adriamycin

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Doxorubicin is derived from the soil fungus *Streptomyces peucetius*. Doxorubicin damages DNA by inhibition of the enzyme topoisomerase II. This enzyme is responsible for DNA functions. When topoisomerase is inhibited, the DNA segments cannot perform transcription, leading to breaks in the DNA strands and cell death. Secondarily, this mechanism causes cell death by blocking synthesis of RNA and proteins. Doxorubicin also forms free radicals (OH) that can attack DNA and lead to oxidation of DNA. In dogs, the half-life has varied from 8.7 hours to 11 hours, with volume of distribution 0.6-0.7 L/kg and clearance 52-83 L/kg/hr. In cats the pharmacokinetics are highly variable with half-lives ranging from 11 minutes to 9.5 hours. Other antitumor antibiotics include mitoxantrone, actinomycin D, and bleomycin.

Indications and Clinical Uses

Doxorubicin is used for treatment of various neoplasia, including hemangiosarcoma and lymphoma. Doxorubicin is commonly used in humans for the treatment of breast tumors, various sarcomas, and osteosarcoma. In veterinary medicine it has been used for lymphoma, osteosarcoma, and other carcinomas and sarcomas. It is considered one of the most effective single agents in the treatment of lymphoma. It is used commonly in cancer protocols with other agents.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects limit the frequency and cumulative doses that can be administered. Bone marrow toxicity is the major adverse effect that limits the frequency of acute administration, and the cardiotoxicity is the major effect that limits the chronic administration. The nadir of bone marrow depression (leukopenia) is at 7 to 10 days. The stem cells are usually spared and recovery occurs within 21 days following each dose. Cardiac toxicity is caused by an acute effect during administration seen as arrhythmias and decreased systolic function and a chronic effect that is manifest as cardiomyopathy and congestive heart failure. Cardiac toxicity is dose related. The risk of chronic effects increases as total cumulative doses exceed 200-240 mg/m². In some dogs, cardiac changes can be observed as soon as after 120 mg/m² cumulative dose. Dexrazoxane

(Zincard) is a potent chelator of iron and has been used to decrease the adverse cardiac effects in some patients. Alopecia is common in people but primarily is seen only in dogs that have continuously growing hair (e.g., poodles). Cats may lose their whiskers. Gastrointestinal acute side effects—*anorexia, vomiting, and diarrhea*—were the most common acute side effects. Hypersensitivity (allergic) reactions are not life-threatening, but they can occur commonly. They are probably not true allergic reactions, but are simply the result of mast cell degranulation that occurs independently of IgG binding. Signs of this reaction are head shaking (ear pruritus) and generalized urticaria and erythema. Cats are more sensitive to adverse effects than dogs, so lower doses are used in cats. Adverse effects in cats include *anorexia, vomiting, and renal injury*. In horses, adverse effects included *bone marrow suppression, hair loss, dermatitis, and other skin reactions*.

Contraindications and Precautions

Do not use in animals with cardiomyopathy. Monitor CBC in patients before and after treatment. If significant leukopenia (particularly neutropenia of fewer than 1000 cells) is present, withhold treatment or use a lower-dose intensity. Use cautiously in dogs with known mutation deficiency in the MDR membrane transporter (p-glycoprotein) (e.g., Collie and related breeds). These dogs are more prone to toxicity.

Drug Interactions

Doxorubicin is commonly administered with other anticancer drugs, antiemetics, and antihistamines without adverse effects. However, doxorubicin is a p-glycoprotein substrate and should not be used with drugs that are p-glycoprotein inhibitors (e.g., cyclosporine or ketoconazole). (See Appendix for list of inhibitors.)

Instructions for Use

Regimen listed may differ for various tumors. To prepare solution, the total dose is diluted in a saline fluid solution of 25 or 50 mL and infused slowly over 20-30 minutes, but preferably over 60 minutes. Extending duration of infusion to 2-3 hours may decrease some adverse effects. For cats, mix 1 mg/mL in saline solution and administer IV over 5-10 minutes with fluids. In cats SQ fluids (22 mL/kg) may be administered with doxorubicin. This drug is very irritating and special care must be made to ensure that extravasation from the vein does not occur. For canine lymphoma, some oncologists believe that remission of cancer is best achieved when five treatments are administered (target 150-180 mg/m² cumulative dose). In chemotherapy protocols it is sometimes administered with cyclophosphamide. Animals may require antiemetic and antihistamine (diphenhydramine) prior to therapy. Most often it is administered on a body surface area rate (mg/m²); however, dose according to body weight (mg/kg) may be safer for small dogs (see Small Animal Dosage section). In cats, additional SQ fluids are administered to prevent renal toxicity.

Patient Monitoring and Laboratory Tests

Monitor ECG during therapy. ECGs should be performed periodically in dogs to look for evidence of myocardial toxicity. CBC should be monitored regularly and prior to each treatment because of risk of myelotoxicity.

Formulations

Doxorubicin is available in a 2-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 30 mg/m² q21days IV.
- Dogs >15 kg body weight: 30 mg/m².
- Dogs <15 kg body weight: 1 mg/kg.

Cats

- 20 mg/m² (approximately 1.25 mg/kg) q3wks IV. In some cats, higher doses of 25 mg/m² appear to be equally tolerated.

Large Animal Dosage

Horses

- 70 mg/m², IV every 3 weeks for 6 cycles.

Regulatory Information

Withdrawal times are not established for animals that produce food.

This drug should not be used in animals intended for food because it is an anticancer agent.

Doxycycline Hyclate, Doxycycline Monohydrate

doks-ih-sye'kleen

Trade and other names: Vibramycin, Monodox, Doxy Caps, and generic brands

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Tetracycline antibiotic. Mechanism of action of tetracyclines is to bind to the 30S ribosomal subunit and inhibit protein synthesis. The action of tetracyclines is usually bacteriostatic. It has a broad spectrum of activity including bacteria, some protozoa, *Rickettsia*, and *Ehrlichia*.

Indications and Clinical Uses

Doxycycline is usually the drug of choice for treating tick-borne diseases in animals. Efficacy has been demonstrated in research studies and in some clinical studies. It is used for treating infections caused by bacteria, some protozoa, *Rickettsia*, and *Ehrlichia*. Doxycycline administered to cats with infections caused by *Mycoplasma*, or *Chlamydophilia felis* (formerly *Chlamydia psittaci*) at 10-15 mg/kg once daily PO, or 5 mg/kg q12h PO, has been effective in eliminating the organism and improving clinical signs. In dogs at 5 mg/kg q12h PO for 3-4 weeks has cleared *Ehrlichia canis* from blood and tissues. Doxycycline is often added to heartworm treatment because of the activity against the organism *Wolbachia*. This combination, although controversial, may improve microfilaricidal effect when combined with ivermectin, improve response to adulticidal treatment with melarsomine, and decrease injury to pulmonary vessels. In horses, it has been used to treat Ehrlichiosis, but also has been used to treat other diseases (e.g., respiratory infections) when oral treatment is indicated.

Precautionary Information

Adverse Reactions and Side Effects

Tetracyclines may cause renal tubular necrosis at high doses and can affect bone and teeth formation in young animals. However, doxycycline has not been reported to cause these problems in animals. Doxycycline administered orally to cats has caused esophageal irritation, tissue injury, and esophageal stricture. This may be caused by solid-dose formulations (primarily doxycycline hyclate rather than doxycycline monohydrate) becoming entrapped in the esophagus. Passage into the stomach by giving the cat water or food after administration is advised to prevent this effect. Doxycycline given IV to horses has been fatal; however, it has been administered safely to horses PO, although diarrhea is possible. In two equine studies there were no adverse effects reported from oral administration. In another study, one of the horses in a pharmacokinetic trial developed signs of enteritis and colic.

Contraindications and Precautions

Do not administer to young animals because it can affect bone and teeth formation. However, it has been better tolerated in children than other tetracyclines. If solid-dose forms are administered to cats, lubricate the tablet/capsule, or follow with food or water to ensure passage into stomach. Do not administer rapidly IV. Do not administer solution IM or SQ. Do not administer IV to horses under any circumstances; acute death has been reported from this use.

Drug Interactions

Tetracyclines bind to compounds containing calcium, which decreases oral absorption. However, this is less of a problem with doxycycline than with other tetracyclines. Doxycycline has been mixed with milk prior to oral administration to children without decreasing efficacy.

Instructions for Use

Many pharmacokinetic and experimental studies have been conducted in small animals. Doxycycline is ordinarily considered the drug of choice for *Rickettsia* and *Ehrlichia* infections in dogs. Doxycycline is more effective than enrofloxacin for *Ehrlichia*. When used with ivermectin (6 mcg/kg weekly) for heartworm treatment, doxycycline was administered at a dose of 10 mg/kg per day intermittently for several months (e.g., 20 months out of 36 months). To prepare doxycycline intravenous infusion solution, add 10 mL to a 100-mg vial or 20 mL to a 200-mg vial and then further dilute for IV use in 100 to 1000 mL of LRS or 5% dextrose. Infuse over 1 to 2 hours (see Stability and Storage section).

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are ≤ 2 mcg/mL for streptococci and ≤ 4 for other organisms. Tetracycline is used as a marker to test susceptibility for other drugs in this class, such as doxycycline, minocycline, and oxytetracycline.

Formulations

Doxycycline is available in a 10-mg/mL oral suspension, 50- or 100-mg tablets, and 50- and 100-mg capsules (doxycycline hyclate). Doxycycline monohydrate is available as 50- or 100-mg tablets or capsules. A controlled-release formulation (Oracea) contains 10-mg delayed release and 30-mg immediate release in one capsule. Doxycycline hyclate injection is available in a 100- and 200-mg injection vial.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Avoid mixing with cations such as iron, calcium, aluminum, and zinc. However, doxycycline tablets have been mixed with milk and immediately administered to children without loss of potency. Doxycycline hyclate for injection will retain potency for 12 hours at room temperature or 72 hours refrigerated after reconstitution at concentrations up to 1 mg/mL. IV solutions are stable in LRS or 5% dextrose for 6 hours at room temperature. Protect IV solutions from light. If frozen after reconstitution with sterile water, solutions of 10 mg/mL are potent for 8 weeks. If doxycycline is prepared in a compounded formulation it may be unstable. Doxycycline hyclate formulated in Ora Plus and Ora Sweet as a suspension retained potency for only 14 days. Other suspensions prepared for animals also may be unstable. Observe for dark color change (dark brown) as evidence of loss of potency.

Small Animal Dosage

Dogs and Cats

- 3-5 mg/kg q12h PO or IV. 10 mg/kg q24h PO.
- *Rickettsia* (dogs): 5 mg/kg q12h.
- *Ehrlichia* (dogs): 5 mg/kg q12h for at least 14 days.
- Heartworm treatment: 10 mg/kg per day, PO, administered intermittently (4 to 6 week intervals) in combination with either ivermectin (6 mcg/kg weekly) or ivermectin + melarsomine.

Birds

- Mix four 100-mg doxycycline hyclate capsules with 1 L water (400 mg/L). Shake to make solution and offer as only source of water to birds to eliminate bacteria. Alternatively, 25 mg/kg PO, q12h, ×3 weeks.

Large Animal Dosage

- Dose: 10-20 mg/kg q12h PO. For *Lawsonia intracellularis*: 20 mg/kg PO, q24h, for 3 weeks.
- Horses: *Do not administer IV.*

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Dronabinol

droe-nab'ih-nole

Trade and other names: Marinol

Functional classification: Antiemetic

Pharmacology and Mechanism of Action

Antiemetic from the cannabinoid class. The site of action is unknown, but there is some evidence that the active ingredient may affect opiate receptors, or they may affect other receptors in the vomiting center. For dronabinol, the oral absorption is good, but bioavailability is low because of high first-pass effects. The volume of distribution is high.

Indications and Clinical Uses

Cannabinoids have been used in people who have not responded to any other antiemetic drugs (e.g., patients who are receiving anticancer drugs). They have also gained recent popularity to increase the appetite in patients with terminal disease, cancer, and AIDS. Their use has not been reported in veterinary patients, but they have been used by some veterinarians to increase the appetite in cats.

Precautionary Information

Adverse Reactions and Side Effects

Cannabinoids are relatively well tolerated in people, but side effects include drowsiness, dizziness, ataxia, and disorientation. Withdrawal signs may occur after abrupt discontinuation after repeated doses.

Contraindications and Precautions

No known contraindications.

Drug Interactions

No drug interactions reported for animals.

Instructions for Use

Dronabinol is a form of synthetic marijuana (THC) and is available as an antiemetic prescription drug. Most clinical use in animals has been anecdotal. It has been administered to decrease vomiting and improve appetite associated with chemotherapy.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Dronabinol is available in 2.5-, 5-, and 10-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 5 mg/m² PO, up to 15 mg/m² for antiemetic administration prior to chemotherapy.
- Appetite stimulation: start at 2.5 mg before meals.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Edetate Calcium Disodium

ed'eh-tate kal'see-um dye-soe-dee-um

Trade and Other Names: Calcium disodium versenate and calcium disodium ethylenediaminetetra-acetate (EDTA)

Functional Classification: Antidote

Pharmacology and Mechanism of Action

Chelating agent. Readily chelates with lead, zinc, cadmium, copper, iron, and manganese.

Indications and Clinical Uses

Edetate calcium disodium is indicated for treatment of acute and chronic lead poisoning. It is sometimes used in combination with dimercaprol.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects reported in animals. In people, allergic reactions (release of histamine) have occurred after intravenous administration.

Contraindications and Precautions

Do not use edetate disodium to substitute for edetate calcium disodium because it will chelate calcium in the patient.

Drug Interactions

No specific drug interactions are reported. However, it has the potential to chelate other drugs if mixed together.

Instructions for Use

Edetate calcium disodium may be used with dimercaprol. It is equally effective when administered IV or IM, but intramuscular injection may be painful. Ensure adequate urine flow before the first dose is administered.

Patient Monitoring and Laboratory Tests

Monitor lead concentrations to assess treatment.

Formulations

Edetate calcium disodium is available in a 20-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

- 25 mg/kg q6h for 2-5 days SQ, IM, or IV.

Large Animal Dosage

- 25 mg/kg q6h for 2-5 days SQ, IM, or IV.

Regulatory Information

Withdrawal time: 2 days for meat; 2 days for milk (extralabel).

Edrophonium Chloride

ed-roe-foe'nee-um klor'ide

Trade and Other Names: Tensilon and generic brands

Functional Classification: Antimyasthenic, anticholinesterase

Pharmacology and Mechanism of Action

Cholinesterase inhibitor. Edrophonium causes cholinergic effects by inhibiting metabolism of acetylcholine. Its effects do not last long and is used for short-term use only.

Indications and Clinical Uses

Because edrophonium is short acting, it ordinarily is only used for diagnostic purposes (e.g., myasthenia gravis). It also has been used to reverse neuromuscular blockade of nondepolarizing agents (pancuronium).

Precautionary Information

Adverse Reactions and Side Effects

Edrophonium is short acting and side effects are minimal. Overdose in nonmyasthenia animals may cause salivation, retching, vomiting, and diarrhea. If this is observed, administer atropine at 0.02-0.04 mg/kg. Excessive muscarinic/cholinergic effects may occur with high doses; these may also be counteracted with atropine.

Contraindications and Precautions

Edrophonium will potentiate effects of other cholinergic drugs. Cats are especially sensitive to edrophonium (see dose differences in Small Animal Dosage section).

Drug Interactions

Use cautiously with other cholinergic drugs.

Instructions for Use

Edrophonium is used only for determination of diagnosis of myasthenia gravis. An alternative drug for this purpose is neostigmine methylsulfate (Prostigmin) at 40 mcg/kg IM or 20 mcg/kg IV.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Edrophonium is available in a 10-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 0.11-0.22 mg/kg IV (maximum dose is 5 mg per dog).

Cats

- 0.25-0.5 mg/cat IV.

Large Animal Dose

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. Because of a short half-life, no risk of residue is anticipated in food animals.

RCI Classification: 3

Enalapril Maleate

eh-nal'ah-prill mal'ee-ate

Trade and Other Names: Enacard (veterinary preparation) and Vasotec (human preparation)

Functional Classification: Vasodilator, angiotensin-converting enzyme (ACE) inhibitor

Pharmacology and Mechanism of Action

ACE inhibitor. Like other ACE inhibitors, it inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and will also stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. The ability of aldosterone to cause sodium and water retention contributes to congestion.

Enalapril, like other ACE inhibitors, will cause vasodilation and decrease aldosterone-induced congestion, but ACE inhibitors also contribute to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins.

Indications and Clinical Uses

Enalapril, like other ACE inhibitors, is used to treat hypertension and CHF. Efficacy for CHF is good and can be used with other drugs such as pimobendan, furosemide, digoxin, and spironolactone. It is primarily used in dogs. In addition to its use for treatment of congestive heart failure, enalapril has been used to delay onset of CHF in dogs with mitral regurgitation. The benefit of enalapril and other ACE inhibitors for occult heart disease is controversial; some studies have shown a benefit and others have not. Enalapril has been used in some cats in heart failure or with systemic hypertension. Unfortunately, approximately 50% of cats with hypertension do not respond to enalapril, and ACE inhibitors are not considered a primary treatment for hypertension in cats.

ACE inhibitors also have been shown to be beneficial in the management of certain types of kidney disorders (nephropathy) and for renal hypertension. Renal benefits result from limiting systemic and glomerular capillary hypertension, the antiproteinuric effect to decrease in urine protein-to-creatinine ratio, and retarding the development of glomerular sclerosis and tubulointerstitial lesions. ACE inhibitors have decreased proteinuria in patients, but long-term benefits on survival have not been established. The benefits of ACE inhibitor treatment in cats with chronic renal disease are somewhat modest and have little effect on survival time or long-term prognosis.

Large animal uses have not been established, but in horses the metabolite enalaprilat at 0.5 mg/kg IV completely inhibited ACE activity but did not change blood pressure or other hemodynamic variables in response to exercise.

Precautionary Information

Adverse Reactions and Side Effects

Enalapril may cause azotemia in some patients; carefully monitor patients receiving high doses of diuretics.

Contraindications and Precautions

Discontinue ACE inhibitors in pregnant animals; they cross the placenta and have caused fetal malformations and death of the fetus.

Drug Interactions

Use cautiously with other hypotensive drugs and diuretics. Nonsteroidal anti-inflammatory drugs (NSAIDs) may decrease vasodilating effects.

E

Instructions for Use

Doses are based on clinical trials conducted in dogs. For dogs, start with once-daily administration and increase to q12h if needed. Other drugs used for treatment of heart failure may be used concurrently.

Patient Monitoring and Laboratory Tests

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

Formulations

Enalapril is available as Vasotec (human preparation) in 2.5-, 5-, 10-, and 20-mg tablets and as Enacard (veterinary preparation) in 1-, 2.5-, 5-, 10-, and 20-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Enalapril, compounded in a variety of oral suspensions and flavorings, was stable for 60 days. Above pH of 5, degradation occurs more quickly.

Small Animal Dosage

Dogs

- 0.5 mg/kg q12-24h PO. In some animals it may be necessary to increase dose to 1 mg/kg per day, administered as 0.5 mg/kg q12h.

Cats

- 0.25-0.5 mg/kg q12-24h PO.
- 1-1.25 mg/cat/day PO.

Large Animal Dosage

- There are no clinical studies available to establish doses for horses.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Enflurane

en-floor'ane

Trade and Other Names: Ethrane

Functional Classification: Inhalant anesthetic

Pharmacology and Mechanism of Action

Inhalant anesthetic. Like other inhalant anesthetics, the mechanism of action is uncertain. Enflurane produces a generalized, reversible, depression of the CNS. The inhalant anesthetics vary in their solubility in blood, their potency, and the rate of induction and recovery. Those with low blood/gas partition coefficients are associated with the most rapid rates of induction and recovery. Enflurane has a vapor pressure of 175 mm Hg (at 20°C), a blood/gas partition coefficient of 1.8, and a fat/blood coefficient of 36.

Indications and Clinical Uses

Enflurane, like other inhalant anesthetics, is used for general anesthesia in animals. It has a minimum alveolar concentration (MAC) value of 2.37%, 2.06%, and 2.12% in cats, dogs, and horses, respectively.

Precautionary Information

Adverse Reactions and Side Effects

Like other inhalant anesthetics, enflurane produces vasodilation and increased blood flow to cerebral blood vessels. This may increase intracranial pressure. Like other inhalant anesthetics, it produces a dose-dependent myocardial depression with accompanying decrease in cardiac output. It also depresses respiratory rate and alveolar ventilation. Like other inhalant anesthetics it increases the risk of ventricular arrhythmias, especially in response to catecholamines.

Contraindications and Precautions

No specific contraindications are reported for animals.

Drug Interactions

Other sedatives and anesthetics (e.g., opiates, benzodiazepines, phenothiazines, alpha-2 agonists) will lower the requirement for inhalent gas anesthesia.

Instructions for Use

Titrate dose for each individual with anesthetic monitoring.

Patient Monitoring and Laboratory Tests

Monitor anesthesia parameters. During anesthesia, monitor heart rate and rhythm and respiratory rate.

Formulations

Enflurane is available as a solution for inhalation.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- Induction: 2%-3% Maintenance: 1.5%-3%

Large Animal Dosage

- MAC value: 1.66%.

Regulatory Information

No withdrawal times are established for food animals. Clearance is rapid and short withdrawal times are suggested. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Enilconazole

en-il-kah'nah-zole

Trade and Other Names: Imaverol and ClinaFarm-EC

Functional Classification: Antifungal

Pharmacology and Mechanism of Action

Azole antifungal agent for topical use only. Like other azoles, enilconazole inhibits membrane synthesis (ergosterol) in fungus and weakens the cell wall. It is highly active against dermatophytes.

Indications and Clinical Uses

Enilconazole is used only topically. It is used as a topical agent to apply on the skin for treatment of dermatophytes; as a spray, it is used to treat the environment. It may be applied to animal bedding, stalls, and cages. In addition to dermatologic use, enilconazole has been instilled into the nasal sinus of dogs for treatment of nasal aspergillosis.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported. However, it is reported that if used on cats, they should be prevented from licking fur after application until the drug has dried.

Contraindications and Precautions

No specific contraindications are reported.

Drug Interactions

No specific interactions are reported. However, like other azoles, systemic treatment may result in cytochrome P450 enzyme inhibition.

Instructions for Use

It is used only topically. Imaverol is available only in Canada as 10% emulsion. In the US, Clinafarm EC is available for use in poultry units as 13.8% solution. Dilute solution to at least 50:1 and apply topically every 3-4 days for 2-3 weeks. Enilconazole also has been instilled as 1:1 dilution into nasal sinus for nasal aspergillosis. Enilconazole also has been used—in a diluted form—as a spray to kill fungi on bedding, equine tack, and cages.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations Available

Enilconazole is available as 10% or 13.8% emulsion.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. When the emulsion is mixed, it should be used immediately and not stored.

Small Animal Dosage

- Nasal aspergillosis: 10 mg/kg q12h instilled into nasal sinus for 14 days (10% solution diluted 50/50 with water).
- Dermatophytes: dilute 10% solution to 0.2% and wash lesion with solution four times at 3 to 4-day intervals. Solution may be sponged directly on animal. Allow solution to air dry.

Large Animal Dosage

Horses

- Dilute 10% solution to 0.2% and wash lesions with solution four times at 3 to 4-day intervals.
- Treatment of aspergillus rhinitis: infuse in nasal catheter a 2% solution every 12 hours (25-100 mL).

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Enoxaparin sodium

en-oks'ah-pare-in

Trade and Other Names: Lovenox and low-molecular-weight heparin (LMWH)

Functional Classification: Anticoagulant

Pharmacology and Mechanism of Action

Low-molecular-weight heparin (LMWH), also known as fragmented heparin. LMWH is characterized by a molecular weight composed of approximately 5000, compared to conventional heparin (unfractionated) with a molecular weight of approximately 15,000. Subsequently, the absorption, clearance, and activity of LMWH differ from unfractionated heparin (UFH). LMWHs produce their effect by binding to antithrombin (AT) and increasing antithrombin III-mediated inhibition of synthesis and activity of coagulation factor Xa. However, LMWH, unlike conventional heparin, produces less inhibition of thrombin (factor IIa). LMWH's activity is described by the Anti-factor Xa/Anti-factor IIa ratio. Enoxaparin has a ratio of 3.8:1 (conventional unfractionated heparin ratio is 1:1). In people, LMWHs have several advantages compared to UFH and include greater anti-Xa/IIa activity, more complete and predictable absorption from injection, longer duration, less frequent administration, reduced risk of bleeding, and a more predictable anticoagulant response. However, in dogs and cats, the half-life of LMWH is much shorter than in humans, reducing some of this advantage. In dogs the half-life of enoxaparin is approximately 5 hours; in cats it is estimated to be 1.9 hours, which requires much more frequent administration in either species to maintain anti-Xa

activity compared to humans. LMWHs used in veterinary medicine include tinzaparin (Innohep), enoxaparin (Lovenox), and dalteparin (Fragmin).

Indications and Clinical Uses

Enoxaparin, like other LMWHs, is used to treat hypercoagulability disorders and prevent coagulation disorders such as thromboembolism, venous thrombosis, disseminated intravascular coagulopathy (DIC), and pulmonary thromboembolism. Clinical indications are derived from uses of conventional heparin or extrapolated from human medicine. There have been few clinical studies to examine efficacy of LMWH in animals. Previously published doses extrapolated from humans have been shown *not* to produce adequate and consistent anti-Xa activity in dogs and cats, and the doses listed in this entry are needed for therapy.

Precautionary Information

Adverse Reactions and Side Effects

Although better tolerated than regular heparin, bleeding is a risk. However, LMWHs produce less bleeding problems than administration of conventional heparin. LMWHs are associated with a lower incidence of heparin-induced thrombocytopenia in people, but heparin-induced thrombocytopenia from any form of heparin has not been a clinical problem in animals. If excessive anticoagulation and bleeding occur as a result of an overdose, protamine sulfate should be administered to reverse heparin therapy. Protamine dose is 1.0 mg protamine for every 1.0 mg enoxaparin administered by slow IV infusion. Protamine complexes with heparin to form a stable, inactive compound.

Contraindications and Precautions

Do not administer IM to prevent hematoma; administer SQ only. LMWH is excreted by renal clearance in animals; therefore, if renal disease is present, the elimination will be prolonged. Rebound hypercoagulability may occur after discontinuation of heparin treatment; therefore, it may be advised to taper the dose slowly when discontinuing treatment.

Drug Interactions

Do not mix with other injectable drugs. Use cautiously in animals that are already receiving other drugs that can interfere with coagulation, such as aspirin and warfarin. Although a specific interaction has not been identified, use cautiously in animals that may be receiving certain chondroprotective compounds such as glycosaminoglycans for treatment of arthritis. Some antibiotics, such as cephalosporins, may inhibit coagulation.

Instructions for Use

Dosing recommendations extrapolated from human medicine are not appropriate for animals. Animal owners should be warned that LMWHs are expensive compared to conventional heparin. When dosing, do not interchange doses on a unit-for-unit basis with heparin or other low-molecular-weight heparins because they differ in manufacturing process, molecular weight distribution, anti-Xa and anti-IIa activities, units, and dosage.

Patient Monitoring and Laboratory Tests

Monitor patients for clinical signs of bleeding problems. When administering LMWH, aPTT and PT clotting times are not reliable indicators of therapy, although prolonged aPTT is a sign of overdosing. Anti-Xa activity is considered the preferred

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laboratory measure of LMWH activity in people, but the use of this parameter is controversial in animals. Peak anti-Xa activity occurs 3-4 hours after dosing and the target range for anti-Xa activity should be 0.5-1.0 U/mL for cats and 0.5-2.0 U/mL for dogs.

Formulations

Enoxaparin is available in 30 mg in 0.3 mL, 40 mg in 0.4 mL, 60 mg in 0.6 mL, 80 mg in 0.8 mL, 100 mg in 1 mL injection, 100 mg/mL injection, 120 mg per 0.8 mL, 150-mg/mL injection, and 300 mg per 3 mL

Stability and Storage

Store in a tightly sealed container protected from light. The pH of the injection is 5.5 to 7.5.

Small Animal Dosage

Dogs

- 0.8 mg/kg SQ, q6h (see monitoring section for dose adjustment).

Cats

- 1 mg/kg SQ, q12h, up to 1.25 mg/kg SQ, q6h (see monitoring section for dose adjustment).

Large Animal Dosage

Horses

- Prophylaxis: 0.5 mg/kg q24h SQ and 1 mg/kg q24h SQ for high-risk patients.

Regulatory Information

Extralabel withdrawal times are not established. However, 24-hour withdrawal times are suggested because this drug has little risk from residues.

Enrofloxacin

en-roe-floks'ah-sin

Trade and Other Names: Baytril

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Fluoroquinolone antibacterial drug. Enrofloxacin acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. Enrofloxacin is a bactericidal with a broad spectrum of activity. In most animal species, enrofloxacin is metabolized to ciprofloxacin. Ciprofloxacin is an active desmethyl metabolite of enrofloxacin and may contribute in an additive fashion to the antibacterial effects. At the peak concentration, ciprofloxacin may account for approximately 10% and 20% of the total concentration in cats and dogs, respectively. Susceptible bacteria include *Staphylococcus*, *Escherichia coli*, *Proteus*, *Klebsiella*, and *Pasteurella*. *Pseudomonas aeruginosa* is moderately sensitive but requires higher concentrations. Enrofloxacin has poor activity against *Streptococcus* and anaerobic bacteria.

Indications and Clinical Uses

Enrofloxacin, like other fluoroquinolones, is used to treat susceptible bacteria in a variety of species. Treatment has included infections of skin and soft tissue, UTIs in dogs and cats, *Chlamydophila felis* infections in cats, and ulcerative colitis caused by *Escherichia coli* in dogs. In horses it has been used for a variety of soft

tissue infections and respiratory infections, although this use is based primarily on anecdotal experience. Enrofloxacin is approved for the treatment and control of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis*, and *Streptococcus suis*. It is also approved for treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *P. multocida*, and *Haemophilus somni* (previously *Haemophilus somnus*). Enrofloxacin has been shown effective for treating *Rickettsia* infections in dogs. However, it is not effective for treating *Ehrlichia* (see Doxycycline). Enrofloxacin is also used in most exotic animal species because of its safety and activity against a wide variety of pathogens.

Precautionary Information

Adverse Reactions and Side Effects

High concentrations may cause CNS toxicity, especially in animals with renal failure. It may cause occasional vomiting and, at high doses, may cause some nausea and diarrhea. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4 weeks to 28 weeks of age. Large, rapidly growing dogs are the most susceptible. Cats are relatively resistant to cartilage injury, but foals are susceptible. Blindness in cats that is caused by retinal degeneration has been reported. Affected cats have had permanent blindness. This may be a dose-related effect. Cats administered doses of 20 mg/kg developed retinal degeneration but did not at 5 mg/kg. Therefore, dose restrictions in cats have been used. Administration of concentrated solution (100 mg/mL) given orally to horses has caused oral mucosal lesions. When injected, this solution (pH 10.5) may be irritating to some tissues.

Contraindications and Precautions

Avoid use in young dogs because of risk of cartilage injury. Do not administer to young foals; injury to articular cartilage has been reported. Use cautiously in animals that may be prone to seizures, such as epileptics. Do not administer to cats at doses greater than 5 mg/kg/day.

Drug Interactions

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, and calcium, may decrease absorption.

Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur. Enrofloxacin may precipitate in an IV line if injected directly into IV fluids.

Instructions for Use

Low dose of 5 mg/kg/day is used for sensitive organisms with minimum inhibitory concentration (MIC) values of 0.12 mcg/mL or less or urinary tract infection. A dose of 5-10 mg/kg/day is used for organisms with MIC of 0.12-0.5 mcg/mL (e.g., gram-positive bacteria). A dose of 10-20 mg/kg/day is used for organisms with MIC of 0.5-1.0 mcg/mL (e.g., *Pseudomonas aeruginosa*). The solution is not approved for intravenous use, but it has been administered via this route safely if given slowly. Enrofloxacin was not absorbed in cats after transdermal application in a pluronic gel vehicle. Concentrated enrofloxacin solution (cattle formulation at 100 mg/mL) is basic (pH 10.5); therefore it can be irritating to some animals when

280 Enrofloxacin

injected IM. Do not inject more than 20 mL at each site. Also, this formulation may precipitate out of solution if pH is decreased by other solutions.

Patient Monitoring and Laboratory Tests

Susceptibility testing: For small animals, CLSI break points for sensitive organisms are ≤ 0.5 mcg/mL. MIC values ≥ 4 are considered resistant. If MIC values are 1 or 2 mcg/mL, higher doses may be justified. For cattle, the break point for sensitive organisms is ≤ 0.25 mcg/mL. Other fluoroquinolones may be used in some cases to estimate susceptibility to this fluoroquinolone, but a test using a specific drug is recommended. Ciprofloxacin break point for susceptibility is ≤ 1.0 mcg/mL. However, if ciprofloxacin is used to treat *Pseudomonas* it may be several times more active than other fluoroquinolones. Enrofloxacin may cause a false-positive result on urine glucose tests when using tablet (e.g., Clintest) copper reduction test.

Formulations

Enrofloxacin is available in 22.7- and 68-mg tablets; Taste Tabs are 22.7, 68, and 136 mg. It is also available in a 22.7-mg/mL injection and a 100-mg/mL preparation for large animals (Baytril-100).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has been evaluated and it was found to be stable with many mixtures. However, do not mix with solutions that contain ions that may chelate with enrofloxacin (iron, magnesium, aluminum, and calcium). If administered IV, it is recommended to first dilute the solution in fluids (e.g., 1:10 dilution) and infuse slowly. The 100-mg/mL solution is alkaline and contains benzyl alcohol and l-arginine as a base. If pH of this solution is lowered, it may precipitate. The 22.7-mg/mL formulation has a pH of 11.5 and may not be compatible with some solutions.

Small Animal Dosage

Dogs

- 5-20 mg/kg/day IM, PO, or IV.

Cats

- 5 mg/kg/day PO or IM. (Avoid intravenous use in cats.)

Exotic Animals

- Usually 5 mg/kg/day or in reptiles, every other day.

Birds

- 15 mg/kg q12h IM or PO.

Large Animal Dosage

Horses

- 5 mg/kg q24h IV.
- 7.5-10 mg/kg q24h PO.
- 5 mg/kg of 100 mg/mL solution (Baytril-100) IM.

Cattle (BRD)

- Single dose: 7.5-12.5 mg/kg once SQ (3.4 to 5.7 mL per 100 pounds).
- Multiple-dose:: 2.5 to 5 mg/kg SQ (1.1 to 2.3 mL per 100 pounds) once daily for 3 to 5 days.

Swine (SRD)

- 7.5 mg/kg SQ, behind the ear.

Regulatory Information

Cattle withdrawal time: 28 days for meat. Not to be used in lactating dairy cattle or calves intended to be used as veal. Do not use in female dairy cattle 20 months of age or older. Pig withdrawal time: 5 days.

Extralabel use of fluoroquinolones in animals that produce food is illegal.

Ephedrine Hydrochloride

eh-fed'rin hye-droe-klor'ide

Trade and Other Names: Generic brands

Functional Classification: Adrenergic agonist

E

Pharmacology and Mechanism of Action

Adrenergic agonist. Decongestant. Ephedrine acts as an agonist on alpha-adrenergic receptors and beta₁-adrenergic receptors but has less effect on beta₂ receptors.

Indications and Clinical Uses

Ephedrine is used as a vasopressor (e.g., when it is administered during anesthesia). It also has been used as a CNS stimulant. Oral formulations have been used to treat urinary incontinence because of action on bladder sphincter muscle. However, this is no longer recommended and most oral dose forms are no longer available.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are related to excessive adrenergic activity (e.g., peripheral vasoconstriction and tachycardia).

Contraindications and Precautions

Use in animals with cardiovascular disease is not recommended.

Drug Interactions

No specific drug interactions are reported. However, ephedrine will potentiate any other adrenergic agonist.

Instructions for Use

The most current use is from injection primarily in acute situations to increase blood pressure. Oral use for urinary incontinence in dogs has diminished because of lack of available formulations.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm in patients.

Formulations

Ephedrine is available in a 25- and 50-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- Urinary incontinence: 4 mg/kg or 12.5-50 mg/dog q8-12h PO.
- Vasopressor: 0.75 mg/kg IM or SQ, repeat as needed.

282 Epinephrine

Cats

- Urinary incontinence: 2-4 mg/kg q12h, PO.
- Vasopressor: 0.75 mg/kg IM or SQ, repeat as needed.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

Withdrawal time: No withdrawal times are established. Ephedrine is metabolized after administration, and a short withdrawal is recommended.

RCI Classification: 2

Epinephrine

eh-pih-nef'rin

Trade and Other Names: Adrenaline and generic brands

Functional Classification: Adrenergic agonist

Pharmacology and Mechanism of Action

Adrenergic agonist. Epinephrine nonselectively stimulates alpha-adrenergic and beta-adrenergic receptors. Epinephrine is a potent adrenergic agonist with a prompt onset and a short duration of action.

Indications and Clinical Uses

Epinephrine is used primarily for emergency situations to treat cardiopulmonary arrest and anaphylactic shock. It is administered IV, IM, or endotracheal for acute use. Vasopressin (arginine vasopressin) has replaced epinephrine in some cardiopulmonary resuscitation protocols. Epinephrine has been used in horses to test for diagnosis of anhidrosis, but terbutaline sulfate challenge is used more frequently for this test.

Precautionary Information

Adverse Reactions and Side Effects

Overdose will cause excessive vasoconstriction and hypertension. High doses can cause ventricular arrhythmias. When high doses are used for cardiopulmonary arrest, an electrical defibrillator should be available.

Contraindications and Precautions

Avoid repeated administration in patients.

Drug Interactions

Epinephrine will interact with other drugs that are used to either potentiate or antagonize alpha-adrenergic or beta-adrenergic receptors. It is incompatible with alkaline solutions (e.g., bicarbonate), chlorine, bromine, and salts of metals or oxidizing solutions. Do not mix with bicarbonates, nitrates, citrates, and other salts.

Instructions for Use

Doses are based on experimental studies, primarily in dogs. Clinical studies are not available. Intravenous doses are ordinarily used, but endotracheal administration is acceptable when intravenous access is not available. The intraosseous route also has been used, and doses are equivalent to intravenous doses. When the endotracheal route is used, the dose is higher and duration of effect may be longer than with

intravenous administration. When administering doses endotracheally, one can dilute the dose in a volume of 2-10 mL of saline. There appears to be no advantage to intracardiac injection compared to intravenous administration. Solutions are available in 1:1000 and 1:10,000 (either 1 mg/mL or 0.1 mg/mL). Generally, only the 1:10,000 solution is given IV. 1:1000 solutions are intended for SQ and IM use.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during treatment.

Formulations

Epinephrine is available in a 1-mg/mL (1:1,000) injection solution and 0.1-mg/mL (1:10,000) injection solution. The 1:10,000 is most often used IV, and the 1:1000 solution is used IM or SQ. Ampules for people are designed to deliver 1 mg/person (approximately 14 mcg/kg).

Stability and Storage

It is compatible with plastic in syringes. When solution becomes oxidized, it turns brown. Do not use if this color change is observed. It is most stable at pH of 3-4. If pH of solution is >5.5, it becomes unstable.

Small Animal Dosage

Cardiac arrest: 10-20 mcg/kg IV. 100-200 mcg/kg (0.1-0.2 mg/kg) endotracheal (may be diluted in saline before administration).

Anaphylactic shock: 2.5-5 mcg/kg IV or 50 mcg/kg endotracheal (may be diluted in saline).

Vasopressor therapy: 100-200 mcg/kg (0.1-0.2 mg/kg) IV (high dose) or 10-20 mcg/kg (0.01-0.02 mg/kg) IV (low dose). Administer low dose first, and if no response use high dose.

Large Animal Dosage

1 mg/mL (1:1000) solution.

Anaphylactic shock (cattle, pigs, horses, and sheep): 20 mcg/kg (0.02 mg/kg) IM or 1 mL per 45 kg (1 mL per 100 pounds). 5-10 mcg/kg (0.005-0.01 mg/kg) IV or 0.25 to 0.5 mL per 45 kg (100 pounds).

Regulatory Information

No withdrawal times are established. Epinephrine is rapidly metabolized after administration, and 0 days is recommended for withdrawal.

RCI Classification: 2

Epoetin Alpha (Erythropoietin)

ee-poe'eh-tin

Trade and Other Names: Epogen, epoetin alfa, "EPO," (r-HuEPO), and Erythropoietin

Functional Classification: Hormone

Pharmacology and Mechanism of Action

Human recombinant erythropoietin. Hematopoietic growth factor that stimulates erythropoiesis.

Indications and Clinical Uses

Epoetin alpha is used to treat nonregenerative anemia. It has been used to treat myelosuppression caused by disease or chemotherapy. It also has been used to treat chronic anemia associated with chronic renal failure. The value of epoetin alpha to improve anemia in cats with chronic renal failure has been established in several studies. In some animals, anemia is also caused by iron deficiency and can be combined with ferrous sulfate at a dose of 50-100 mg per cat daily.

Precautionary Information

Adverse Reactions and Side Effects

Because this product is a human-recombinant product, it may induce local and systemic allergic reactions in animals. Injection site pain and headache have occurred in people. Seizures also have occurred. Delayed anemia may occur because of cross-reacting antibodies against animal erythropoietin (reversible when drug is withdrawn). Antiepoetin antibodies may increase with long-term use, which may occur in as high as 30% of treated cats, leading to failure of treatment.

Contraindications and Precautions

Stop therapy with epoetin when joint pain, fever, anorexia, or cutaneous reactions are observed.

Drug Interactions

No interactions are reported.

Instructions for Use

The use of epoetin alpha has been limited primarily to dogs and cats. The only form currently available is a human recombinant product. It is used in animals when hematocrit falls below 25%. In cats, 100 units/kg SQ three times a week is administered until a target hematocrit of 30%-40% is attained. Thereafter, twice-weekly injections are used. Maintenance dose is usually in a range of 75-100 units/kg SQ once or twice a week.

Patient Monitoring and Laboratory Tests

Monitor hematocrit. Dose should be adjusted to maintain hematocrit in a range of 30%-34%.

Formulations Available

Epoetin alpha is available in 2000 units/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 35 or 50 units/kg three times a week, up to 400 units/kg/wk SQ (adjust dose to maintain hematocrit of 30%-34%).

Cats

- Start with 100 units/kg SQ three times weekly; reduce to twice weekly and to once weekly when target hematocrit of 30%-40% is attained. In most cats, maintenance dose is 75-100 units/kg SQ twice weekly.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

No withdrawal times are established for food animals. Erythropoietin in any form is prohibited to be on the premises of racing horses.

RCI Classification: 2

Epsiprantel

ep-sih-pran'til

Trade and Other Names: Cestex

Functional Classification: Antiparasitic

E

Pharmacology and Mechanism of Action

Anticestodal agent similar to praziquantel. The action of epsiprantel on parasites is related to neuromuscular toxicity and paralysis via altered permeability to calcium. Susceptible parasites include canine cestodes *Dipylidium caninum* and *Taenia pisiformis* and feline cestodes *D. caninum* and *T. taeniaeformis*.

Indications and Clinical Uses

Like praziquantel, epsiprantel is used primarily to treat infections caused by tapeworms.

Precautionary Information

Adverse Reactions and Side Effects

Vomiting occurs at high doses. Anorexia and transient diarrhea have been reported. Epsiprantel is safe in pregnant animals.

Contraindications and Precautions

Do not use in animals younger than 7 weeks. All doses are single dose.

Drug Interactions

No drug interactions are reported.

Instructions for Use

Administer as directed to treat tapeworm infections.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Epsiprantel is available in 12.5-, 25-, 50-, or 100-mg coated tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 5.5 mg/kg PO.

Cats

- 2.75 mg/kg PO.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Ergocalciferol

er-go-kal-sif'eh-role

Trade and Other Names: Calciferol and Drisdol

Functional Classification: Vitamin

Pharmacology and Mechanism of Action

Vitamin D analogue. Vitamin D promotes absorption and utilization of calcium.

Indications and Clinical Uses

Ergocalciferol is used for vitamin D deficiency and as treatment of hypocalcemia associated with hypoparathyroidism.

Precautionary Information

Adverse Reactions and Side Effects

Overdose may cause hypercalcemia.

Contraindications and Precautions

Avoid use in pregnant animals because it may cause fetal abnormalities. Use cautiously with high doses of preparations containing calcium.

Drug Interactions

No drug interactions are reported.

Instructions for Use

Ergocalciferol should not be used for renal secondary hypoparathyroidism because of inability to convert to active compound. Doses for individual patients should be adjusted by monitoring serum calcium concentrations.

Patient Monitoring and Laboratory Tests

Monitor serum calcium concentration.

Formulations

Ergocalciferol is available in 400-unit tablets (OTC), 50,000-unit tablets (1.25 mg), and 500,000-unit/mL (12.5 mg/mL) injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

- 500-2000 units/kg/day PO.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Ertapenem

er-tah-pen'em

Trade and Other Names: Invanz

Functional Classification: Antibacterial

E

Pharmacology and Mechanism of Action

Ertapenem is a beta-lactam antibiotic of the carbapenem (penem) class with a broad spectrum of activity. Its action on cell walls is similar to other beta-lactams, which is to bind penicillin-binding proteins (PBP) that weaken or interfere with cell wall formation. In *Escherichia coli*, it has strong affinity toward PBPs 1a, 1b, 2, 3, 4, and 5 with preference for PBPs 2 and 3. Ertapenem is stable against hydrolysis by a variety of beta-lactamases, including penicillinases, and cephalosporinases and extended spectrum beta-lactamases. Spectrum includes gram-negative bacilli, including *Enterobacteriaceae*. Ertapenem is not as active against *Pseudomonas aeruginosa* as other carbapenems. It is also active against most gram-positive bacteria, except methicillin-resistant strains of *Staphylococcus* and *Enterococcus*. In people the half-life is longer than other carbapenems (4 hours) because of high protein binding (95%), which allows for less frequent dosing. However, in dogs these advantages do not exist. The protein binding in dogs is 46%, the volume of distribution is 0.28 L/kg, and the half-life is only 1.3 hours.

Indications and Clinical Use

Ertapenem is indicated primarily for resistant infections caused by bacteria resistant to other drugs. It may be valuable for treating resistant infections caused by *Escherichia coli* and *Klebsiella pneumoniae*. The use of ertapenem has not been as common as for meropenem or imipenem. High protein binding and long half-life in people have allowed less frequent administration compared to other carbapenems. However, dosing protocols have not been tested in dogs and cats.

Precautionary Information

Adverse Reactions and Side Effects

Carbapenems pose similar risks as other beta-lactam antibiotics, but adverse effects are rare. There is a risk of CNS toxicity (seizures and tremors) with high doses.

Contraindications and Precautions

Some slight yellowish discoloration may occur after reconstitution. Slight discoloration will not affect potency. However, a darker amber or brown discoloration may indicate oxidation and loss of potency.

Drug Interactions

Do not mix in vial or syringe with other antibiotics.

Instructions for Use

Doses in animals have been based on extrapolation from human studies rather than efficacy trials.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are ≤ 4 mcg/mL for all organisms. Most bacteria have a MIC less than 2 mcg/mL. Sensitivity to imipenem can be used as a marker for ertapenem.

Formulations

Ertapenem is available in a 1-g vial for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 30 mg/kg q8 IV or SQ.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Erythromycin

eh-rith-roe-mye'sin

Trade and Other Names: Gallimycin-100, Gallimycin-200, Erythro-100, and generic brands

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Macrolide antibiotic. Like other macrolides, it inhibits bacteria by binding to the 50S ribosome and inhibiting protein synthesis. The spectrum of activity of erythromycin is limited primarily to gram-positive aerobic bacteria; it has little or no effect on gram-negative bacteria. The spectrum of activity also includes mycoplasma. In cattle, it is also active against respiratory pathogens such as *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni* (formerly *Haemophilus somnus*). Erythromycin effects on gastrointestinal motility are via stimulation of motilin receptors to increase smooth muscle activity. In dogs the half-life is 1.3 hours IV and 2.9 hours oral, with only 11% bioavailability. In cats, the half-life is less than 1 hour.

Indications and Clinical Uses

Erythromycin is used in a variety of species to treat infections caused by susceptible bacteria. Infections treated include respiratory infections (pneumonia), soft tissues infections caused by gram-positive bacteria, and skin and respiratory infections. In foals it is used to treat *Rhodococcus equi* pneumonia, often in combination with

rifampin. In some species, including horses, it has been used at low doses to stimulate intestinal motility but demonstration of this activity has been limited in clinical patients. In horses the dose of erythromycin to stimulate GI motility is lower than the antibacterial dose (1 mg/kg), but the clinical efficacy for this use has not been shown. In experimental calves, 8.8 mg/kg IM significantly increased rumen motility. At a dose of 10 mg/kg IM in cows undergoing surgery for LDA, it increased rumen contractions.

The use of erythromycin has diminished because of decreased availability of some dose forms (erythromycin estolate), adverse effects in small animals (vomiting), short half-life that requires frequent dosing, and diarrhea in horses. Other macrolides (e.g., azithromycin and clarithromycin in small animals and horses, and tilmicosin and tulathromycin in cattle) are used more often instead of erythromycin.

Precautionary Information

Adverse Reactions and Side Effects

Diarrhea in large animals is the most common adverse effect. This is believed to be caused by a disruption of the normal bacterial intestinal flora. This is caused usually from oral administration. Nursing mares have developed diarrhea through exposure to treated foals. Hyperthermia (febrile syndrome) in association with erythromycin treatment has been observed in foals.

In small animals the most common side effect is vomiting (probably caused by cholinergic-like effect or motilin-induced motility). In small animals, it also may cause diarrhea. In rodents and rabbits, the diarrhea caused by erythromycin can be serious and even fatal.

Contraindications and Precautions

Do not administer orally to rodents or rabbits. Do not administer erythromycin solutions intended for intramuscular administration by intravenous injection. Only the gluceptate and lactobionate salts should be used intravenously (gluceptate rarely available).

Drug Interactions

Erythromycin, like other macrolides, is known to inhibit the cytochrome P450 enzymes and may decrease the metabolism of other coadministered drugs. See Appendix.

Instructions for Use

There are several forms of erythromycin, including the ethylsuccinate and estolate esters and stearate salt for oral administration. However, the estolate form is only available as a suspension. There are no convincing data to suggest that one form is absorbed better than another, and dosage is included for all. Only erythromycin gluceptate and lactate are to be administered IV (gluceptate rarely available). A motilin-like effect to stimulate GI motility occurs at low dose and has been studied primarily in experimental horses. Erythromycin may be administered to cattle in conjunction with surgical procedures to stimulate rumen motility postsurgery.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms is ≤ 0.25 mcg/mL for streptococci and ≤ 0.5 for other organisms. Susceptibility to erythromycin tends to predict susceptibility to other macrolide antibiotics.

Formulations

Erythromycin is available in several forms that contain either a 250- or 500-mg erythromycin base. Oral formulations include 25- and 50-mg/mL erythromycin estolate suspension, 40-mg/mL erythromycin ethylsuccinate suspension, 400-mg ethylsuccinate tablets, and 250- and 500-mg erythromycin stearate tablets. Intravenous formulations include erythromycin lactobionate, but erythromycin gluceptate is rarely available. Erythromycin phosphate, a feed additive available as a powder, has been administered in horses and shown to produce adequate absorption. Erythromycin phosphate is 260 mg/g, which is equivalent to 231-mg erythromycin base per gram. This is available as an OTC feed additive for poultry.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Protect from freezing. Erythromycin base is most stable at pH 7-7.5. In acidic solution it may decompose. Ethylsuccinate formulations are stable for 14 days.

Small Animal Dosage

Dogs and Cats

- 10-20 mg/kg q8-12h PO.
- Prokinetic effects (GI): 0.5-1 mg/kg q8-12h PO or IV.

Large Animal Dosage

Horses

- *Rhodococcus equi*: Erythromycin phosphate or erythromycin estolate 37.5 mg/kg q12h PO or 25 mg/kg q8h PO. Note that in horses, erythromycin base (plain tablets) are poorly absorbed and other forms should be used. (See Instructions for Dosing regarding dosage forms.)
- Erythromycin lactiobionate injection: 5 mg/kg q4-6h IV. To stimulate GI motility: 1 mg/kg.

Cattle

- Abscesses, pododermatitis: 2.2-8.8 mg/kg q24h IM.
- Pneumonia: 2.2-8.8 mg/kg q24h IM or 15 mg/kg q12h IM.
- Stimulate rumen motility: calves 8.8 mg/kg IM; cows 10 mg/kg IM

Regulatory Information

Cattle withdrawal times: 6 days meat (at 8.8 mg/kg). Do not use in female dairy cattle older than 20 months of age. Do not slaughter treated animals within 6 days of last treatment. To avoid excess trim, do not slaughter within 21 days of last injection.

In Canada, withdrawal time for meat is 14 days and 72 hours for milk.

Esmolol Hydrochloride

ez'moe-lole hye-droe-klor'ide

Trade and Other Names: Brevibloc

Functional Classification: Beta blocker, antiarrhythmic

Pharmacology and Mechanism of Action

Beta blocker. Selective for beta₁ receptor. The difference between esmolol and other beta blockers is the short duration of action is attributed to metabolism by red blood cell esterases; it has a half-life of only 9-10 minutes.

Indications and Clinical Uses

Esmolol is indicated for short-term control of systemic hypertension and tachyarrhythmias. It has been used for emergency therapy or short-term treatment. Long-term treatment is not possible because of short half-life. Ordinarily, if an animal shows a positive response to esmolol, it can be switched to longer-acting beta blockers (e.g., propranolol).

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects related to beta₁-blocking effects on heart include myocardial depression, reduced cardiac output, and bradycardia.

Contraindications and Precautions

When administering to patients with dilated cardiomyopathy, consider the risk of negative cardiac effects. Use cautiously in patients with bronchospasm. Esmolol is contraindicated in patients with bradycardia or AV block.

Drug Interactions

Use cautiously with digoxin, morphine, or warfarin.

Instructions for Use

Esmolol is indicated for short-term intravenous therapy only. Doses are based primarily on empiricism or extrapolation of human dose. No clinical studies have been reported in animals.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during treatment.

Formulations

Esmolol is available in 10-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

0.5 mg/kg (500 mcg/kg) IV, which may be given as 0.05-0.1 mg/kg slowly every 5 min.

CRI (Constant rate infusion): 0.5 to 1 mg/kg slowly over a 30-second period followed by 50-200 mcg/kg/min infusion.

Large Animal Dosage

Horses

0.2 mg/kg over 1 minute, IV. After 10 minutes, administer 0.5 mg/kg over 1 minute, IV.

CRI: 0.5 mg/kg IV, followed by 25 mcg/kg/min IV.

Regulatory Information

Withdrawal times are not reported. However, because of short duration of action and rapid metabolism, a short withdrawal period is suggested.

RCI Classification: 3

Estradiol Cypionate

ess-trah-dye'ole sip'ee-oh-nate

Trade and Other Names: ECP, Depo-Estradiol, and generic brands

Functional Classification: Hormone

Pharmacology and Mechanism of Action

Estradiol is used for estrogen replacement in animals. It also has been used to induce abortion in animals.

Indications and Clinical Uses

Estradiol is a semisynthetic estrogen compound. Its effects will mimic that of estrogen in animals. The most common use in small animals has been to terminate pregnancy.

Estradiol benzoate also has been used to terminate pregnancy (5-10 mg/kg divided into two or three subcutaneous injections). Estradiol cypionate formulation had high efficacy (95%), but it had serious adverse effects and is not recommended. Estradiol cypionate is longer acting and more potent than other estrogen formulations.

Precautionary Information

Adverse Reactions and Side Effects

Estradiol has a high risk of causing endometrial hyperplasia and pyometra. There is a dose-dependent risk of bone marrow toxicity in animals, particularly dogs. Estradiol cypionate injections have produced leukopenia, thrombocytopenia, and fatal aplastic anemia. Because stem cells can be affected, the bone marrow toxicity may not be reversible.

Contraindications and Precautions

Estradiol is contraindicated in pregnancy, unless used to terminate pregnancy. Do not administer to ferrets.

Drug Interactions

No drug interactions are reported for animals. It should not be used with other drugs that may suppress the bone marrow. In people, it has been recommended that these estrogen compounds not be used with other drugs that may cause hepatotoxicity. Estradiol may increase cyclosporine concentrations.

Instructions for Use

To terminate pregnancy, 22 mcg/kg is administered once IM during days 3-5 of estrus or within 3 days of mating. However in one study, a dose of 44 mcg/kg was more efficacious than a dose of 22 mcg/kg when given during estrus or diestrus.

Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow suppression.

Formulations

Estradiol is available in a 2-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

22-44 mcg/kg IM (total dose not to exceed 1 mg).

Cats

250 mcg/cat IM, between 40 hrs and 5 days of mating.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not use in food-producing animals.

Estriol

ess-tree-ole

Trade and Other Names: Theelol (previously called Oestriol), Incurin (Europe)

Functional Classification: Hormone

Pharmacology and Mechanism of Action

Estriol is an estrogen hormone. It differs from DES or other estrogens because it is naturally occurring and occupies the receptor for a shorter duration compared to synthetic compounds. When used to treat urinary incontinence, its effects are believed to be caused by increasing sensitivity of alpha-adrenergic receptors in urinary smooth muscle.

Indications and Clinical Uses

Estriol is an estrogen replacement. In small animals, it has most often been used to treat urinary incontinence that is associated with estrogen deficiency. Success rate may be limited. Estriol has increased sphincter tone in urethra of female dogs but has limited efficacy when used in clinical treatment.

Precautionary Information

Adverse Reactions and Side Effects

Estriol has not been associated with pyometra or bone marrow suppression compared to estradiol.

Contraindications and Precautions

Estriol is contraindicated in pregnancy. Do not administer to ferrets.

Drug Interactions

No drug interactions are reported for animals. It should not be used with other drugs that may suppress the bone marrow. In people, it has been recommended that these estrogen compounds not be used with other drugs that may cause hepatotoxicity.

Instructions for Use

To treat urinary incontinence, it has been used in combination with phenylpropanolamine (PPA); however, treatment addition of PPA may not improve efficacy compared to estrogen drugs used alone.

Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow suppression.

Formulations

Estriol is not usually available in commercial forms but can be compounded for animals.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 2 mg per dog, PO, q24h (may be combined with phenylpropanolamine). After starting with 2 mg per dog per day, after 1 week reduce dose to 1.5 mg per dog per day for 1 week, then 1 mg per dog per day for 1 week, and a gradually tapered regimen, and increased interval (every other day, every third day, etc.) until a goal of 0.5 mg per dog, once per week is achieved.

Cats

- No dose established.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not use in food-producing animals.

Etidronate Disodium

eh-tih-droe'na-te dye-soe'dee-um

Trade and Other Names: Didronel

Functional Classification: Antihypercalcemic agent

Pharmacology and Mechanism of Action

Bisphosphonate drug. These drugs are a group of drugs characterized by a germinal bisphosphonate bond. They slow the formation and dissolution of hydroxyapatite crystals. Their clinical use resides in their ability to inhibit bone resorption. These drugs decrease bone turnover by inhibiting osteoclast activity and retard bone resorption and decrease rate of osteoporosis.

Indications and Clinical Uses

The bisphosphonate group of drugs, which includes etidronate, is used primarily in people to treat osteoporosis and hypercalcemia of malignancy. In animals they are used to decrease calcium in conditions that cause hypercalcemia, such as cancer and vitamin D toxicosis. Studies in people have shown that bisphosphonates may have action in cancer-induced bone disease that is more significant than the effect on osteolysis and bone resorption and also may decrease the tumor burden. Drugs in this class include pamidronate, etidronate, and pyrophosphate. In dogs, more experimental work has been performed with pamidronate than other drugs in this group. Some bisphosphonates have been used to treat navicular disease in horses, but this work is only preliminary and used injectable formulations.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects not reported for animals. In people, GI problems are common. Esophageal lesions have occurred because of reaction from contact with mucosa. If used in animals, ensure that tablets are completely swallowed.

Contraindications and Precautions

No contraindications have been identified in animals.

Drug Interactions

No drug interactions have been reported in animals. If mixed with other solutions or drugs, avoid mixtures containing calcium.

E

Instructions for Use

At high doses, etidronate may inhibit mineralization of bone. In people, alendronate has replaced etidronate because of side effects. There are no clinical studies demonstrating efficacy of etidronate in animals; the use is extrapolated from human medicine and anecdotal experience.

Patient Monitoring and Laboratory Tests

Monitor serum calcium and phosphorus. Monitor urea nitrogen, creatinine, urine-specific gravity in treated animals, and food intake.

Formulations

Etidronate is available in 200- and 400-mg tablets and 50-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 5 mg/kg/day PO.

Cats

- 10 mg/kg/day PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established; 24 hour withdrawal times are suggested because this drug has little risk from residues.

Etodolac

ee-toe'doe-lak

Trade and Other Names: EtoGesic (veterinary preparation) and Lodine (human preparation)

Functional Classification: Nonsteroidal anti-inflammatory drug (NSAID)

Pharmacology and Mechanism of Action

Like other NSAIDs, etodolac has analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the cyclo-oxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations; and COX-2 activity is important for some biological effects. In dogs, etodolac has a half-life of 7.6 to 14 hours, depending on the study and feeding conditions. In dogs it shows either little preference of COX-2 or COX-1 (nonselective) or slight COX-2 selectivity in vitro. It is not known if selectivity for COX-2 affects efficacy or risk of adverse effects. In horses, etodolac is relatively COX-2 selective and is more potent than in dogs. The half-life in horses is only 3 hours, but a duration of effect of approximately 24 hours has been observed in horses with lameness.

Indications and Clinical Uses

Etodolac is indicated for treatment of osteoarthritis in dogs. It also is used as an analgesic and may be used for other painful conditions. Like other NSAIDs, etodolac is expected to reduce fever. Uses in cats have not been established. Etodolac has been used in some horses to relieve pain associated with abdominal surgery and to treat lameness (e.g., caused by navicular disease). Dose regimens are different for horses compared with other animals.

Precautionary Information

Adverse Reactions and Side Effects

NSAIDs may cause GI ulceration. Other adverse effects caused by NSAIDs include decreased platelet function and renal injury. In clinical trials with etodolac at recommended doses, some dogs showed weight loss, loose stools, or diarrhea. At high doses (above label dose), etodolac caused GI ulceration in dogs. Etodolac has been associated with keratoconjunctivitis sicca (KCS) in dogs, which in some cases has been severe. Resolution of KCS has occurred in only 10%-15% of cases after discontinuing medication. Improvement in KCS was greater if treatment duration was short. In horses, at high doses GI toxicity has been observed.

Contraindications and Precautions

Do not administer to animals prone to GI ulcers. Do not administer with other ulcerogenic drugs, such as corticosteroids. Do not administer to dogs that may be prone to developing KCS. Do not administer to animal with compromised renal function.

Drug Interactions

Use NSAIDs cautiously with other drugs known to cause GI injury (e.g., corticosteroids). The efficacy of angiotensin-converting enzyme (ACE) inhibitors and diuretics (furosemide) may be diminished when administered concurrently with NSAIDs. Etodolac may cross-react with sulfonamides in sensitive animals.

Instructions for Use

Administer as directed and avoid concurrent use of other medications that may increase GI toxicity. Most of the use in dogs has been associated with treatment of osteoarthritis. In horses, it has been shown experimentally to improve lameness associated with navicular disease. When used in horses for this purpose, it was given at 23 mg/kg orally once or twice daily for 3 days. Treated horses improved with either regimen and showed no signs of adverse effects. Experimental horses treated with 20 or 23 mg/kg did not demonstrate adverse effects, but long-term safety has not been reported.

Patient Monitoring and Laboratory Tests

Monitor for signs of GI ulcers and bleeding. Monitor tear production periodically in dogs treated with etodolac and observe for ocular signs of KCS. Monitor liver enzymes in dogs treated with NSAIDs periodically for signs of liver toxicosis. Monitor urea nitrogen and creatinine in treated animals for signs of renal injury. Etodolac has had varying effects on T4, free T4, and TSH concentrations in dogs. One study showed no effect, and another study showed a decrease in T4 and free T4 in treated dogs after 2 weeks.

Formulations

Etodolac is available in 150- and 300-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Etodolac is insoluble in water but is soluble in alcohol or propylene glycol.

Small Animal Dosage

Dogs

- 10-15 mg/kg once daily PO.

Cats

Dose not established.

Large Animal Dosage

Horses

- 23 mg/kg q24h PO. Long-term safety with this regimen has not been established (see Instructions for Dosing).

Regulatory Information

No withdrawal times have been established. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Famciclovir

fam-sye'kloe-veer

Trade and Other Names: Famvir

Functional Classification: Antiviral

Pharmacology and Mechanism of Action

Antiviral drug. Famciclovir is a synthetic purine analogue (acyclic nucleoside analogue). It is converted to the antiviral drug penciclovir and has antiviral activity against herpes virus type 1 and 2. The action is related to the affinity for the enzyme thymidine kinase (TK), which converts penciclovir into penciclovir triphosphate, which inhibits viral DNA polymerase to prevent DNA chain elongation—thus inhibiting viral DNA chain elongation. It is used for treatment of various forms of herpes virus infection in humans and also has been used for treatment of viral infections in animals. However, feline herpes virus 1 (FHV1) is resistant to acyclovir and valciclovir, and studies are lacking on the susceptibility of other herpes viruses. Other antiviral drugs used in animals include acyclovir, penciclovir, and valacyclovir.

Indications and Clinical Uses

Although in vitro testing does not indicate high activity against the virus, famciclovir has been used to treat feline herpes virus (FHV1) associated with conjunctivitis, rhinosinusitis, keratitis, and FHV1-associated dermatitis. In treated cats there was improvement of conjunctivitis, decreased conjunctival inflammation, decreased ocular discomfort, and decreased tearing.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects were identified in limited studies performed in cats.

Contraindications and Precautions

Reduce dose in animals with compromised renal function.

Drug Interactions

No interaction identified.

Instructions for Use

The dose listed for cats is based on limited studies in which 62.5 mg per cat was studied initially, but later evidence suggested that a higher dose of 125 mg per cat was more effective.

Patient Monitoring and Laboratory Tests

Monitor BUN and creatinine during use.

Formulations

Famciclovir is available in 125-, 250-, and 500-mg tablets.

Stability and Storage

Store tablets and capsules in tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Cats

- Treatment of feline herpes: 62.5 mg per cat, PO, q8h, for 3 weeks. However, a higher dose of 125 mg per cat q8h may be more effective.

Large Animal Dosage

Horses

- No doses have been established.

Regulatory Information

Because of mutagenicity, it should not be administered to animals intended for food.

Famotidine

fah-moe'tih-deen

Trade and Other Names: Pepcid

Functional Classification: Antiulcer agent

F

Pharmacology and Mechanism of Action

Histamine₂ antagonist (H₂ blocker). Stimulation of acid secretion in the stomach requires activation of histamine type 2 receptors (H₂ receptor), gastrin receptors, and muscarinic receptors. Famotidine and related H₂ blockers inhibit the action of histamine on the histamine H₂ receptor of parietal cells and inhibits gastric parietal cell gastric acid secretion. It increases stomach pH to help heal and prevent gastric and duodenal ulcers.

Indications and Clinical Uses

Famotidine, like other H₂-receptor blockers, is used to treat ulcers and gastritis in a variety of animals. Although it is often used for animals with vomiting, there are no efficacy data to indicate that it is effective. There are no efficacy data to support its use for preventing nonsteroidal anti-inflammatory drug (NSAID)-induced bleeding and ulcers. Famotidine has been used by veterinarians as a preferred H₂ blocker, but there is a lack of evidence to demonstrate superiority over other drugs in this class. Some studies have demonstrated efficacy at 1 mg/kg in dogs, while other studies have not demonstrated differences between a placebo in dogs for increasing stomach pH.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects usually are seen only with decreased renal clearance. In people, CNS signs may occur with high doses. The intravenous solution contains benzyl alcohol, aspartic acid, and mannitol. Give intravenous injections slowly to cats (over 5 minutes) because rapid intravenous injections may cause hemolysis.

Contraindications and Precautions

Intravenous solutions contain benzyl alcohol. IV injections to small animals, especially cats, should be done slowly.

Drug Interactions

Famotidine and other H₂-receptor blockers block secretion of stomach acid. Therefore, they will interfere with oral absorption of drugs dependent on acidity, such as ketoconazole, itraconazole, and iron supplements. Unlike cimetidine, famotidine is not associated with inhibition of microsomal P450 enzymes.

Instructions for Use

Administer with food for best absorption. Clinical studies for famotidine have not been performed; therefore optimal doses for ulcer prevention and healing are not known. Dose recommendations are extrapolated from human use or from anecdotal experience. Experimental studies in dogs have shown that doses of 0.1-0.2 mg/kg inhibit stomach acid secretion, but other clinical studies have shown that doses of 1.0 mg/kg suppress stomach acid for 24 hours. For intravenous use, dilute with IV solutions (e.g., 0.9% saline) to a total volume of 5-10 mL.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Famotidine is available in 10-mg tablets, 8 mg/mL oral suspension, and 10-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Famotidine is soluble in water. Compounded formulations in cherry syrup have been stable for 14 days. Diluted intravenous solutions in saline are stable for 48 hours at room temperature.

Small Animal Dosage

Dogs

- 0.1-0.2 mg/kg q12h PO, IV, SQ, or IM. Doses as high as 0.5-1 mg/kg have been administered, but there is no evidence that higher doses will improve efficacy.

Cats

- 0.2 mg/kg q24h, up to 0.25 mg/kg q12h IM, SQ, PO, or IV (slowly over 5 minutes).

Large Animal Dosage

Horses

- 1-2 mg/kg q6-8h PO.

Regulatory Information

No restrictions on use in animals not intended for food.

RCI Classification: 5

Febantel

feh-ban'tel

Trade and Other Names: Rintal and Vercom. Drontal Plus also contains two other drugs.

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Febantel is an antiparasitic that interferes with carbohydrate metabolism in parasitic worms. It suppresses mitochondrial reactions via inhibition of fumarate reductase and interferes with glucose transport. It is metabolized to a benzimidazole compound that binds to structural protein tubulin and prevents polymerization to microtubules, which results in incomplete digestion and absorption of nutrients by parasite.

A formulation of febantel, pyrantel, and praziquantel (Drontal Plus) has been used in cats for treatment of *Giardia*, roundworms, hookworms, and whipworms.

Indications and Clinical Uses

Febantel is indicated in the control and treatment of larvae and adult stages of intestinal nematodes. In horses, it is used for removal of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*), ascarids (*Parascaris equorum*, sexually mature and immature), pinworms (*Oxyuris equi*, adult and fourth-stage larvae), and the various small strongyles.

In dogs and cats it is used for treatment of hookworms (*Ancylostoma caninum* and *Uncinaria stenocephala*), ascarids (*Toxocara canis* and *Toxascaris leonina*), and whipworms (*Trichuris vulpis*). In dogs, it is used in combination with praziquantel for treatment of hookworms (*A. caninum* and *U. stenocephala*), whipworms (*T. vulpis*), ascarids (*T. canis* and *T. leonina*), and tapeworms (*Dipylidium caninum* and *Taenia pisiformis*).

In cats it is used in combination with praziquantel for removal of hookworms (*A. tubaeforme*), ascarids (*Toxocara cati*), and tapeworms (*D. caninum* and *Taenia taeniaeformis*).

Febantel has been used with pyrantel (Drontal Plus) for treatment of *Giardia*.

Precautionary Information

Adverse Reactions and Side Effects

Vomiting and diarrhea may occur after dosing.

Contraindications and Precautions

Do not use in pregnant animals. Do not use in animals with liver or kidney dysfunction.

Drug Interactions

No drug interactions reported.

Instructions for Use

For horses, the paste may be administered on the base of the tongue or added to a portion of the normal grain ration. For most effective results, re-treat in 6-8 weeks. Febantel suspension may be used in combination with trichlorfon oral liquid when combining 1 part febantel suspension with 5 parts trichlorfon liquid.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Febantel is available in an equine paste: 45.5% febantel (455 mg/mL), suspension: 9.3% (2.75 g per ounce) febantel, and 27.2- and 163.3-mg tablets.

Febantel is also available in combinations; each gram of paste contains 34 mg of febantel and 3.4 mg of praziquantel.

Febantel, pyrantel, and praziquantel are available for small animals.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 10 mg/kg febantel alone or in combination with 1 mg/kg praziquantel PO, with food once daily for 3 days.

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- Puppies: 15 mg/kg febantel alone or in combination with 1.5 mg/kg praziquantel PO, with food once daily for 3 days.
- For treatment of *Giardia*, it has been combined with pyrantel (27-35 mg/kg febantel + 27-35 mg/kg pyrantel) q24h, PO x 3 days.

Cats

- 10 mg/kg febantel alone or in combination with 1 mg/kg praziquantel PO, in the food once daily for 3 days.
- Kittens: 15 mg/kg febantel alone or in combination with 1.5 mg/kg praziquantel.

Large Animal Dosage

Cattle

- 7.5 mL/100 kg body weight PO.

Sheep and Goats

- 1 mL/20 kg body weight or 5 mL/25 kg PO.

Horses

- 6 mg/kg PO.

Regulatory Information

Not for use in horses intended for food. No other regulatory restrictions are listed.

Felbamate

fel'bah-mate

Trade and Other Names: Felbatol

Functional Classification: Anticonvulsant

Pharmacology and Mechanism of Action

Anticonvulsant. The action to treat seizures in animals may be via antagonism at the N-methyl-D-aspartate (NMDA) receptor and block effects of excitatory amino acids. The half-life in dogs is 5-6 hours, which may require frequent administration.

Indications and Clinical Uses

Felbamate is used to treat epilepsy in dogs when they are refractory to other anticonvulsants. It has been used in conjunction with other anticonvulsants. However, the use in animals has declined because of the availability of other drugs to treat refractory seizures such as levetiracetam, zonisamide, gabapentin, and pregabalin.

Precautionary information

Adverse Reactions and Side Effects

Not documented with use in dogs. In people the most severe reactions have been hepatotoxicity and aplastic anemia.

Contraindications and Precautions

It may increase phenobarbital concentrations.

Drug Interactions

Possible interactions exist with drugs that either alter or are substrates for hepatic cytochrome P450 enzymes. See Appendix. It may increase phenobarbital concentrations if used concurrently.

Instructions for Use

Dosing has been empirically in dogs. There are no controlled studies to document efficacy, but it is usually administered when animals have been refractory to other drugs, such as phenobarbital or bromide.

Patient Monitoring and Laboratory Tests

Monitoring of plasma concentrations is helpful to assess therapy. Assays may be available in some commercial laboratories. Ideal plasma concentrations have not been established for animals. However, concentrations in humans of 24 to 137 mcg/mL in plasma have been effective (mean of 78 mcg/mL).

Formulations

Felbamate is available in 12- mg/mL oral liquid and 400- and 600-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Start with 15-20 mg/kg q8h PO. Maximum dose is approximately 70 mg/kg q8h PO.
- Small dogs: 200 mg/dog q8h PO, and increase to a maximum dose of 600 mg/dog q8h.
- Large dogs: 400 mg/dog q8h. Increase dose gradually by 200 mg (15 mg/kg); increments until seizure control. Maximum dose for large dogs is 1200 mg/dog q8h.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No withdrawal times have been established. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Fenbendazole

fen-ben'dah-zole

Trade and Other Names: Panacur and SafeGuard

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Benzimidazole antiparasitic drug. Like other benzimidazoles, fenbendazole produces a degeneration of the parasite microtubule and irreversibly blocks glucose uptake in parasites. Inhibition of glucose uptake causes depletion of energy stores in parasite, eventually resulting in death. However, there is no effect on glucose metabolism in mammals.

Indications and Clinical Uses

Fenbendazole is effective for treatment of numerous helminth intestinal parasites in animals, including *Toxacara*, *Toxascaris*, *Ancylostoma*, and *Trichuris*. In dogs it is

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effective for most intestinal helminth parasites and also against nematodes. Fenbendazole has been effective for treatment of *Giardia*, but higher doses are needed and there may be failure rates as high as 50%. It is effective in cats for treatment of lungworms, flukes, and a variety of helminth parasites.

Precautionary Information

Adverse Reactions and Side Effects

It has a good safety margin, but vomiting and diarrhea have been reported. When evaluated at doses of three and five times the recommended dose at three times the recommended duration, fenbendazole was well tolerated and no adverse effects were reported. It has been safe to use during pregnancy. There have been rare reports of pancytopenia associated with fenbendazole administration.

Contraindications and Precautions

No known contraindications. It may be used in all ages of animals.

Drug Interactions

There are no known drug interactions.

Instructions for Use

Dose recommendations based on clinical studies by manufacturer. Granules may be mixed with food. Paste may be given to horses and cattle. Presence of food does not affect oral absorption. In studies for treatment of *Giardia*, it was safer than other treatments.

Patient Monitoring and Laboratory Tests

Fecal monitoring may be performed to determine the efficacy of treatment for intestinal parasites.

Formulations Available

Fenbendazole is available in 22.2% (222 mg/g) Panacur granules, 10% (92 g/32 oz), and 100-mg/mL oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 50 mg/kg/day for 3 days PO. Duration may be extended to 5 days for severe parasitic infestations.

Cats

- 50 mg/kg/day for 3 days PO.
Duration may be extended to 5 days for severe parasitic infestations.

Large Animal Dosage

Horses

Intestinal parasites, such as strongyles, pinworms, and ascarids: Panacur granules or paste is administered at a dose of 5.1 mg/kg (2.3 mg/pound) PO. Two packets of 1.15 g each will treat a 450-kg (1000-pound) horse. Re-treatment in 6-8 weeks may be necessary. Panacur paste can be administered to horses at a dose of 5 mg/kg PO. Re-treatment at 6-8 weeks may be necessary. For treatment of ascarids (*Parascaris equorum*) in horses, a higher dose of 10 mg/kg is recommended.

Sheep and Goats

- 5 mg/kg PO.

Cattle

- 5 mg/kg PO.

Regulatory Information

Cattle withdrawal time (meat): 8 days. There is no withdrawal period for milk.

Goat withdrawal time: 6 days meat; 0 days milk.

Fenoldopam mesylate

fe-nol'- doe- pam

Trade and Other Names: Corloпам

Functional Classification: Vasodilator

F

Pharmacology and Mechanism of Action

Fenoldopam is a dopamine agonist. It is specific for the dopamine D₁ receptors and therefore has been used to produce smooth muscle relaxation and vasodilation in vascular beds that have D₁ receptors. It has no activity on D₂ receptors and only a small effect on alpha-adrenergic receptors. Because of this activity, fenoldopam has more specificity than dopamine, which has been used for similar indications. The use of fenoldopam is usually confined to increasing renal perfusion to treat acute renal failure. The half-life in animals is very short (1-7 minutes in dogs), so it is usually administered via constant rate infusion.

Indications and Clinical Uses

The use of fenoldopam in veterinary medicine is limited to a few research studies (primarily in cats) and some anecdotal evidence of efficacy for treating acute renal failure. The use in people is to treat severe hypertension, to prevent renal ischemia, to increase gastrointestinal perfusion, and to treat acute renal failure. The use is limited to short-term in-hospital use when rapid treatment of hypertension is needed.

Precautionary Information**Adverse Reactions and Side Effects**

The most common side effect is hypotension. The half-life of fenoldopam is short; therefore, if hypotension is observed, decrease the infusion rate. Other adverse effects have not been described for small animals. In people adverse effects can include increased intraocular pressure (risk in glaucoma), low potassium, and tachycardia.

Contraindications and Precautions

No known contraindications.

Drug Interactions

Use cautiously with other vasodilators; excessive hypotension can occur. Do not use with beta blockers.

Instructions for Use

Administer by constant rate infusion (CRI). Do not administer bolus doses. Onset of effects should occur within 15 minutes of starting the CRI. Dose recommendations are based on some limited research studies and anecdotal clinical experience from

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veterinarians. There have been no well-controlled studies of efficacy in animals, and the use is largely extrapolated from human recommendations. It is recommended that the solution is added to fluids to make a 40-mcg/mL solution for infusion. For example, add 1 mL (10 mg) to 250 mL.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and blood pressure during treatment.

Formulations Available

Fenoldopam is available as a 10-mg/mL injection. The pH range is 2.8 to 3.8.

Stability and Storage

Fenoldopam solution can be mixed with sodium chloride solution (0.9%) or 5% dextrose solution for infusion. Once mixed in fluids, it is stable under normal ambient light and temperature conditions for at least 24 hours. After 24 hours, discard the solution.

Small Animal Dosage

Dogs

0.8 mcg/kg/min CRI.

Cats

0.5 mcg/kg/min CRI.

Large Animal Dosage

Foals

0.04 mcg/kg/min.

Regulatory Information

There are no withdrawal times established for food animals. Because fenoldopam has a very short half-life, residues in food animals are not expected to be a problem.

Fentanyl Citrate

fen'tah-nil sih'trate

Trade and Other Names: Sublimaze and generic brands; Fentora buccal tablets

Functional Classification: Analgesic, Opioid

Pharmacology and Mechanism of Action

Synthetic opiate analgesic. Fentanyl is approximately 80 to 100 times more potent than morphine. Fentanyl is an agonist for the mu-opiate receptors on nerves and inhibits release of neurotransmitters involved with transmission of pain stimuli (such as Substance P). The central sedative and euphoric effects are related to mu-receptor effects in the brain. Fentanyl has a wide safety profile with doses as high as 300 times the recommended dose not being lethal in spontaneously breathing dogs. It is highly lipophilic—approximately 1000 times more lipophilic than morphine, which produces rapid diffusion into the CNS. In dogs the half-life is approximately 3-6 hours, and in cats it is approximately 2.5 hours. Clearance is high in dogs and oral absorption is very low. Fentanyl can be absorbed from the skin or oral mucous membrane, but it is not orally bioavailable if swallowed.

Indications and Clinical Uses

Fentanyl citrate is used as an intravenous bolus or as a constant rate infusion (CRI) in animals for relief of pain, an adjunct for anesthesia, or as a sedative in combination with other CNS sedatives. Fentanyl administered IV will produce

antinociceptive effects for approximately 2 hours. Most of the doses are based on empiricism and experimental studies. Oral buccal tablets have been used in people for treatment of breakthrough pain, but there has been only anecdotal experience with this use in animals. See Fentanyl, Transdermal for information about transdermal form. Clinical use is primarily in dogs and cats. In horses at doses needed to produce analgesia it is associated with a high degree of restlessness, tachycardia, increased locomotor activity, and excitement (see Adverse Reactions and Side Effects section). In horses there has been poor efficacy at lower doses.

Precautionary Information

Adverse Reactions and Side Effects

Fentanyl has adverse effects similar to morphine. Like all opiates, side effects are predictable and unavoidable. Side effects include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses. As with other opiates, a slight decrease in heart rate is expected. In most cases this decrease does not have to be treated with anticholinergic drugs (e.g., atropine), but it should be monitored. In horses, undesirable and even dangerous behavior can follow rapid intravenous opioid administration. Horses should receive a preanesthetic of acepromazine or an α_2 agonist.

Contraindications and Precautions

Fentanyl citrate is a Schedule II controlled substance. Tolerance and dependence occurs with repeated administration. Cats and horses are prone to excitement after administration, especially IV.

Drug Interactions

There are no specific drug interactions, but fentanyl will decrease other anesthetic requirements. Fentanyl will potentiate other opiates and CNS depressants.

Instructions for Use

No clinical studies have been reported. In addition to fentanyl injection, transdermal fentanyl is available. Oral transmucosal (buccal) forms and soluble muco-adhesive film strips are available for human administration but have not been adequately tested in animals. For SQ injection, fentanyl citrate may be mixed with bicarbonate solution (see stability section below) to decrease pain from injection.

Patient Monitoring and Laboratory Tests

Monitor analgesic response. Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

Formulations Available

Fentanyl citrate is available as a 250-mcg/5 mL injection (50 mcg/mL). Fentora buccal tablets are 100, 200, 400, 600, and 800 mcg. Fentanyl buccal soluble film (Onsolis) is 200, 400, 600, 800, and 1200 mcg per film strip.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water and slightly soluble in alcohol. It is a Schedule II drug, so store in a locked compartment. Compounded into a transmucosal gel has not been effective. The pH of fentanyl citrate is 5.2. If bicarbonate solution is added (1:10 or 1:20 dilution) the pH increases to 8.0, which may decrease pain from injection if injected immediately after mixing.

Small Animal Dosage

Dogs and Cats

- Anesthetic uses: 0.02-0.04 mg/kg q2h IV, SQ, or IM or if administered with acepromazine or diazepam, use 0.01 mg/kg IV, IM, or SQ.
- Analgesic agent, 0.005-0.01 mg/kg q2h IV, IM, or SQ.
CRI: 0.003 mg/kg IV (3 mcg/kg) loading dose, followed by 0.005 mg/kg/hr (5 mcg/kg/hr) in dogs or 0.002 mg/kg/hr (2 mcg/kg/hr) in cats.
- Fentanyl buccal film strip: No dose is established for animals. In people, the starting dose is 200 mcg, then increased as needed.

Large Animal Dosage

Small Ruminants

5-10 mcg/kg (0.005-0.010 mg/kg) IV.

Regulatory Information

Schedule II controlled drug by DEA. No withdrawal information is available for food-producing animals.

RCI Classification: 1

Fentanyl, Transdermal

fen'tah-nil

Trade and Other Names: Duragesic

Functional Classification: Analgesic, Opioid

Pharmacology and Mechanism of Action

Synthetic opiate analgesic. Fentanyl is approximately 80 to 100 times more potent than morphine. Fentanyl is an agonist for the mu-opiate receptors on nerves and inhibits release of neurotransmitters involved with transmission of pain stimuli (such as Substance P). The central sedative and euphoric effects are related to mu-receptor effects in the brain. The fentanyl transdermal system delivers fentanyl through the skin at a constant rate to produce systemic effects. Absorption is determined by the surface area for absorption.

Patches are available that deliver 25, 50, 75, and 100 mcg/hr. Absorption can be variable in animals (e.g., rate of release of fentanyl has varied from 27% to 98% [mean 71%] of the theoretical value). Cats absorbed the fentanyl at an average rate of approximately one third that of the theoretical delivery rate, but one patch will maintain consistent concentrations of fentanyl in the plasma for at least 118 hours. Fentanyl transdermal patches (two or three 100-mcg/hr patches) have been applied to the skin of horses to relieve pain. In horses, the duration is less than in dogs or cats and may have to be reapplied every 48 hours.

Indications and Clinical Uses

Transdermal absorption and effective plasma concentrations have been demonstrated for cats, dogs, horses, and goats. Fentanyl transdermal has the same properties as fentanyl citrate administered IV, except in this formulation it is administered transdermal to produce pain relief and as an adjunct to other drugs in perioperative patients and in patients with chronic pain. In dogs, fentanyl transdermal patches (50 mcg/hr) are appropriate for most average-size dogs. Transdermal fentanyl has been shown effective to relieve postoperative pain in dogs. Transdermal fentanyl has

been well tolerated in cats. Fentanyl patches (25 mcg/hr) were effective and safe to relieve pain from onychectomy surgery in cats. Cats that have received fentanyl patches have had improvement in temperament, attitude, and appetite. Transdermal fentanyl has been used alone or combined with nonsteroidal anti-inflammatory drugs (NSAIDs) for treating severe pain in horses and may provide pain relief that is superior to NSAIDs alone.

Precautionary Information

Adverse Reactions and Side Effects

Severe adverse effects have not been reported. The patch may cause slight skin irritation at the site of application. If patch delivery of fentanyl is high, some signs of opiate overdose may occur (e.g., excitement in cats or sedation in dogs); however, these reactions are rare. Adverse effects have not been reported from the use in horses. If adverse effects are observed in animals (e.g., respiratory depression, excess sedation, or excitement in cats), remove patch and, if necessary, administer naloxone.

Contraindications and Precautions

Transdermal fentanyl is a Schedule II controlled substance. Use cautiously in animals of small body weight (e.g., small toy dogs and young or debilitated cats). Animal owners should be advised of the high risks to humans if transdermal patches are applied to humans. Fentanyl is absorbed through intact human skin.

Drug Interactions

There are no specific drug interactions, but transdermal fentanyl will decrease other anesthetic requirements. Transdermal fentanyl will potentiate other opiates and CNS depressants.

Instructions for Use

Transdermal fentanyl incorporates fentanyl into adhesive patches applied to skin of dogs and cats. Studies have determined that patches release sustained levels of fentanyl for 72-108 hours in dogs and cats. One 100-mcg/hr patch is equivalent to 10 mg/kg of morphine every 4 hours IM. Studies have determined that 25-mcg/hr patches are appropriate for cats. If rate of delivery is too high for cats and adverse reactions are suspected, covering half the adhesive surface area will reduce rate of delivery. A single 50-mcg/hr patch is appropriate for dogs weighing 10-20 kg. In horses, two or three 100-mcg/hr patches achieved rapid plasma concentrations within effective ranges in adults, but it was highly variable. Duration of effect in horses is less than in dogs or cats at only 48 hours. Follow manufacturer's recommendations carefully when applying patches.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone. Monitor for signs of excitement in cats.

Formulations Available

Transdermal fentanyl is available in 25-, 50-, 75-, and 100-mcg/hr patches. In May 2009 the formulation was switched to a matrix vehicle instead of a reservoir system. These have been bioequivalent to previous formulations in people.

310 Ferrous Sulfate

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not open fentanyl patch membrane.

Small Animal Dosage

Dogs

• 10-20 kg: 50-mcg/hr patch q72h.

Cats

25-mcg patch q120 h.

Large Animal Dosage

Horses

Adults: Two or three transdermal patches of 100 mcg/hr each (10 mg fentanyl, equivalent to 35-110 mcg/kg delivered transdermally).

Foals: One transdermal patch of 100 mcg/hr.

Sheep and Goats

• 100-mcg/hr patch. (Absorption has been inconsistent.)

Regulatory Information

Schedule II controlled drug by DEA.

Fentanyl should not be administered to animals that produce food. Withdrawal times are not established.

Ferrous Sulfate

fare'us sul'fate

Trade and Other Names: Ferospace and generic brands (OTC)

Functional Classification: Mineral supplement, iron supplement

Pharmacology and Mechanism of Action

Iron supplement. Replaces iron in animals that are deficient or with iron-deficiency anemia.

Indications and Clinical Uses

Iron supplements are indicated in patients with diseases caused by iron deficiency.

Precautionary Information

Adverse Reactions and Side Effects

High doses cause stomach ulceration. Feces become dark with oral administration.

Contraindications and Precautions

Do not use in animals prone to gastric ulcers. High doses or accidental ingestion may cause severe ulcers and perforation and should be treated as an emergency.

Drug Interactions

Iron supplements will interfere with oral absorption of other drugs such as fluoroquinolones, tetracyclines, and other drugs that may chelate with iron. Cimetidine and other antacids will decrease oral absorption because an acid environment favors absorption.

Instructions for Use

Recommendations based on dose needed to increase hematocrit. In some animals, injectable Iron Dextran is used instead of oral therapy.

Patient Monitoring and Laboratory Tests

Monitor hematocrit, serum iron levels, and total iron-binding capacity.

Formulations

OTC oral formulations are available; 250 mg ferrous sulfate contains 50 mg elemental iron. Injectable forms are usually Iron Dextran. (Iron Dextran is listed in a separate monograph.)

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with other drugs because chelation may occur. Ferrous sulfate is soluble in water.

Small Animal Dosage

Dogs

- 100-300 mg/dog q24h PO.

Cats

- 50-100 mg/cat q24h PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Extralabel withdrawal times are not established. However, 24-hour withdrawal times are suggested because this drug has little risk from residues.

Finasteride

fin-ass'ter-ide

Trade and Other Names: Proscar

Functional Classification: Hormone antagonist

Pharmacology and Mechanism of Action

Finasteride is a synthetic steroid type-II 5 alpha reductase inhibitor. It inhibits conversion of testosterone to dihydrotestosterone (DHT).

Indications and Clinical Uses

Because DHT stimulates prostate growth, finasteride has been used for benign prostatic hypertrophy (BPH). In dogs with BPH, finasteride has been shown to reduce prostatic size without adversely affecting testosterone production or semen quality.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects reported in dogs.

Contraindications and Precautions

Finasteride is contraindicated in pregnant animals.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Doses are based on clinical studies in dogs and information for other animals has not been reported. One study in dogs found significant effects at 0.1 mg/kg q24h. Another study used a dose range of 0.1 to 0.5 mg/kg q24h and reported reduction in prostate size.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Finasteride is available in 5-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

- 0.1 mg/kg q24h PO.
- Dogs 10-50 kg: 5-mg tablet q24h PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No withdrawal times are established. Do not use in animals intended for food.

Firocoxib

feer-oh-koks'ib

Trade and Other Names: Previcox and Equioxx

Functional Classification: Anti-inflammatory

Pharmacology and Mechanism of Action

Firocoxib is a nonsteroidal anti-inflammatory drug (NSAID). Like other drugs in this class, firocoxib produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the cyclooxygenase (COX) enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known whether there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Firocoxib, using in vitro assays, is more COX-1 sparing compared to older NSAIDs and is a selective inhibitor of COX-2. The COX-1/COX-2 ratio is greater than for other drugs, indicating that firocoxib is a selective COX-2 inhibitor in dogs, horses, and cats. It has not been established if the specificity for COX-1 or COX-2 is related to efficacy or safety. Firocoxib has a half-life of 7.8 hours in dogs, 9-12 hours in cats, and 30-40 hours in horses. It is highly protein bound (96%-98%). Oral absorption is 38% in dogs, 79% in horses, and 54%-70% in cats. Feeding delays absorption but does not diminish overall absorption. In horses, oral absorption is 79%, with oral paste at a dose of 0.1 mg/kg.

Indications and Clinical Uses

Firocoxib is used to decrease pain, inflammation, and fever. It has been used for the acute and chronic treatment of pain and inflammation in dogs. One of the most common uses is osteoarthritis, but it also has been used for pain associated with surgery. In horses it is used for osteoarthritis. In cats, firocoxib has been demonstrated to be effective for attenuating acute febrile responses. Use in cats is limited to short-term use or long-term use at low doses.

Precautionary Information

Adverse Reactions and Side Effects

GI problems are the most common adverse events associated with NSAIDs and can include vomiting, diarrhea, nausea, ulcers, and erosions of the GI tract. Both acute and long-term safety and efficacy have been established for dogs. In field trials, vomiting was the most often reported adverse effect. In studies performed in dogs, higher doses (five times dose) caused GI problems. In horses, mucosal recovery after intestinal ischemia was less than other non-selective NSAIDs. In studies of young juvenile dogs, administration of firocoxib was associated with periportal fatty hepatic changes in some animals. Renal toxicity, especially in dehydrated animals or animals with preexisting renal disease, has been observed for some NSAIDs. Behavior changes have occurred in dogs and horses, but they are rare.

In horses, gastrointestinal problems (diarrhea, loose stool) have been reported in field trials, but they are rare at approved doses. At doses exceeding labeled dose or duration in horses, ulcers, azotemia, renal injury, erosions of skin and oral mucosa, and prolonged bleeding times have been observed.

Contraindications and Precautions

Dogs and cats with preexisting GI problems or renal problems may be at a greater risk of adverse effects from NSAIDs. There is no information on the safety of firocoxib in the treatment of breeding, pregnant, or lactating animals, but adverse effects have not been reported in breeding animals.

In horses, do not exceed recommended duration of treatment. During animal safety studies in horses, toxicity occurred at recommended doses if administration exceeded 30 days.

Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors.

Instructions for Use

Use according to manufacturer's dosing guidelines. Chewable tablets can be administered with or without food. Long-term studies have not been completed in cats, and only single-dose studies have been reported.

Patient Monitoring and Laboratory Tests

Monitor GI signs for evidence of diarrhea, GI bleeding, or ulcers. Because of risk of renal injury, monitor renal parameters (water consumption, BUN, creatinine, and urine-specific gravity) periodically during treatment.

Formulations

Firocoxib is available in 57- and 227-mg tablets. Equine oral paste is available as 8.2 mg/g of paste (0.82% w/w).

314 Florfenicol

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 5 mg/kg once daily PO.

Cats

- 1.5 mg/kg once. Long-term safety in cats has not been determined.

Large Animal Dosage

Horses

- 0.1 mg/kg q24h, PO for up to 14 days.

Regulatory Information

Do not administer to animals that produce food. Do not administer to horses that are used for human consumption.

In racing horses, it is not permitted to be used 12 hours prior to competition.

Florfenicol

flore-fen'ih-kole

Trade and Other Names: Nuflor, Nuflor Gold, Resflor (flunixin and florfenicol) Aquaflor (fish form)

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Florfenicol is a thiamphenicol derivative with the same mechanism of action as chloramphenicol (inhibition of protein synthesis). However, it is more active than either chloramphenicol or thiamphenicol. Florfenicol has a broad spectrum of antibacterial activity that includes all organisms sensitive to chloramphenicol, gram-negative bacilli, gram-positive cocci, and other atypical bacteria such as mycoplasma. Florfenicol is highly lipophilic, which provides high enough concentrations to treat intracellular pathogens and cross some anatomical barriers (penetration across the blood–brain barrier in cattle is 46%). The half-life of florfenicol is 2–3 hours in cattle after IV administration, but it is prolonged (18 hours) after IM injection. In dogs the half-life is shorter, with values of 1.1 and 1.2 after IV and oral administration, respectively. The half-life in cats is approximately 4 hours and 7.8 hours after IV and oral administration, respectively.

Indications and Clinical Uses

Because florfenicol is a derivative of chloramphenicol, it has been used in situations in which chloramphenicol is unavailable or illegal. (Chloramphenicol is illegal to use in food animals in the United States.) Florfenicol has been shown to be effective for treatment of bovine respiratory disease (BRD) in cattle associated with *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni* (formerly *Haemophilus somnus*). Administration of florfenicol (40 mg/kg once SQ) at time of arrival to the feedlot decreased the incidence of BRD. It also is used for treatment of bovine interdigital phlegmon (foot rot, acute interdigital necrobacillosis, and infectious

pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus* and for treatment of infectious bovine keratoconjunctivitis caused by *Moraxella bovis*. ResflorGold contains both florfenicol and flunixin. It is used for the same Bovine Respiratory Disease pathogens and provides anti-inflammatory activity with the addition of flunixin meglumine, including BRD-associated pyrexia in beef and non-lactating dairy cattle.

In pigs it is used for treatment of swine respiratory disease (SRD) caused by *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Salmonella choleraesuis*, and *Streptococcus suis*. In cats, effective concentrations can be achieved with twice-daily administration. In dogs, the half-life is short and frequent administration is necessary to produce effective concentrations. Florfenicol also has been administered to fish. There is a feed-additive formulation that also has been approved for catfish (10 mg/kg).

Precautionary Information

Adverse Reactions and Side Effects

Use in dogs and cats has been limited; therefore, adverse effects have not been reported. Chloramphenicol has been linked to dose-dependent bone marrow depression and similar reactions may be possible with florfenicol. However, there does not appear to be a risk of aplastic anemia as for chloramphenicol. At high doses, florfenicol may cause testicular degeneration. In horses, doses of 20 mg/kg q48h IM changed the bacterial flora and increased risk of diarrhea.

Contraindications and Precautions

Long-term use in animals may cause bone marrow suppression. Administration to horses has caused diarrhea, colitis, and elevations in bilirubin. Administration to horses is not recommended. Do not administer more than 10 mL in a single site.

Drug Interactions

No drug interactions are reported for animals. However, chloramphenicol is well known to inhibit cytochrome P450 enzymes and decrease metabolism of other drugs (see Appendix). Therefore, it is possible, but not documented, that florfenicol could cause drug interactions.

Instructions for Use

Dose form is only approved for use in cattle and pigs, and doses listed have not been thoroughly evaluated in small animals. Doses listed are derived from pharmacokinetic studies. Sustained effect in cattle from intramuscular and subcutaneous administration does not appear to be long lasting in dogs. Injectable formulation for cattle has been administered, if necessary, orally to small animals, but the taste is bitter.

Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow depression. Susceptibility testing: laboratories have used chloramphenicol to test for susceptibility to florfenicol. CLSI break points for sensitive organisms are ≤ 4 mcg/mL for streptococci and ≤ 8 mcg/mL for other organisms.

Formulations

Florfenicol is available in 300-mg/mL injectable solution (cattle), or 23-mg/mL solution to be added to drinking water for pigs (400 mg per gallon). Medicated feed formulation contains 500 g/kg to be added to fish feed. Flunixin is combined with florfenicol in Resflor Gold, which has 300 mg florfenicol and 16.5 mg flunixin per mL with vehicles of 2-pyrrolidone, 35 mg malic acid, and triacetin.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Light yellow or straw color does not affect potency. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 20 mg/kg q6h IM or PO.

Cats

- 22 mg/kg q8h IM or PO.

Large Animal Dosage

Cattle, BRD

- 20 mg/kg q48h SQ or IM (in the neck).
- 40 mg/kg SQ as a single injection (Nufloor Gold), or q72h SQ in the neck region (also combined with flunixin meglumine at 2.2 mg/kg, and Nufloor Gold at 40 mg/kg).

Horses

Although florfenicol has been administered, some references cite adverse effects after administration. Until more safety data become available, it is suggested to avoid use of florfenicol in horses.

Pigs

- 15 mg/kg IM in the neck q48h.
- Administer in drinking water at 400 mg per gallon (100 parts per million) for 5 consecutive days.

Regulatory Information

Cattle withdrawal time (meat): 28 days if administered IM; 38 days if administered SQ. Nufloor Gold withdrawal time (40 mg/kg SQ) is 44 days.

A withdrawal period has not been established in preruminating calves.

Do not use in calves to be processed for veal; not to be used in dairy cattle 20 months of age or older or in veal calves younger than 1 month.

Pig withdrawal time: 16 days after last treatment when administered in water; 13 days after last treatment when administered with feed.

Fluconazole

floo-kahn'ah-zole

Trade and Other Names: Diflucan and generic brands

Functional Classification: Antifungal

Pharmacology and Mechanism of Action

Azole antifungal drug. Fungistatic. Fluconazole inhibits ergosterol synthesis in fungal cell membrane and has activity against dermatophytes, systemic fungi, and yeasts, including *Candida*, *Coccidioides*, and *Cryptococcus* spp.. However, it has weak activity against molds such as *Aspergillus* or *Zygomycetes*. Compared to other oral azole antifungals, fluconazole is absorbed more predictably and completely, even on an empty stomach. The half-life in dogs, cats, and horses is approximately 14-15, 13-25, and 38 hours, respectively.

Indications and Clinical Uses

Fluconazole is effective against dermatophytes, yeasts, and a variety of systemic fungi. In dogs, cats, horses, and exotic animals, it is used to treat systemic fungal infections,

yeast infections, and dermatophytes, including *Malassezia* dermatitis. In cats it has been used to treat *Cryptococcus*. In dogs, it is not as active against coccidioidomycosis as other azole antifungal drugs, but it has been effective in some patients. Higher doses may be needed (e.g., 10 mg/kg q12h) for coccidioidomycosis. Because it is water soluble, it has been used to treat fungal cystitis.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported from fluconazole administration. Compared to ketoconazole, it has less effect on endocrine function. However, increased liver enzyme concentrations and hepatopathy are possible.

Contraindications and Precautions

Use cautiously in pregnant animals. At high doses in laboratory animals, it has caused fetal abnormalities.

Drug Interactions

Fluconazole can be an inhibitor of cytochrome P450 enzymes, which can increase other drug concentrations. It will cause an increase in cyclosporine concentrations in dogs. It may also cause other reactions as a result of inhibition of metabolizing enzymes.

Instructions for Use

Doses for fluconazole are primarily based on studies performed in cats for treatment of cryptococcosis. Efficacy for other infections has not been reported. The primary difference between fluconazole and other azoles is that fluconazole attains higher concentrations in the CNS. Oral absorption of fluconazole is more predictable than itraconazole and ketoconazole and less affected by fasting.

Patient Monitoring and Laboratory Tests

Monitor hepatic enzymes periodically in treated animals. Susceptibility testing is possible, but ranges are only established for *Candida*.

Formulations

Fluconazole is available in 50-, 100-, 150-, and 200-mg tablets, 10- and 40-mg/mL oral suspension, and 2-mg/mL intravenous injection.

Stability and Storage

Fluconazole is stable for 14 days after reconstituting oral suspension. Because it is water soluble at a concentration of 8-10 mg/mL, it also may be compounded in formulations for administration to small animals. However, long-term stability, beyond 15 days, of compounded formulations has not been determined.

Small Animal Dosage

Dogs

- 5 mg/kg q12h, PO. In refractory cases increase dose to 10 mg/kg q12h, PO.
- *Malassezia* treatment: 5 mg/kg q12h PO.

Cats

- 50 mg/cat per once daily PO, or in refractory cases increase to 50 mg per cat q12h, PO. In most cases it is administered once daily.

Large Animal Dosage

Horses

- 5 mg/kg q24h PO.

Regulatory Information

No withdrawal times are established for animals intended for food (extralabel use).

Flucytosine

floo-sye'toe-seen

Trade and Other Names: Ancobon

Functional Classification: Antifungal

Pharmacology and Mechanism of Action

Antifungal drug. Action is to penetrate fungal cells and is converted to fluorouracil, which acts as antimetabolite.

Indications and Clinical Uses

Flucytosine is an antifungal drug that has been limited in veterinary medicine to treat cryptococcal meningitis. It should be used in combination with amphotericin B (but not azole antifungal drugs) for treatment of cryptococcosis to improve efficacy and decrease resistance.

Precautionary Information

Adverse Reactions and Side Effects

Anemia and thrombocytopenia are the most common adverse effects.

Contraindications and Precautions

No specific contraindications have been identified for animals.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Flucytosine is used primarily to treat cryptococcosis in animals. Efficacy is based on its ability to attain high concentrations in cerebrospinal fluid (CSF). Flucytosine may be synergistic with amphotericin B.

Patient Monitoring and Laboratory Tests

Monitor CBC during treatment.

Formulations Available

Flucytosine is available in 250- and 500-mg capsules and 75-mg/mL oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Compounded oral suspensions have been stable for 60 days.

Small Animal Dosage

Dogs and Cats

- 25-50 mg/kg q6-8h PO, up to a maximum dose of 100 mg/kg q12h PO.
- Cryptococcal meningitis: 20-40 mg/kg q6h PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No withdrawal times are established for animals that are intended for food (extralabel use).

Fludrocortisone Acetate

floo-droe-kor'tih-sone ass'ih-tate

Trade and Other Names: Florinef

Functional Classification: Corticosteroid

F

Pharmacology and Mechanism of Action

Mineralocorticoid replacement therapy. Fludrocortisone has high potency of mineralocorticoid activity compared to glucocorticoid activity. Fludrocortisone acts to mimic the action of aldosterone in the body, specifically to increase reabsorption of sodium in renal tubules.

Indications and Clinical Uses

Fludrocortisone is used as replacement therapy in animals with adrenocortical insufficiency (Addison's disease). Because of its glucocorticosteroid activity, some animals may not require additional supplementation with glucocorticoids when administering fludrocortisone. Desoxycorticosterone pivalate (DOCP) is used as an alternative in dogs when an intermittent injectable is desired rather than daily oral doses of fludrocortisone.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are primarily related to glucocorticoid effects with high doses. Polyuria/polydipsia may occur in some animals. Long-term treatment for hypoadrenocorticism may result in glucocorticoid side effects. Administration of fludrocortisone causes a significant reduction in urine aldosterone.

Contraindications and Precautions

Although used as a mineralocorticoid, it may produce glucocorticoid side effects. Use cautiously in animals that may be at risk for corticosteroid side effects.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Dose should be adjusted by monitoring patient response (i.e., monitoring electrolyte concentrations). In some patients, it is administered with a glucocorticoid and sodium supplementation (e.g., prednisolone/prednisone at a dose of 0.2-0.3 mg/kg/day).

Patient Monitoring and Laboratory Tests

Monitor patient's electrolytes (especially sodium and potassium). Dose adjustment should be based on electrolyte monitoring to maintain these within a desired range.

Formulations

Fludrocortisone is available in 100-mcg (0.1-mg) tablets.

320 Flumazenil

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is insoluble in water. When crushed tablets were prepared in various suspensions, they were stable for 14 days.

Small Animal Dosage

Dogs

15-30 mcg/kg/day (0.015-0.03 mg/kg) PO.

Cats

- 0.1-0.2 mg/cat q24h PO. To test for primary aldosteronism, administer 0.05 mg/kg q12h, × 4 days.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Extralabel withdrawal times are not established. However, 24-hour withdrawal times are suggested because this drug has little risk from residues.

RCI Classification: 4

Flumazenil

floo-may'zeh-nil

Trade and Other Names: Romazicon

Functional Classification: Antidote

Pharmacology and Mechanism of Action

Benzodiazepine receptor antagonist. Flumazenil blocks the action of benzodiazepines, such as diazepam, from the action on the GABA receptor.

Indications and Clinical Uses

Flumazenil has no therapeutic benefits of its own, but it is used as a reversal agent after benzodiazepine administration in people (not commonly used in veterinary medicine). Because of high first-pass effects, it cannot be administered orally; it must be injected.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects reported in animals.

Contraindications and Precautions

Flumazenil may precipitate a seizure if used with tricyclic antidepressants (TCAs) or other drugs that can lower seizure threshold.

Drug Interactions

Flumazenil may increase risk of seizures when used with other drugs known to inhibit the inhibitory neurotransmitter GABA.

Instructions for Use

Flumazenil is used primarily to block effects of benzodiazepine drugs. It has been used to reverse overdoses of benzodiazepines (e.g., diazepam). Although it has been used experimentally for treating hepatic encephalopathy, its efficacy for this condition is not established.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Flumazenil is available in a 100-mcg/mL (0.1 mg/mL) injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 0.02 mg/kg (20 mcg/kg) IV.
- To reverse benzodiazepines: 0.2 mg (total dose), as needed, IV.

Large Animal Dosage

Horses, Cattle, Swine, and Sheep

To reverse benzodiazepines: 20 mcg/kg IV (0.02 mg/kg).

Regulatory Information

Do not use in animals intended for food.

Flumethasone

floo-meth'ah-sonē

Trade and Other Names: Flucort

Functional Classification: Corticosteroid

Pharmacology and Mechanism of Action

Potent glucocorticoid anti-inflammatory drug. Potency is listed by one reference as approximately 15 times that of cortisol and in veterinary references as 30 times that of cortisol and 6 to 7 times the potency of prednisolone. Anti-inflammatory effects are complex but primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. Use is for treatment of inflammatory and immune-mediated disease.

Indications and Clinical Uses

Flumethasone, like other corticosteroids, is used to treat a variety of inflammatory and immune-mediated diseases. The dosing section contains the range of doses for replacement therapy, anti-inflammatory therapy, and immunosuppressive therapy. Flumethasone is used more often in large animals than small animals. Large-animal uses include treatment of inflammatory conditions, especially musculoskeletal disorders. In horses, flumethasone has been used for treatment of recurrent airway obstruction (RAO, formerly called chronic obstructive pulmonary disease [COPD]). In cattle, corticosteroids have been used in the treatment of ketosis.

Precautionary Information

Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic–pituitary–adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, and delayed wound healing and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and UTIs. In horses, additional adverse effects include risk of laminitis.

Contraindications and Precautions

Use cautiously in patients prone to ulcers or infection and in animals in which wound healing is necessary. Use cautiously in animals with renal failure or diabetes and in pregnant animals.

Drug Interactions

Administration of corticosteroids with nonsteroidal anti-inflammatory drugs (NSAIDs) will increase the risk of GI injury.

Instructions for Use

Doses are based on severity of underlying disease. For example, anti-inflammatory conditions require lower doses than immune-mediated conditions. For all conditions, cats often require higher doses than dogs. Note that the approved label dose for cattle and horses is in the range of 1.25 to 5 mg per animal or approximately 0.003–0.006 mg/kg (3–6 mcg/kg) for an adult animal. Considering that the potency of flumethasone may be similar to dexamethasone, many experts feel that the dose should be higher, in the range of 0.04–0.15 mg/kg.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an adrenocorticotropic hormone (ACTH) stimulation test to monitor adrenal function.

Formulations

Flumethasone is available in a 0.5-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- Anti-inflammatory uses: 0.15–0.3 mg/kg q12–24h IV, IM, or SQ.

Large Animal Dosage

Horses

- 1.25–2.5 mg per animal, as a single dose, IM or IV (approximately 0.003–0.006 mg/kg). This is the dose frequently listed on the product label. However, many experts prefer doses of 0.04–0.15 mg/kg, as a single dose IV or IM.

Cattle

- 1.25–5 mg/animal as a single dose IV or IM. This is the dose frequently listed on the product label. However, many experts prefer doses of 0.04–0.15 mg/kg, as a single dose IV or IM.

Regulatory Information

There are no US withdrawal times established.

In Canada, cattle withdrawal time (meat): 4 days.

RCI Classification: 4

Flunixin Meglumine

floo-nix'in meg'loo-meen

Trade and Other Names: Banamine and generic brands

Functional Classification: Nonsteroidal anti-inflammatory drug (NSAID)

F

Pharmacology and Mechanism of Action

Flunixin is an NSAID. Flunixin and other NSAIDs produce analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the cyclo-oxygenase (COX) enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known whether there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Flunixin is not selective for either COX-1 or COX-2. Other anti-inflammatory effects may occur (such as effects on leukocytes) but have not been well characterized. In horses, the half-life is 2 hours, oral absorption of paste is 77%, and absorption of granules is 85%. However, access to hay will delay peak concentrations and oral absorption from granules and paste mixed with feed may be more erratic. In cattle the half-life is 3-4 hours IV, but it is longer when administered IM. Oral absorption in cattle is 60%.

Indications and Clinical Uses

Flunixin is used primarily for short-term treatment of moderate pain and inflammation. It has been used to treat abdominal pain in horses, to decrease signs of sepsis in horses, and to decrease clinical signs associated with coliform mastitis in cattle. In horses, as an adjunctive treatment for sepsis, it is used at a low dose of 0.25 mg/kg. It has been used as an adjunctive treatment, with antibiotics, for treatment of bovine respiratory disease (BRD). Flunixin has been combined with antibiotics for treatment of BRD (e.g., florfenicol in Resflor) in which it reduces inflammatory lung reactions. Flunixin has been used as a single dose for treatment of diarrhea in dairy calves. Flunixin at 2.2 mg/kg IV in cows with endotoxin mastitis did not affect milk production, but it decreased fever and improved rumen motility. ResflorGold contains both florfenicol and flunixin. It is used for the same Bovine Respiratory Disease pathogens and provides anti-inflammatory activity with the addition of flunixin meglumine, including BRD-associated pyrexia in beef and non-lactating dairy cattle.

In pigs it is used for pyrexia associated with swine respiratory disease.

In dogs and cats it has been used occasionally, but treatment is usually confined to one or two treatments because of risk of gastrointestinal toxicity (ulcers and perforation).

Precautionary Information

Adverse Reactions and Side Effects

Most severe adverse effects are related to the GI system. Flunixin causes gastritis and GI ulceration with high doses or prolonged use. In horses, flunixin administration may affect recovery after ischemic injury to the intestine. Reduced renal perfusion has also been documented. Therapy in dogs should be limited to 4 consecutive days. In horses, if given IM it can result in myositis and abscess at the injection site.

Contraindications and Precautions

Avoid use in pregnant animals near term. Do not use in calves to be processed for veal. Do not use in bulls intended for breeding because reproductive effects in this class of cattle have not been studied. Flunixin is approved for IV treatment in some food animals, but if the dose is administered IM or SQ, there is an increased risk of meat residues.

Drug Interactions

Ulcerogenic effects are potentiated when administered with corticosteroids. Coadministration with phenylbutazone will increase the risk of hypoproteinemia and gastric ulcers in horses. Flunixin, like other NSAIDs, may interfere with the action of diuretics such as furosemide and angiotensin-converting enzyme (ACE) inhibitors.

Coadministration with enrofloxacin in dogs increased flunixin plasma concentrations because of reduced clearance.

Instructions for Use

Flunixin is not approved for small animals but has been shown in experimental studies to be an effective prostaglandin synthesis inhibitor. It is approved for use in small animals in Europe.

Patient Monitoring and Laboratory Tests

Monitor for signs of GI bleeding and ulcers during treatment.

Formulations

Flunixin is available in 250-mg packet granules in a 10-g packet and 10- and 50-mg/mL injection. It is also available as a paste, and each 30-g syringe contains flunixin meglumine equivalent to 1500 milligrams of flunixin. Flunixin is combined with florfenicol in Resflor Gold, which has 300 mg florfenicol and 16.5 mg flunixin per mL with vehicles of 2-pyrrolidone, 35 mg malic acid, and triacetin.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 1.1 mg/kg once IV, IM, or SQ.
- 1.1 mg/kg/day 3 day/week PO.
- Ophthalmic: 0.5 mg/kg once IV.

Large Animal Dosage

Horses

- 1.1 mg/kg q24h for up to 5 days IV or IM. Note: In foals it has been shown that doses as low as 0.25 mg/kg inhibit prostaglandin synthesis during sepsis. Horses with colic are often treated with low doses of 0.25 mg/kg IV q8h.
- Paste: 1.1 mg/kg q24h PO.
- Granules: 1.1 mg/kg/day PO (one packet per 500 pounds).

Cattle

- 1.1 to 2.2 mg/kg (slowly) once a day for up to 3 days IV.
- In combination with florfenicol (Resflor Gold): 40 mg/kg florfenicol and 2.2 mg/kg flunixin administered SQ.

Pigs

- 2.2 mg/kg, once IM.

Regulatory Information

Cattle withdrawal time: 4 days meat and 36 hours milk. Risk of residues is higher if dose is administered IM or SQ, and the withdrawal time should be extended to at least 30 days for meat and 72 hours for milk if this route is used. If administered orally in cattle, the meat withdrawal time should be at least 8 days and the milk withdrawal time should be 48 hours.

Pig withdrawal time: 12 days.

RCI Classification: 4

Fluorouracil

floo-roe-yoo'rah-sil

Trade and Other Names: 5-Fluorouracil, Adrucil

Functional Classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Antimetabolite. Action is via inhibition with nucleic acid synthesis. Fluorouracil is used in anticancer protocols.

Indications and Clinical Uses

Fluorouracil is used in cancer protocols used in dogs. It has been used as a component with other combination cancer regimens.

Precautionary Information

Adverse Reactions and Side Effects

Fluorouracil causes mild leukopenia, thrombocytopenia, and CNS toxicity.

Contraindications and Precautions

Do not use in cats.

Drug Interactions

No drug interactions are reported for animals.

326 Fluoxetine Hydrochloride

Instructions for Use

Consult anticancer treatment protocol for precise dosage and regimen.

Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow toxicity.

Formulations

Fluorouracil is available in a 50-mg/mL vial.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 150 mg/m² once/week IV.

Cats

- Do not use.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in food animals because it is an anticancer agent.

Fluoxetine Hydrochloride

floo-oks'eh-teen hye-droe-klor'ide

Trade and Other Names: Prozac (human formulation); Reconcile (veterinary formulation)

Functional Classification: Behavior modification, SSRI

Pharmacology and Mechanism of Action

Antidepressant drug. Fluoxetine, like other drugs in this class, is classified as a selective serotonin reuptake inhibitor (SSRI). Its mechanism of action appears to be via selective inhibition of serotonin reuptake and downregulation of 5-HT₁ receptors. SSRIs are more selective for inhibiting serotonin reuptake than the tricyclic antidepressant (TCA) drugs. Fluoxetine is metabolized to norfluoxetine, which is an active metabolite. Oral absorption in dogs is 72% with a half-life of 6-10 hours. The metabolite norfluoxetine has a longer half-life of 48-57 hours. In cats, oral absorption is 100% with a half-life of 34-47 hours; the metabolite norfluoxetine has a half-life of 51-55 hours. Absorption in cats from transdermal administration is only 10%. Another SSRI used in animals is paroxetine (Paxil).

Indications and Clinical Uses

Fluoxetine, like other SSRIs, is used to treat behavioral disorders such as separation anxiety, canine compulsive behaviors, and dominance aggression. In cats, it has been effective for decreasing urine spraying (1 mg/kg/day). In trials comparing fluoxetine with clomipramine for treating urine marking in cats, both drugs were equally effective for long-term use. In both dogs and cats SSRI have been used for pain syndromes, but there are no studies of efficacy published for this indication. However, the urine marking returned after discontinuation of the drug.

In horses, fluoxetine has been used for “cribbing behavior” and other behavior disorders.

Precautionary Information

Adverse Reactions and Side Effects

Fluoxetine has fewer adverse effects (especially antihistamine and antimuscarinic effects) compared to other antidepressant drugs. The most common reaction in clinical trials was lethargy and decreased appetite. During clinical trials in dogs adverse reactions included vomiting, lethargy, depression, trembling, and shaking in some dogs. In rare cases it may cause seizures. In dogs, at high doses of 10-20 mg/kg it caused tremors, anorexia, aggressive behavior, nystagmus, emesis, and ataxia. Occasionally some of these signs may be seen at lower doses. In cats, nervousness or increased anxiousness has been observed. However, in trials used for treating urine spraying, few adverse effects were reported. In cats 5 mg/kg produced tremors and 3 mg/kg produced anorexia and vomiting. However, cats have tolerated doses up to 50 mg/kg.

Contraindications and Precautions

Use cautiously in animals prone to aggression because it may decrease inhibition. In early pregnancy it appears to be safe but has caused pulmonary hypertension in experimental animals late in pregnancy.

Drug Interactions

Do not use with other behavior-modifying drugs such as other SSRIs or TCAs. Do not use with monoamine oxidase inhibitors (MAOIs). Administration with selegiline may induce a reaction. Because it is highly metabolized by the liver, it may be subject to interactions caused by cytochrome P450 inhibitors.

Instructions for Use

Always use in conjunction with comprehensive behavior modification protocol. Clinical efficacy of fluoxetine for separation anxiety in dogs has been established from clinical studies. Because of long half-life, accumulation in plasma may take several days to weeks. There may be a delay in the onset of action of 2 weeks.

In some animals, paroxetine (Paxil) is preferred, which is available in tablets and has been used for smaller-size animals. Do not use transdermally; absorption is low.

Patient Monitoring and Laboratory Tests

Use in animals has been relatively safe, and one should only monitor behavior changes.

Formulations

Fluoxetine is available in veterinary formulations of 8-, 16-, 32-, and 64-mg tablets and in human formulations of 10-, 20-, and 40-mg capsules, 10-mg tablets, and 4-mg/mL oral solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water at 14 mg/mL and in alcohol at 100 mg/mL. Fluoxetine hydrochloride solution has been mixed with various juices, and flavorings and found to be stable for 8 weeks. In one trial it was mixed in tuna-flavored water for cats and retained effectiveness.

Small Animal Dosage

Dogs

- 1-2 mg/kg, once daily, PO.

Cats

- 0.5-4 mg/cat q24h PO (0.5-1 mg/kg per day). Start with 1/4 tablet (2.5 mg) per cat.
- Urine marking: 1 mg/kg q24h PO and increase to 1.5 mg/kg if there has been inadequate response.

Large Animal Dosage

- Horses: 0.25-0.5 mg/kg PO once daily, mixed with grain.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 2

Fluticasone Propionate

(floo-tik'ah-sone proe-pee-oe-nayt)

Trade and Other Names: Flovent

Functional Classification: Corticosteroid

Pharmacology and Mechanism of Action

Potent glucocorticoid anti-inflammatory drug with potency of 18 times that of desamethasone. In patients with inflammatory airway diseases, glucocorticoids have potent anti-inflammatory effects on the bronchial mucosa. Glucocorticoids bind to receptors on cells and inhibit the transcription of genes for the production of mediators (cytokines, chemokines, adhesion molecules) involved in airway inflammation. A decrease in the synthesis of inflammatory mediators such as prostaglandins, leukotrienes, and platelet-activating factor caused by glucocorticoids also may be important. Glucocorticoids also play a role in enhancing the action of adrenergic agonists on beta-2 receptors in the bronchial smooth muscle, either by modifying the receptor or augmenting muscle relaxation after a receptor has been bound. Corticosteroids also may prevent downregulation of beta-2 receptors. Topical (inhaled) corticosteroids such as fluticasone or budesonide are used to avoid systemic effects. They typically have high first-pass effects and low systemic exposure if swallowed. Because of low systemic effects, fluticasone produces less systemic steroid effects than prednisolone, such as effects on water consumption, appetite, and systemic immunity.

Indications and Clinical Uses

Fluticasone is used as an inhaled (topical) corticosteroid for treatment of airway disease. Most of the use has been established for cats, but it also could be used for dogs, horses, or other animals in which a special adapter can be used to deliver the drug via a metered-dose inhaler. In dogs and cats the most common use is for inflammatory airway diseases such as asthma, bronchitis, or bronchospasm. For example, if a cat is given 2 puffs twice a day of a potent inhaled corticosteroid (e.g., budesonide, fluticasone) and allowed 5-7 breaths (10 sec) from a chamber (spacer), it may reduce the need for oral prednisolone in cats with feline asthma. When doses were compared in experimental cats, the low dose of 44 mcg twice daily was as effective as 110 or 220 mcg twice daily.

In horses the most common use is for recurrent airway obstruction (RAO), formerly called chronic obstructive pulmonary disease (COPD).

Precautionary Information

Adverse Reactions and Side Effects

Although fluticasone systemic absorption is low, some systemic exposure will occur in animals. Side effects can occur but are not expected to be as severe as with systemic corticosteroids. Adrenal suppression is expected to occur in treated animals (suppressed ACTH response) but may recover once treatment is discontinued.

Contraindications and Precautions

Use cautiously in patients with oral or respiratory tract infections because immunosuppression may occur.

Drug Interactions

Some systemic effects are possible but minimal. Administration of corticosteroids with nonsteroidal anti-inflammatory drugs (NSAIDs) will increase the risk of GI injury.

F

Instructions for Use

The use is based on administration of fluticasone for treatment of airway diseases. It is delivered via a metered-dose inhaler. These inhalers can be used in animals if special adaptations, such as a spacer device, which are available for use in pediatrics or for cats and horses, are used. When treating dogs and cats, doses listed in the dosing section can be used initially, then adjusted depending on response.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform adrenocorticotropic hormone (ACTH) stimulation test to monitor adrenal function. Fluticasone, although minimally absorbed systemically, will suppress the ACTH response.

Formulations

Metered-dose inhaler at 44, 110, or 220 mcg per puff.

Stability and Storage

Store in original container (metered-dose inhaler). Do not puncture container or attempt to remove drug from pressurized container. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

Start with 220 mcg per dose, q12h.

Cats

Start with 44 mcg per dose (one puff from a 44 mcg inhaler), twice daily. Increase the dose as needed, to 110 mcg, then to 220 mcg.

Horses

1300-2600 mcg per horse (6-12 puffs from 220 mcg inhaler) twice daily.

Regulatory Information

There are no US withdrawal times established.

RCI Classification: not established.

Fomepizole

foh-meh'pih-zole

Trade and Other Names: 4-Methylpyrazole, Antizol-Vet, and Antizole (human preparation)

Functional Classification: Antidote

Pharmacology and Mechanism of Action

Fomepizole is an antidote for ethylene glycol (antifreeze) and methanol intoxication. It inhibits the dehydrogenase enzyme that converts ethylene glycol to toxic metabolites.

Indications and Clinical Uses

Fomepizole is used for treatment of acute ethylene glycol toxicosis in dogs and cats. In people, it is used for this purpose but also is registered for methanol poisoning. It should be used early for maximum success. Fomepizole was safe and effective in dogs in clinical trials if used within 8 hours of poisoning. In cats, it is effective if administered at high doses within 3 hours of ethylene glycol ingestion.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects have been reported.

Contraindications and Precautions

Treatment should be initiated early for optimum effect. In cats, treatment should be initiated within 3 hours, using a dose that is higher than for dogs.

Drug Interactions

Fomepizole will inhibit the metabolism of other drugs and compounds that share a similar pathway as alcohol. Use cautiously with any other coadministered drugs.

Instructions for Use

The only use documented is for emergency management of ethylene glycol intoxication. Experimental studies have demonstrated effectiveness in dogs and cats (high doses in cats). In cats administration of ethanol infusion is also effective. Administer 0.9% sodium chloride before administration of fomepizole. If used for treating methanol intoxication, include administration of folinic acid (Leukovorin) at a dose of 1 mg/kg.

Patient Monitoring and Laboratory Tests

Monitor renal function during treatment. Monitor urine output.

Formulations

Fomepizole is available in a 5% solution in a 1.5-mL vial (Antizol-Vet) and 1-g/mL solution (Antizol), a human preparation. 1.5 g may be added to 30 mL saline solution for injection (50 mg/mL).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 20 mg/kg initially IV, then 15 mg/kg at 12- and 24-hour intervals, then 5 mg at 36 hours.

Cats

- 125 mg/kg initially, followed by 31.3 mg/kg at 12, 24, and 36 hours after the initial dose. Continue doses every 12 hours until ethylene glycol is no longer detected. If analysis of ethylene glycol is not available, treat with 31 mg/kg every 12 hours through 60 hours.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No withdrawal times are established for animals intended for food. There is little risk of residues in food animals.

Fosfomycin tromethamine

fos-foe-mye'-sin troe-meth'-ah-meen

Trade and Other Names: Monurol

Functional Classification: Antibacterial (urinary)

Pharmacology and Mechanism of Action

Fosfomycin is a urinary antimicrobial. It inhibits cell walls of susceptible bacteria and may decrease virulence by inhibiting the adherence of bacteria to bladder mucosa. It produces adequate concentrations in urine to manage urinary tract infections. In people it is used as a single dose to treat acute UTI. In dogs the half-life is short (1.3 hours IV and 2.2 hours oral) and oral absorption is 30%.

Indications and Clinical Uses

Fosfomycin is used as treatment, or adjunctive treatment, for urinary tract infections. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. In women it is used as a single dose to treat acute urinary tract infections.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects have been reported. It has been safe and well-tolerated in dogs up to 120-200 mg/kg.

Contraindications and Precautions

Do not administer in dry form; mix with water. There are no other known contraindications. Fosfomycin should not be substituted for antibiotics with established efficacy.

Drug Interactions

No known drug interactions.

Instructions for Use

Fosfomycin has been used to treat urinary tract infections in animals, primarily when other drugs have failed or were inactive as a result of resistance. Alternatively, fosfomycin has been used intermittently (pulse therapy) to prevent recurrences of urinary tract infections. The efficacy of any of these indications is not established in animals.

Patient Monitoring and Laboratory Tests

Monitor urinary tract infection with culture and urinalysis.

Formulations

Fosfomycin is available in a 3-g packet. The packet also contains saccharin and sucrose for flavoring. This packet may be mixed with water and administered immediately orally.

Stability and Storage

Store in original package, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Precise doses are not established for small animals. 40-80 mg/kg q8h, PO has been recommended. Additional cited doses used are empiric and include a recommendation of a 3-g packet divided equally into three daily doses (1 g dissolved in 30 mL) and administered daily to dogs.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No withdrawal times are established for animals intended for food.

Furazolidone

fyoo-rah-zole'ih-done

Trade and Other Names: Furoxone

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Furazolidone is an oral antiprotozoal drug with activity against *Giardia*, and it may have some activity against bacteria in intestine. It is used for only local treatment of intestinal parasites; it is not used for systemic therapy.

Indications and Clinical Uses

Furazolidone has been used to treat protozoal intestinal parasites. However, because efficacy and safety of other oral antiprotozoal drugs are better established, they are used more often.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects not reported in animals. In people, mild anemia, hypersensitivity, and disturbance of intestinal flora have been reported.

Contraindications and Precautions

No contraindications reported for animals.

Drug Interactions

Do not use with monoamine oxidase inhibitors (MAOIs).

Instructions for Use

Clinical studies have not been reported for animals. Doses and recommendations are based on extrapolation from humans. Other drugs, such as fenbendazole, may be preferred for treating *Giardia*.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Furazolidone has been discontinued in the U.S. It may be available through some compounding pharmacies. Previously available tablet was 100 mg.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

- 4 mg/kg q12h for 7-10 days PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. For extra-label use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Furosemide

fyoo-roe'seh-mide

Trade and Other Names: Lasix and generic brands

Functional Classification: Diuretic

Pharmacology and Mechanism of Action

Furosemide is a loop diuretic that inhibits the $\text{Na}^+/\text{K}^+/\text{2Cl}^-$ cotransporter in the ascending thick loop of Henle. It is often called high-ceiling diuretics because it is more effective than other diuretics. Furosemide decreases the sodium, chloride, and potassium reabsorption from the tubule. Subsequently, these ions are retained in the renal tubule and presented to the distal nephron. Dilute urine is produced because water is retained in the tubule when it reaches the distal tubule. In addition, there is an associated urine loss of Mg^{++} and Ca^{++} . An additional mechanism of action is via prostaglandin synthesis. Furosemide increases intrarenal prostaglandin production (e.g., PGI_2), which increases renal blood flow. Synthesis of prostaglandins also may cause vasodilation in other tissues. The plasma half-life in animals is short (1.5-3 hours); therefore, this is a short-acting drug. Oral absorption can be highly variable, but in horses oral absorption is so low that this is not a viable method of administration.

Indications and Clinical Uses

In small animals, furosemide is the drug of choice to treat conditions that cause edema: pulmonary edema, liver disease, heart disease, and vascular disease. It increases urine production and can be used to treat acute renal failure. In addition, furosemide will increase K^+ and Ca^{++} excretion and is used to treat hyperkalemia and hypercalcemia. In horses, furosemide has been used to treat edema and syndromes associated with congestion. The most common use in horses is pretreatment prior to racing. Although it appears to produce faster racing times, the mechanism is unclear. It may decrease body weight via water loss and may decrease exercise-induced pulmonary hemorrhage (EIPH). However, the efficacy to reduce EIPH has been controversial in horses. In cattle, furosemide also is used for treating conditions of edema (e.g., udder edema) and for treatment of heart failure and pulmonary hypertension.

In all animals, duration of effect is short, approximately 2-4 hours.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are primarily related to diuretic effect (loss of fluid and electrolytes). In dogs, hyponatremia is more common than hypokalemia. Tolerance and activation of the renin-angiotensin-aldosterone system (RAAS) occur with repeated administration, in which the diuretic effect is attenuated.

Contraindications and Precautions

Administer conservatively in animals receiving angiotensin-converting enzyme (ACE) inhibitors to decrease the risk of azotemia. Repeated administration may increase aldosterone levels via activation of RAAS.

Drug Interactions

Concurrent use with aminoglycoside antibiotics or amphotericin B may increase risk of nephrotoxicity and ototoxicity. Administration of nonsteroidal anti-inflammatory drugs (NSAIDs) with furosemide may diminish the effect. The pH of solution is 8-9.8. Furosemide is stable with alkaline drugs, but do not mix with acidifying drug solutions with pH <5.5.

Instructions for Use

Recommendations are based on extensive clinical use of furosemide in animals. The onset of effect after an injection is usually 5 minutes, with the peak at 30 minutes and a duration of approximately 2 hours. Constant rate infusions (CRI) in dogs and horses can be more effective than intermittent bolus. Long-term repeated administration may attenuate the effects because of tolerance and activation of the RAAS.

Patient Monitoring and Laboratory Tests

Monitor electrolyte concentrations (particularly potassium) and hydration status in patients during treatment.

Formulations

Furosemide is available in 12.5-, 20-, 40-, 50-, and 80-mg tablets; 20-, 40-, and 80-mg tablets (human preparation); 10-mg/mL oral solution (syrup), and 50-mg/mL injection. Tablets usually can be easily split.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with acidic solutions. It is compatible in plastic syringes and infusion sets. Furosemide is poorly soluble in water but may be mixed with 5% dextrose, 0.9% saline, or lactated Ringer's solution at a concentration of 10 mg/mL. These solutions are stable for 8 hours. It is more soluble if the pH is >8, but it readily precipitates when pH is <5.5. Compounded oral formulations in syrups and other flavorings are stable if kept at alkaline pH or in alcohol. However, lower pH will result in instability of formulation. If discoloration occurs, discard formulation.

Small Animal Dosage

Dogs

- 2-6 mg/kg q8-12h (or as needed) IV, IM, SQ, or PO. A common initial dose when treating heart failure patients is 2 mg/kg q12h PO, then lower to 1-2 mg/kg q12h, PO.
- In acute cases where intensive treatment is needed, administer 2 mg/kg IV, followed by 2 mg/kg every 30 minutes, until improvement is seen.
- CRI: 0.66 mg/kg bolus dose IV, followed by 0.66 mg/kg/hr for 8 hours.

Cats

- Start with 1 mg/kg, then increase as needed, within a range of 1-4 mg/kg q8-24h IV, IM, SQ, or PO.

Large Animal Dosage

Horses

- 1 mg/kg q8h or 250 to 500 mg/horse at 6-8 hour intervals IM or IV.
- CRI: 0.12 mg/kg IV followed by 0.12 mg/kg/hr IV.

Cattle

- 500 mg/animal once a day or 250 mg/animal twice a day IM or IV.

Regulatory Information

Cattle withdrawal times: 2 days meat and 48 hours milk.

Horses: Most racing regulations specify that a 250-mg/horse dose may be given by a single intravenous injection no later than 4 hours before racing post time. In most horses this will not produce violations above 100 ng/mL urine threshold at 4 hours.

Gabapentin

gab'ah-pen-tin

Trade and other names: Gabapetin, Neurontin, and generic brands

Functional classification: Anticonvulsant, analgesic

Pharmacology and Mechanism of Action

Anticonvulsant and analgesic. Gabapentin is an analogue of the inhibitory neurotransmitter GABA; however, it is not an agonist or antagonist for the GABA receptor. The mechanism of anticonvulsant action and analgesic effects is not clear, but there is evidence that the mechanism of action appears to be via blocking calcium-dependent channels. Gabapentin inhibits the alpha-2-delta ($\alpha_2 \delta$) subunit of the N-type voltage-dependent calcium channel on neurons. Via inhibition, it reduces calcium influx that is needed for release of neurotransmitters—specifically, excitatory amino acids—from presynaptic neurons. Blocking the channels has little effect on normal neurons, but it may suppress simulated neurons involved in seizure activity and pain. Half-life in dogs and cats is only 3-4 hours, which may necessitate frequent administration. In horses the half-life is 8 hours (range 6.7-12 hrs), but the oral absorption is only 16%. Another related drug is pregabalin (Lyrica), which is used in people for neuropathic pain and has also been used in dogs. Gabapentin is eliminated entirely by renal clearance in people, but there is 30-40% hepatic metabolism in dogs. Therefore, some interactions are possible with drugs that affect hepatic clearance, or with hepatic disease may compromise hepatic function.

Indications and Clinical Uses

Gabapentin is used as an anticonvulsant and to treat chronic pain syndromes, including neuropathic pain. It is used to treat neuropathic pain that does not respond to nonsteroidal anti-inflammatory drugs (NSAIDs) or opiates. However, studies demonstrating efficacy for pain treatment in dogs and cats are currently lacking. When used to treat epilepsy, it (or pregabalin) is usually considered when the seizures have become refractory to other drugs. Clinical efficacy studies in veterinary medicine are lacking for either use, and treatment regimens have been mostly derived from anecdotal evidence or extrapolation from human medicine.

Precautionary Information

Adverse Reactions and Side Effects

Sedation and ataxia are reported adverse effects. As dose increases in dogs (see dosing section), sedation is more likely. In people a withdrawal syndrome from abrupt discontinuation has been described, but it is not reported in animals. The oral solution contains xylitol, which is an artificial sweetener that can be toxic to dogs and produces hypoglycemia and liver injury with high doses exceeding 0.1 g/kg. With standard doses of gabapentin oral solution, the toxic level of xylitol is not likely to be exceeded, but one should be cautious about adding other drugs that also contain xylitol.

Contraindications and Precautions

No known contraindications.

Drug Interactions

Antacids decrease oral absorption.

Instructions for Use

Gabapentin has been used in some animals as an anticonvulsant when they are refractory to other drugs. It can be used with other drugs such as phenobarbital and bromide. It also has been used to treat neuropathic pain syndromes and can be used with NSAIDs and opioids. Efficacy for each of these indications is anecdotal; there are no controlled studies published.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Gabapentin is available in 100-, 300-, and 400-mg capsules; 100-, 300-, 400-, 600-, and 800-mg scored tablets; and 50-mg/mL oral solution.

Stability and Storage

If stored at high temperatures and high humidity, there may be degradation within 9 weeks. Split tablets and intact tablets are stable after storage at room temperature for 9 weeks. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Anticonvulsant dose: 2.5-10 mg/kg q8-12h PO.
- Neuropathic pain: Start with 5-15 mg/kg q12h, PO, and increase dose gradually to as high as 40 mg/kg, q8-12h, PO, if necessary.

Cats

- Anticonvulsant dose: 5-10 mg/kg q12h, PO
- Neuropathic pain: 5-10 mg/kg q12h, PO.

Large Animal Dosage

Horses

- Neuropathic pain: 2.5 mg/kg, q12h, PO.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Gemfibrozil

jem-fih'broe-zil

Trade and other names: Lopid

Functional classification: Antihyperlipidemic agent

Pharmacology and Mechanism of Action

Gemfibrozil is an agent that lowers cholesterol, reduces plasma triglyceride and very-low-density-lipoprotein (VLDL), and increases high-density lipoproteins (HDL). Mechanism results from inhibition of peripheral lipolysis and reduced hepatic extraction of free fatty acids.

Indications and Clinical Uses

It is used for treatment of hyperlipidemia. It has been used in dogs for treatment of some hyperlipidemia syndromes, but the efficacy has not been reported.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals.

Contraindications and Precautions

No reported contraindications in animals.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Used primarily in people to treat hyperlipidemia, but it is used occasionally in dogs. Clinical studies have not been performed in animals.

Patient Monitoring and Laboratory Tests

Monitor cholesterol concentrations.

Formulations

Gemfibrozil is available in 600-mg tablets and 300-mg capsules (Canada only).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 7.5 mg/kg q12h PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Gentamicin Sulfate

jen-tah-mye'sin sul'fate

Trade and other names: Gentocin, Garasol, Garacin, and generic

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Aminoglycoside antibiotic. Action is to inhibit bacteria protein synthesis via binding to 30S ribosome. Bactericidal. Gentamicin has a broad spectrum of activity that includes most bacterial isolates in animals, including staphylococci and gram-negative bacilli of the *Enterobacteriaceae*. It is not very active against streptococci and anaerobic bacteria. The pharmacokinetics have been studied in many domestic

and exotic animal species. The half-life is typically 1-2 hours in mammals, and the volume of distribution is approximately 0.2-0.3 L/kg. Clearance is via glomerular filtration.

Indications and Clinical Uses

Gentamicin has a rapid, bactericidal action and is indicated for acute serious infections, such as those caused by gram-negative bacilli. Gentamicin has been administered IM, SQ, and IV. It is not absorbed after oral administration, and this use is restricted to labeled use in pigs. Gentamicin, like other aminoglycosides, can be used with beta-lactam antibiotics because it broadens the spectrum when used with drugs such as penicillins, ampicillin, or cephalosporins. Although gentamicin is generally active against most gram-negative bacilli, amikacin is more consistently active against resistant strains. The only approved use in food animals is oral treatment in pigs for swine dysentery.

Precautionary Information

Adverse Reactions and Side Effects

Nephrotoxicity is the most dose-limiting toxicity. Ensure that patients have adequate fluid and electrolyte balance during therapy. Electrolyte depletion will increase the risk of nephrotoxicity. High levels of calcium and protein in the diet will decrease the risk of nephrotoxicity. Ototoxicity and vestibulotoxicity also are possible but have not been reported in animals. With high doses, neuromuscular toxicity is possible, although rare.

Contraindications and Precautions

Do not administer to animals with compromised renal function, renal insufficiency, or renal failure. There should be adequate renal clearance for clearance of gentamicin. Use in young animals is accepted, except higher doses may be necessary.

Drug Interactions

When used with anesthetic agents, neuromuscular blockade is possible. Do not mix in vial or syringe with other antibiotics. Ototoxicity and nephrotoxicity are potentiated by loop diuretics such as furosemide.

Instructions for Use

Dosing regimens are based on sensitivity of organisms. Some studies have suggested that once-daily therapy (combining multiple doses into a single daily dose) is as efficacious as multiple treatments. Activity against some bacteria (e.g., *Pseudomonas aeruginosa*) is enhanced when combined with a beta-lactam antibiotic, such as ceftazidime. Nephrotoxicity is increased with persistently high trough concentrations.

Patient Monitoring and Laboratory Tests

Susceptibility testing: The CLSI minimum inhibitory concentration (MIC) break point for susceptibility is ≤ 2 mcg/mL. Monitor BUN, creatinine, and urine for evidence of renal toxicity. Blood levels can be monitored to measure for problems with systemic clearance. When monitoring trough levels in patient doses once daily, the trough levels should be below the limit of detection. Alternatively, measure half-life from samples taken at 1 hour and 2 to 4 hours postdosing. Clearance should be approximately equal to the glomerular filtration rate (GFR) (>1.0 mL/kg/min), and half-life should be less than 2 hours.

340 Glipizide

Formulations

Gentamicin is available in a 50- and 100-mg/mL solution for injection and a 50-mg/mL oral solution for pigs.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Gentamicin is soluble in water. Do not mix with other drugs, especially in a vial, syringe, or fluid administration set. Inactivation may occur. Avoid long-term storage in plastic containers.

Small Animal Dosage

Dogs

- 2-4 mg/kg q8h or 9-14 mg/kg q24h SQ, IM, or IV.
Once-daily administration is usually the preferred interval.

Cats

- 5-8 mg/kg q24h SQ, IM, or IV.
Once-daily administration is usually the preferred interval.

Large Animal Dosage

Horses

- Adult: 4-6.6 mg/kg q24h IM or IV.
- Foal younger than 2 weeks: 12-14 mg/kg q24h IM or IV.

Pigs

- 15 mg/kg for young pigs and 10 mg/kg for older pigs, once daily, SQ or IM.
- Colibacillosis, swine dysentery: 1.1-2.2 mg/kg for 3 days in drinking water.

Calves

- Younger than 2 weeks: 12-15 mg/kg q24h IV or IM.
- Adult cattle: 5-6 mg/kg q24h IM or IV.

Regulatory Information

With the exception of licensed products for pigs, aminoglycosides should not be administered to food animals because of residue concerns.

Withdrawal time for pigs: 3 days meat at 1.1 mg/kg PO and 40 days meat at 5 mg/kg IM; 14 days meat at 5 mg/kg PO.

If gentamicin is administered systemically to cattle, an extended withdrawal time is necessary because of persistence of residues in kidney. FARAD recommends 18 months. After systemic administration of 5 mg/kg, milk withdrawal time should be 5 days. If gentamicin is administered intramammary (500 mg per quarter), a milk withdrawal time of at least 10 days and a meat withdrawal time of 180 days should be used.

Contact FARAD for additional information at 1-888-USFARAD (1-888-873-2723).

Glipizide

glip-ih'zide

Trade and other names: Glucotrol

Functional classification: Antidiabetic agent, hypoglycemic agent

Pharmacology and Mechanism of Action

Sulfonylurea oral hypoglycemic agent. This drug acts to increase secretion of insulin from beta cells of the pancreas, probably by interacting with sulfonylurea receptors on beta cells or by inhibiting adenosine triphosphate (ATP)–sensitive potassium channels on the pancreatic beta cells, which increases insulin secretion. These drugs also may increase sensitivity of existing insulin receptors. Studies in cats showed that glipizide had a half-life of 17 hours and effective plasma concentration for 50% efficacy (EC_{50}) of 70 mcg/mL.

Indications and Clinical Uses

Glipizide is used as oral treatment in the management of diabetes mellitus, particularly in cats. Response rate in cats is approximately 44%–65% (some reports are 30% or lower). The response rate in dogs is poor. It has been more common to administer the sulfonylurea class of drugs in animals than other oral hypoglycemic drugs because they have had better efficacy. Glipizide is the most common of this class. Other oral hypoglycemic drugs include acetohexamide, chlorpropamide, glyburide (DiaBeta, Micronase), gliclazide, and tolazamide. Metformin is of the biguanide class of oral drugs for diabetes and has not had efficacy as high as glipizide in cats.

Glipizide transdermal absorption from a pluronic transdermal gel (pluronic organogel [PLO]) vehicle is poor in cats (<20%) and inconsistent. This route is not recommended.

Precautionary Information

Adverse Reactions and Side Effects

It may cause dose-related vomiting, anorexia, increased bilirubin, and elevated liver enzymes in some cats (15%). It may exacerbate deposits of amyloid in feline pancreas and increase the loss of pancreatic beta cells. Glipizide may cause hypoglycemia, but less so than insulin. In people, increased cardiac mortality is possible, but this has not been reported in cats.

Contraindications and Precautions

Many cats do not respond and will require insulin therapy. Do not rely on glipizide in cats that are not stable or if they are dehydrated or debilitated.

Drug Interactions

Many drug interactions have been reported in people. It is not known if these occur in animals. Use cautiously with beta blockers, antifungal drugs, anticoagulants, fluoroquinolones, sulfonamides, and others.

Instructions for Use

Oral hypoglycemic agents are successful in people only for noninsulin-dependent diabetes. There has been only limited use in animals. Because response to oral hypoglycemic agents in cats is unpredictable, it is recommended to use a trial first of at least 4 weeks. If the cat responds, the drug can be continued; otherwise, insulin may be indicated. Feed cats a high-fiber diet when using oral hypoglycemic agents. Transdermal glipizide (5-mg dose) in a PLO gel was evaluated in cats. Although the transdermal formulation produced a modest change in glucose concentrations, systemic absorption was only 20%.

Patient Monitoring and Laboratory Tests

Monitor blood glucose levels to determine if the drug is effective. Monitor liver enzymes. It may increase alanine transaminase (ALT) and alkaline phosphatase.

342 Glucosamine + Chondroitin Sulfate

Formulations

Glipizide is available in 5- and 10-mg tablets.

Stability and Storage

Store glipizide in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

No effective dose available.

Cats

- 2.5-7.5 mg/cat q12h PO. Usual dose is 2.5 mg/cat initially, then increase to 5 mg/cat, q12h.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Glucosamine + Chondroitin Sulfate

gloo-koe'seh-meen + kahn-droy'ten sulf'ate

Trade and other names: Cosequin, Glycoflex, and generic brands

Functional classification: Nutritional supplement

Pharmacology and Mechanism of Action

Glucosamine is an amino sugar synthesized from glucose and glutamine. It is a source of glucosamine-6-phosphate and n-acetylglucosamine. It is an intermediate compound, converted to an ester that is incorporated into articular cartilage. Therefore, it is a direct precursor in the formation of glycosaminoglycans in cartilage. Glucosamine is usually administered as a combination of glucosamine HCl and chondroitin sulfate. Other forms include glucosamine sodium sulfate and glucosamine potassium sulfate. Glucosamine has been promoted to stimulate synthesis of synovial fluid, inhibit degradation, and improve healing of articular cartilage. Additional information is available in the section on chondroitin sulfate. Bioavailability studies have produced varying results depending on formulation, assay technique, and species. Oral absorption of glucosamine has varied, ranging from 12% in dogs to only 2.5% (125 mg/kg) or 6% (20 mg/kg) in horses. Although *in vitro* studies have demonstrated benefits to articular cartilage, some studies have questioned whether oral glucosamine is absorbed systemically intact to a high enough extent to provide these benefits. Oral absorption may be affected by the form administered because glucosamine sulfate may be better absorbed than glucosamine hydrochloride.

Indications and Clinical Uses

Glucosamine is used primarily for treatment of degenerative joint disease and is usually found in formulations in combination with chondroitin sulfate. (See Chondroitin sulfate for additional details.) Analyses of published clinical studies in

dogs have concluded that there is a moderate level of evidence to indicate some benefit in osteoarthritis, but results may be inconsistent among studies. Benefits of treatment in horses with lameness also have been reported from oral administration of chondroitin-glucosamine supplements. There is a lack of supporting evidence that systemic administration is effective for reducing recurrent urinary tract infections in animals (via a beneficial effect on bladder mucosa). These compounds are regulated as dietary supplements that modify disease and are not regulated as drugs.

Precautionary Information

Adverse Reactions and Side Effects

In some animals, soft stools and intestinal gas have been reported. In experimental rodents, injections of glucosamine can cause hyperglycemia, insulin resistance, and a decrease in the metabolic action of insulin via the hexosamine pathway. However, the clinical relevance of these findings has not been shown. Clinical studies in dogs have shown that short-term (21 days) administration of glucosamine does not affect glycemic control or cause diabetes mellitus in dogs. Otherwise, adverse effects have not been reported, although hypersensitivity is possible.

Contraindications and Precautions

The safety of glucosamine has not been established in diabetic animals or obese animals that may be prone to developing diabetes. Otherwise, there are no known precautions.

Drug Interactions

No drug interactions are reported. Glucosamine- and chondroitin-containing products may be used safely with nonsteroidal anti-inflammatory drugs (NSAIDs).

Instructions for Use

Doses are based primarily on empiricism and manufacturer's recommendations. There are few published trials of efficacy or dose titrations available to determine optimal dose. Doses listed are general recommendations and may vary among products. Glucosamine hydrochloride is more bioavailable than glucosamine sulfate. Products may vary in their stability, purity, and potency. Use products from a reputable supplier.

Patient Monitoring and Laboratory Tests

No routine patient monitoring is necessary. There is no evidence that glucosamine administration will increase serum glucose. Glucosamine is produced by glucose in the body, but this is an irreversible reaction.

Formulations

Several formulations are available. Veterinarians are encouraged to carefully examine product label to ensure proper strength. One product (Cosequin) is available as regular-strength ("RS") and double-strength ("DS") capsules. Regular strength contains 250 mg glucosamine; 200 mg chondroitin sulfate; and mixed glycosaminoglycans, 5 mg manganese, and 33 mg manganese ascorbate. The DS tablets contain double of each of these amounts. Products for horses contain 3.3 g per scoop, equal to 1800 mg glucosamine and 570 mg chondroitin.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Products may vary in stability and potency.

Small Animal Dosage

- General dosing requirements for glucosamine: 22 mg/kg/day PO, and increased to 44 mg/kg/day PO, in patients that do not initially respond. Alternatively, a better response may be anticipated by starting with the higher dose.

Many preparations are administered in combination with chondroitin. For general dosing, use the Cosequin RS and DS strength as a general guide.

Dogs

- 1-2 capsules per day, and 2-4 capsules for large dogs.

Cats

- 1 capsule daily.

Large Animal Dosage

Horses

- 12 mg/kg glucosamine + 3.8 mg/kg chondroitin sulfate twice daily PO for 4 weeks, then 4 mg/kg glucosamine + 1.3 mg/kg chondroitin sulfate thereafter. It is common to initiate treatment in horses with a higher dose of 22 mg/kg glucosamine + 8.8 mg/kg chondroitin sulfate daily PO.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Glyburide

glye'byoor-ide

Trade and other names: Diabeta, Micronase, Glynase, and Glibenclamide (British name)

Functional classification: Antidiabetic agent, hypoglycemic agent

Pharmacology and Mechanism of Action

Glyburide is a sulfonylurea oral hypoglycemic agent; it is also known as glibenclamide. This drug acts to increase secretion of insulin from pancreas, probably by interacting with sulfonylurea receptors on beta cells or by interfering with adenosine triphosphate (ATP)-sensitive potassium channels on pancreatic beta cells, which increases secretion of insulin. These drugs also may increase sensitivity of existing insulin receptors. It is used as oral treatment in the management of diabetes mellitus, particularly in cats. The response rate is approximately 40%. Sulfonylurea drugs include glipizide (Glucotrol) and glyburide (DiaBeta, Micronase). Metformin is of the biguanide class of oral drugs for diabetes.

Indications and Clinical Uses

Oral hypoglycemic agents are successful in people only for noninsulin-dependent diabetes. There has been only limited use in animals. Glyburide is not effective in dogs but has been used in some cats. Some cats may initially respond to oral hypoglycemic agents but eventually need insulin treatment. Similar drugs include acetohexamide, chlorpropamide, glipizide, gliclazide, and tolazamide. There is more

experience with glipizide than with other drugs, and it should be used as the first choice (see Glipizide section for more details.).

Precautionary Information

Adverse Reactions and Side Effects

It may cause dose-related vomiting, anorexia, increased bilirubin, and elevated liver enzymes in some cats. Glyburide causes hypoglycemia but less so than insulin. In people, increased cardiac mortality is possible.

Contraindications and Precautions

There are no known contraindications in animals.

Drug Interactions

No drug interactions are reported for animals. Many drug interactions have been reported in people. It is not known if these occur in animals because clinical use has been rare. Use cautiously with beta blockers, antifungal drugs, anticoagulants, fluoroquinolones, and sulfonamides.

G

Instructions for Use

Because response to oral hypoglycemic agents in cats is unpredictable, it is recommended to use a trial first of at least 4 weeks. If the cat responds, the drug can be continued. Otherwise, insulin may be indicated. Feed cats a high-fiber diet when using oral hypoglycemic agents.

Patient Monitoring and Laboratory Tests

Monitor blood glucose levels to determine if the drug is effective. Monitor liver enzymes.

Formulations

Glyburide is available in 1.25-, 2.5-, and 5-mg tablets (Diabeta and Micronase). Glynase is available in 1.5-, 3-, and 6-mg micronized tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

No effective doses have been reported.

Cats

- 0.2 mg/kg daily PO. Alternatively start with 0.625 mg ($\frac{1}{2}$ tablet) per cat once daily.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. No withdrawal information is available.

Glycerin

glih'ser-in

Trade and other names: Generic

Functional classification: Diuretic, laxative

Pharmacology and Mechanism of Action

Glycerin has been administered to lower ocular pressure to treat acute glaucoma. However, intravenous mannitol is used more frequently for this purpose. Glycerin has been used as a laxative; it lubricates the stools and adds water to intestinal contents.

Indications and Clinical Uses

Glycerin is an osmotic agent that draws water into the intestine or renal tubule. Administered systemically, it acts as an osmotic diuretic agent, preventing water reabsorption from the renal tubules. Administered orally, it is not absorbed but acts as an osmotic laxative, drawing water into the intestine.

Precautionary Information

Adverse Reactions and Side Effects

Glycerin may cause dehydration with frequent use or high doses.

Contraindications and Precautions

Do not administer to dehydrated animals.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Although glycerin may lower ocular pressure, other drugs are used to treat acute glaucoma.

Patient Monitoring and Laboratory Tests

Monitor ocular pressures. Monitor electrolytes in treated animals.

Formulations Available

Glycerin is available in an oral solution or 40-mg/mL emulsion.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage (Dogs and Cats)

- 1-2 mL/kg q8h PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Glycopyrrolate

glye-koe-peer'oe-late

Trade and other names: Robinul-V

Functional classification: Anticholinergic

Pharmacology and Mechanism of Action

Anticholinergic agent (blocks acetylcholine effect at muscarinic receptor), parasympatholytic. Glycopyrrolate produces atropine-like effects systemically. However, glycopyrrolate may have less effect on CNS compared to atropine because of lower penetration to CNS. It may produce a longer duration of action than atropine.

Indications and Clinical Uses

Glycopyrrolate is used to inhibit vagal effects and increase heart rate in animals. It also will decrease respiratory, salivary, and GI secretions. It may be used as an adjunct to anesthesia when it is necessary to override vagal stimulus.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects attributed to antimuscarinic (anticholinergic) effects. Side effects of therapy include xerostomia, ileus, constipation, tachycardia, and urine retention.

Contraindications and Precautions

Do not use in patients with glaucoma, intestinal ileus, gastroparesis, or tachycardia.

Drug Interactions

No specific drug interactions are reported for animals. However, it is expected that glycopyrrolate, like other anticholinergic drugs, will antagonize drugs that stimulate respiratory and GI secretions and GI motility.

Instructions for Use

Glycopyrrolate is often used in combination with other agents, particularly anesthetic drugs. Although some anesthetic agents such as alpha-2 agonists and opioids are associated with bradycardia, it is rarely necessary to administer anticholinergic agents to reduce the bradycardia.

Patient Monitoring and Laboratory Tests

Monitor heart rate during treatment.

Formulations

Glycopyrrolate is available as a 0.2-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 0.005-0.01 mg/kg IV, IM, or SQ.

Large Animal Dosage

Cattle and Horses

- Use during anesthesia: 0.005-0.01 mg/kg IM or SQ or 0.0025-0.005 mg/kg IV.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Gold Sodium Thiomalate

gold soe'dee-um thye-oh-mah'late

Trade and other names: Myochrysine

Functional classification: Immunosuppressive

Pharmacology and Mechanism of Action

Used for gold therapy (chrysotherapy). Mechanism of action is unknown, but it may relate to immunosuppressive effect on lymphocytes or suppression of sulfhydryl systems.

Indications and Clinical Uses

Gold therapy is used primarily for immune-mediated diseases (such as dermatologic disease) in animals. In people it has been used for rheumatoid arthritis. In animals, there is a lack of controlled clinical trials to document efficacy. Other immunosuppressive drugs are used more commonly.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include dermatitis, nephrotoxicity, and blood dyscrasias.

Contraindications and Precautions

Use cautiously in animals with bone marrow suppression or renal disease.

Drug Interactions

Use with penicillamine will increase risk of hematologic adverse effects.

Instructions for Use

Clinical studies have not been performed in animals. Aurothioglucose generally is used more often than gold sodium thiomalate.

Patient Monitoring and Laboratory Tests

CBC should be monitored periodically during treatment.

Formulations Available

Gold sodium thiomalate is available in 10-, 25-, and 50-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 1-5 mg per animal IM first week, then 2-10 mg IM second week, and then 1 mg/kg once per week IM for maintenance.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Gonadorelin Hydrochloride, Gonadorelin Diacetate Tetrahydrate

goe-nad-oh-rell'in hye-droe-klor'ide, goe-nad-oh-rell'in dye-ass'eh-tate tet-ra-hye'drate

Trade and other names: Factrel, Fertagyl, Cystorelin, Fertelin, OvaCyst, GnRh, and LHRH

Functional classification: Hormone

G

Pharmacology and Mechanism of Action

Gonadorelin stimulates synthesis and release of luteinizing hormone (LH) and, to a lesser degree, follicle-stimulating hormone (FSH).

Indications and Clinical Uses

Gonadorelin is used to induce luteinization and ovulation in animals. Gonadotropin has been used to manage various reproductive disorders in which stimulation of ovulation is desired. In dairy cattle, it is used to treat ovarian follicular cysts.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals.

Contraindications and Precautions

Do not administer to pregnant animals. Extreme care should be used by people, particularly women, handling this medication. Human exposure may pose a risk to pregnant women.

Drug Interactions

No drug interactions in animals are reported.

Instructions for Use

For treatment of dairy cattle, with the diacetate tetrahydrate form, administer 100 mcg per cow as a single intramuscular or intravenous injection for treatment of ovarian cysts. For the hydrochloride formulation, administer 100 mcg IM for the treatment of cystic ovaries (ovarian follicular cysts) in cattle to reduce the time to first estrus.

Patient Monitoring and Laboratory Tests

Monitor treated cattle for ovulation.

350 Gonadotropin, Chorionic

Formulations

Gonadorelin is available in 50-mcg gonadorelin diacetate tetrahydrate per mL (equivalent to 43 mcg/mL of gonadorelin) or 50-mcg gonadorelin (as hydrochloride) in aqueous solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

• 50-100 mcg/dog/day q24-48h IM.

Cats

• 25 mcg/cat once IM.

Large Animal Dosage

Cattle

• 100 mcg/cow IM or IV once. (Equivalent to approximately 2 mL per cow for gonadorelin diacetate tetrahydrate.)

Regulatory Information

No withdrawal times are necessary (zero days).

Gonadotropin, Chorionic

go-nad-o-tro'pin, kor-ee-ahn'ik

Trade and other names: Profasi, Pregnyl, A.P.L., and generic brands

Functional classification: Hormone

Pharmacology and Mechanism of Action

Gonadotropin is also referred to as human chorionic gonadotropin (hCG). Action of hCG is identical to that of luteinizing hormone (LH).

Indications and Clinical Uses

Gonadotropin is used to induce luteinization in animals. Gonadotropin has been used to manage various reproductive disorders where stimulation of ovulation is desired.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals.

Contraindications and Precautions

Do not administer to pregnant animals. Extreme care should be used by people, particularly women, handling this medication. Human exposure may pose a risk to pregnant women.

Drug Interactions

No specific drug interactions are reported.

Instructions for Use

When used in horses, most ovulate 32-40 hours after treatment.

Patient Monitoring and Laboratory Tests

Monitor treated patients for signs of luteinization and estrus.

Formulations

HCG is available in 5000-, 10,000-, and 20,000-unit injections.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 22 units/kg q24-48h IM or 44 units once IM.

Cats

- 250 units/cat once IM.

Large Animal Dosage

Horses

- Ovulation induction: 2500 to 5000 units per mare IM or IV.

Regulatory Information

No regulatory information is available for food animals. Because of low risk of residues, no withdrawal times are suggested.

Granisetron Hydrochloride

grah-nih'seh-tron hye-droe-klor'ide

Trade and other names: Kytril

Functional classification: Antiemetic

Pharmacology and Mechanism of Action

Antiemetic drug from the class of drugs called serotonin antagonists. These drugs act by inhibiting serotonin (5-HT, type 3) receptors. During chemotherapy, there may be 5-HT released from injury to the GI tract that stimulates vomiting centrally, which is blocked by this class of drugs. These drugs also have been used to treat vomiting from other forms of gastroenteritis. Serotonin antagonists used for antiemetic therapy include granisetron, ondansetron, dolasetron, azestron, and tropisetron.

Indications and Clinical Uses

Granisetron, like other serotonin antagonists, is used primarily as an antiemetic during chemotherapy, for which they generally have been superior to other drugs in efficacy. It may be administered prior to chemotherapy to prevent nausea and vomiting. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

None reported in dogs or cats. These drugs have little affinity for other serotonin receptors.

Contraindications and Precautions

No contraindications reported in animals.

Drug Interactions

No interactions are reported. It may be used with cancer chemotherapy agents.

Instructions for Use

There have been only limited uses of this class of antiemetic drugs used in veterinary patients. Most doses have been extrapolated from human uses.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Granisetron is available in 1-mg tablets and 1-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Discard opened vial after 30 days. Compounded solutions are stable in various fluids for 24 hours. Oral compounded formulations have been prepared in juices, syrups, and flavorings and were stable for 14 days.

Small Animal Dosage

Dogs and Cats

- 0.01 mg/kg IV; oral doses have been extrapolated from people (1 mg/person PO).

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available for food animals. Because of low risk of residues, no withdrawal times are suggested.

Griseofulvin

grizs-ee-oh-ful'vin

Trade and other names: Microsize: Fulvicin U/F, Grisactin, and Grifulvin and Ultramicrosize: Fulvicin P/G, and GrisPEG

Functional classification: Antifungal

Pharmacology and Mechanism of Action

Antifungal drug. After systemic administration, griseofulvin is deposited in the keratin precursor cells of the skin and hair. It is rapidly taken up into these tissues within 4-8 hours or 48-72 hours (depending on the study) after administration.

Once it is incorporated into these cells, mitosis of the fungal cells is inhibited by effects on the mitotic spindle, and eventually fungal cells are killed.

Indications and Clinical Uses

Griseofulvin is one of the drugs of choice when systemic treatment is needed for dermatophyte infections caused by *Microsporum* spp., and *Trichophyton* spp. in dogs and cats. It is sometimes used in combination with topical therapy. Griseofulvin is not effective for the treatment of yeasts or bacteria. At least 4 weeks, and sometimes 3 months or more, are needed for successful therapy. Its use has been replaced by azole antifungal drugs in many cases (itraconazole, fluconazole, etc.). It also has a predilection to accumulate in inflammatory sites of the skin and may be effective for treating some noninfectious, inflammatory dermatoses other than dermatomycosis.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects in animals include teratogenicity in cats, anemia and leukopenia in cats, anorexia, depression, vomiting, and diarrhea. In cats, feline immunodeficiency virus (FIV) infection may increase the risk of bone marrow toxicosis. Whether the bone marrow problems are caused by high doses or is an idiosyncratic (non-dose related) reaction is not understood. These effects resolve in cats when treatment is stopped, but irreversible idiosyncratic pancytopenia has been reported.

Contraindications and Precautions

Do not administer to pregnant cats. Caution should be used when administering griseofulvin to cats with viral infections (FIV) because this may exacerbate bone marrow effects.

Drug Interactions

Griseofulvin is an enhancer of cytochrome P450 drug enzymes. Therefore, other concurrent drugs may be metabolized and cleared more quickly if given with griseofulvin.

Instructions for Use

A wide range of doses has been reported. Doses listed here represent the current consensus. Oral absorption is favored in the presence of fat, and administration of the drug with a high-fat meal can tremendously enhance the extent of absorption. Two formulations are available: microsize and ultramicrosize. Administration of a formulation made up of fine particles also will increase absorption. Veterinary formulations are generally composed of microsize preparations, and this is reflected in the dosage regimens. If the ultramicrosized preparations are used, the dose may be decreased by half. Shake oral suspension well before using. Consider 25 mg/kg q12h initially, and then increase to 50-60 mg/kg q12h for problem cases.

Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow toxicity.

Formulations

Griseofulvin is available in 125-, 250-, and 500-mg microsize tablets; 25-mg/mL oral suspension; 125-mg/mL oral syrup; and 100-, 125-, 165-, 250-, and 330-mg ultramicrosized tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Griseofulvin is insoluble in water but is soluble in alcohol.

Small Animal Dosage

Dogs and Cats

- Microsize: 50 mg/kg per day PO, up to a maximum dose of 110-132 mg/kg/day in divided treatments. Start with 25 mg/kg q12h PO and then increase to 50-60 mg/kg q12h PO for refractory cases.
- Ultramicrosize: 30 mg/kg/day in divided treatments PO.

Large Animal Dosage

Horses

- Dermatophytosis: 5.6 mg/kg q24h of the oral microsize powder. Treatment should be continued for minimum of 10 days.

Regulatory Information

No regulatory information is available for food animals. Because of potential for teratogenic effects, do not administer to food animals.

Growth Hormone

Trade and other names: Somatrem, Somatropin, Protropin, Humatrope, and Nutropin

Functional classification: Hormone

Pharmacology and Mechanism of Action

Growth hormone, also known as human growth hormone (hCG). It is administered to correct growth hormone deficiency in animals. Somatrem is a biosynthetic somatotropin.

Indications and Clinical Uses

Growth hormone is used to treat growth hormone deficiencies. The use is rare in veterinary medicine.

Precautionary Information

Adverse Reactions and Side Effects

Growth hormone is diabetogenic in all animals. Excess growth hormone causes acromegaly.

Contraindications and Precautions

No contraindications reported in animals.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

There is only limited clinical experience in animals. Dose form must be reconstituted with sterile diluent before use.

Patient Monitoring and Laboratory Tests

Monitor glucose periodically during treatment.

Formulations

Growth hormone is available in 5- and 10-mg/vial (1 mg is equal to 3 units).

Stability and Storage

Prepared solution is stable if refrigerated for 14 days. Otherwise it is stable for only 24 hours.

Small Animal Dosage

Dogs and Cats

- 0.1 units/kg three times a week for 4-6 weeks SQ or IM. (Usual human pediatric dose is 0.18-0.3 mg/kg/week SQ or IM.)

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not administer to animals that produce food.

Guaifenesin

gwye-fen'eh-sin

Trade and other names: Glyceryl guaiacolate, Guaiphenesin, Geocolate, Guailaxin, Glycotuss, Hytuss, Glytuss, Fenesin, Humabid LA, and Mucinex

Functional classification: Expectorant; muscle relaxant

Pharmacology and Mechanism of Action

Guaifenesin, which is also known as glyceryl guaiacolate, is a compound that has been an older, traditional therapy for treating cough in people, although the efficacy has been questioned for this effect. For respiratory disease, it is administered orally to produce an expectorant effect. This effect is presumably via stimulation of vagal transmission to produce more viscous bronchial secretions.

As an anesthetic adjunct, it is used as a preanesthetic with barbiturates and other drugs. It is a central-acting skeletal muscle relaxant and causes sedation and relaxation via depression of nerve transmission. Pharmacokinetic information is limited, but half-life in ponies is 60-84 minutes. Duration of action in horses is approximately 30 minutes.

Indications and Clinical Uses

Guaifenesin is administered IV (particularly in large animals) as an adjunct to anesthesia and orally in animals as an expectorant. Historically, it also has been used as an analgesic and antipyretic. Most often it is used prior to induction of general anesthesia in horses, but it also has been used in other species. Supporting data for an expectorant effect are lacking. It may increase the volume and reduce the viscosity of secretions in the trachea and bronchi. It may also facilitate removal of secretions.

Precautionary Information

Adverse Reactions and Side Effects

Minor leakage outside the vein from an intravenous injection does not cause tissue injury. However, thrombophlebitis from intravenous injection may occur. Hypotension may occur from high doses. Some hemolysis has been observed from intravenous infusion, but this is not significant at a concentration less than 15%. A vagal effect (e.g., stimulation of secretions) may occur when the drug is used as an expectorant.

Contraindications and Precautions

Do not administer IV if visible precipitate is observed.

Oral formulations for people (cough and cold remedies) may contain other ingredients such as dextromethorphan or decongestants (e.g., phenylephrine or pseudoephedrine). Do not use these combinations in animals sensitive to these drugs, and if possible use only formulations that contain guaifenesin.

Drug Interactions

No significant drug interactions are reported. It has been safely used with acepromazine, xylazine, detomidine, ketamine, thiopental, and pentobarbital.

Instructions for Use

For anesthetic purposes, 5% guaifenesin is prepared from powder (50 g/L) dissolved in sterile water. It dissolves more readily if the water is warm. Infusion of 110 mg/kg can produce transient recumbency, but usually it is administered with other agents.

Patient Monitoring and Laboratory Tests

Monitoring of animals during anesthesia (heart rate, rhythm, and respiratory rate) is suggested. Hypotension is possible; therefore blood pressure should be monitored.

Formulations

Guaifenesin is available in intravenous solutions that are prepared prior to infusion from powder to a 5% solution. It is also available in a 100- and 200-mg tablet; 600-mg extended-release tablets; and 20-mg/mL and 40-mg/mL oral solution. Human over-the-counter formulations may contain other ingredients such as dextromethorphan and decongestants.

Stability and Storage

Guaifenesin is soluble in water and in alcohol. It is more soluble in warm water. It will precipitate if the temperature is 22°C or colder. It should be administered orally shortly after preparation because stability is short. However, 10% solutions have been stable for as long as 7 days. For intravenous use it has been mixed with xylazine and ketamine, without apparent loss of stability.

Small Animal Dosage

Dogs

- Expectorant: 3-5 mg/kg q8h PO.
- Anesthetic adjunct: 2.2 mL/kg/hr of a 5% solution intravenously. Administered with α_2 agonists and ketamine.

Cats

- Expectorant: 3-5 mg/kg q8h PO.

Large Animal Dosage

Horses

- 2.2 mL/kg of a 5% solution (110 mg/kg) infused IV to horses prior to other anesthetic agents, such as ketamine. Guaifenesin solution may be infused rapidly.
- Constant rate infusion (CRI): 2.2 mg/kg/hr IV.

Regulatory Information

Withdrawal time (extralabel): 3 days meat and 48 hours milk.

RCI Classification: 4

Halothane

hal'oe-thane

Trade and other names: Fluothane

Functional classification: Inhalant anesthetic

Pharmacology and Mechanism of Action

Inhalant anesthetic. Halothane is a multi-halogenated ethane. It is characterized by rapid induction and recovery, high potency, and few adverse effects. Like other inhalant anesthetics, the mechanism of action is uncertain. They produce generalized, reversible depression of the CNS. The inhalant anesthetics vary in their solubility in blood, their potency, and the rate of induction and recovery. Those with low blood/gas partition coefficients are associated with the most rapid rates of induction and recovery. Halothane has a vapor pressure of 243 mm Hg (at 20° C), a blood/gas partition coefficient of 2.3, and a fat/blood coefficient of 51. Because of high solubility in fat, its clearance from the body is slower than other agents.

Indications and Clinical Uses

Halothane, like other inhalant anesthetics, is used for general anesthesia in animals. It has a minimum alveolar concentration (MAC) value of 1.04%, 0.87%, and 0.88% in cats, dogs, and horses, respectively. However, it has been replaced by newer inhalant anesthetics (e.g., isoflurane) in many veterinary practices.

Precautionary Information

Adverse Reactions and Side Effects

Like other inhalant anesthetics, halothane produces vasodilation and increased blood flow to cerebral blood vessels. This may increase intracranial pressure. Also like other inhalant anesthetics, it produces a dose-dependent myocardial depression, with accompanying decrease in cardiac output. It also depresses respiratory rate and alveolar ventilation. Like other inhalant anesthetics, it increases the risk of ventricular arrhythmias, especially in response to catecholamines. Hepatotoxicity has been reported in people.

Contraindications and Precautions

Administer with caution to patients with cardiovascular problems.

Drug Interactions

No specific drug interactions. Use of other anesthetics in conjunction with halothane will lower the requirement for halothane dose.

Instructions for Use

Use of inhalant anesthetics requires careful monitoring. Dose is determined by depth of anesthesia.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and rhythm and respiration during anesthesia.

Formulations

Halothane is available in a 250-mL bottle.

Stability and Storage

Halothane is highly volatile and should be stored in a tightly sealed container.

Small Animal Dosage

- Induction: 3%
- Maintenance: 0.5%-1.5%

Large Animal Dosage

- MAC value: 1%

Regulatory Information

No withdrawal times are established for food animals. Clearance is rapid, and short withdrawal times are suggested. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Hemoglobin Glutamer (Oxyglobin)

hee'moe-gloe-bin gloot'am-er

Trade and other names: Oxyglobin

Functional classification: Iron supplement, hemoglobin substitute

H

Pharmacology and Mechanism of Action

Hemoglobin glutamer (bovine) is used as oxygen-carrying fluid in dogs with varying causes of anemia. Oxyglobin is an ultrapurified polymerized bovine hemoglobin. The molecular weight is 64,000-500,000 (average 200,000). Osmolality is 300 mOsm/mL. Colloid osmotic pressure is higher than other colloids, with a colloid osmotic pressure of 43.3. Half-life in dogs is approximately 24 hours (range 18-43 hours). It is metabolized by macrophages, and 95% of a dose is eliminated in 5-9 days.

Indications and Clinical Uses

Hemoglobin glutamer has been used to treat anemia caused by blood loss, hemolysis, or decreased blood cell production. Although approved for dogs, it also has been used in cats.

Precautionary Information**Adverse Reactions and Side Effects**

Circulatory overload is possible, especially with high doses and rapid administration. Patients at the most risk of circulatory overload are those with cardiac disease, respiratory disease, risk of hypertension, cerebral edema, oliguria/anuria caused by renal failure, and cats. Pulmonary hypertension has been observed because of depletion of nitric oxide (NO) and volume overload. Because cats are more sensitive to the adverse effects than dogs, lower dose rates should be used in cats. Other adverse effects have been skin and mucous membrane discoloration, vomiting, diarrhea, and anorexia. Discoloration of skin and mucous membranes can persist for 3-5 days.

Contraindications and Precautions

Hemoglobin glutamer should not be used in dogs with advanced heart disease. Administer with caution to cats because of an increased risk of pulmonary hypertension.

Drug Interactions

Do not administer with other drugs via the same infusion set. Do not mix with other drugs.

360 Heparin Sodium

Instructions for Use

Administer using aseptic technique. In 5-7 days, 90% of dose is eliminated.

Patient Monitoring and Laboratory Tests

Patients receiving hemoglobin glutamer should be monitored carefully. Use of Oxyglobin does not require cross-matching. Monitoring packed cell volume (PCV) or hematocrit is not useful for assessing response to Oxyglobin therapy. Oxyglobin will interfere with other monitoring tests, such as blood chemistry analysis (colorimetric assays). Doses of 30 mL/kg are listed by manufacturer, but many veterinarians use 10-15 mL/kg.

Formulations

Hemoglobin glutamer is available in 13 g/dL polymerized hemoglobin of bovine origin in 125-mL single-dose bags. Availability from manufacturer may be limited.

Stability and Storage

At room temperature, hemoglobin glutamer has a 3-year shelf-life. Once opened, a 125-mL bag should be used within 24 hours because of oxidation of hemoglobin to methemoglobin. Do not freeze.

Small Animal Dosage

Dogs

- One-time dose of 10-30 mL/kg IV or up to a rate of 5-10 mL/kg/hr.

Cats

- One-time dose of 3-5 mL/kg IV, slowly. Maximum rate is 5 mg/kg/hr and not to exceed 13-20 mL/kg in 24 hours.

Large Animal Dosage

No doses reported. Do not use in race horses.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested. However, hemoglobin glutamer (Oxyglobin) is prohibited to be on the premises of racing horses.

RCI Classification: 2

Heparin Sodium

hep'ah-rin soe'dee-um

Trade and other names: Liquaemin and Hepalean (Canada)

Functional classification: Anticoagulant

Pharmacology and Mechanism of Action

Anticoagulant. Heparin produces its action by increasing antithrombin III-mediated inhibition of synthesis and activity of factor Xa. Heparin differs from low-molecular-weight heparin (LMWH) by an equal anti-factor Xa/anti-factor IIa ratio. Heparin has a ratio of 1:1, but the LMWHs have ratios of 2:1 or higher. In people, there is an advantage of LMWH over conventional heparin because the LMWHs have longer half-lives and less frequent administration is needed. However, this may not be an advantage for dogs and cats. See the description

of LMWH for more information (enoxaparin [Lovenox], and dalteparin [Fragmin]).

Indications and Clinical Uses

Heparin is administered to prevent and treat hypercoagulability disorders and prevent coagulation disorders such as thromboembolism, venous thrombosis, disseminated intravascular coagulopathy (DIC), and pulmonary thromboembolism. Use in specific situations in animals is primarily anecdotal or derived from the clinical experience in people. No outcome-based studies to evaluate efficacy have been published to support specific guidelines for therapy. Use for prevention of thrombosis in canine patients with immune-mediated hemolytic anemia has not been effective (300 units/kg q6h). In horses, it is used to prevent thrombosis in patients at risk.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects caused by excessive inhibition of coagulation result in bleeding. Heparin-induced thrombocytopenia, a problem in people, has not been cited as a problem in animals. If excessive anticoagulation and bleeding occur as a result of an overdose, protamine sulfate should be administered to reverse heparin therapy. Protamine should be administered by slow IV infusion. Protamine complexes with heparin to form a stable, inactive compound.

Contraindications and Precautions

Do not use in animals unless able to monitor bleeding because it may be life threatening. Do not inject IM because it may create a hematoma.

Drug Interactions

Use cautiously in animals that are already receiving other drugs that can interfere with coagulation, such as aspirin and warfarin. Although a specific interaction has not been identified, use cautiously in animals that may be receiving certain chondroprotective compounds, such as glycosaminoglycans for treatment of arthritis.

Instructions for Use

Dose adjustments should be performed by monitoring clotting times. For example, dose is adjusted to maintain activated partial thromboplastin time (APTT) at 1.5 to 2 times normal. For information on other forms of heparin, such as LMWHs, see dalteparin or enoxaparin. Duration of anticoagulant effect may vary among patients, but in general, a 200-unit/kg dose in dogs has a duration of effect of approximately 6 hours.

In high-risk patients, doses used include 500 units/kg SQ or IM, followed by reduced doses such as those listed in dosing section q8-12h.

Patient Monitoring and Laboratory Tests

Monitor effect using APTT or anti-Xa activity. Dose is adjusted to maintain APTT at 1.5 to 2 times normal. Target range for anti-Xa activity is 0.35-0.70 units/mL. If anti-Xa activity is greater than 70 Units/mL, reduce dose by 25%.

Formulations

Heparin sodium is available in 1000- and 10,000-units/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats (low-dose prophylaxis)

- 70 units/kg q8-12h SQ.

Dogs

- 100-200 units/kg IV loading dose, then 100-300 units/kg q6-8h SQ. Adjust dose via monitoring and increase to 500-600 units/kg if necessary. In more severe cases, start with 500 units/kg SQ as initial dose, then administer 500 units/kg q12h.

Cats

- 300 units/kg SQ, q8h and increase up to 500 units/kg if necessary.

Large Animal Dosage

- 125 units/kg SQ or IM q8-12h. (Lower doses of 80 units/kg SQ, q12h also have been used in horses.)

Regulatory Information

No regulatory information is available for food animals. Because of low risk of residues, no withdrawal times are suggested.

Hetastarch

het'ah-starch

Trade and other names: HES, Hydroxyethyl starch, Hetastarch, and Hespan

Functional classification: Fluid replacement

Pharmacology and Mechanism of Action

Hetastarch is a synthetic colloid volume expander that is used to maintain vascular volume in animals with circulatory shock. It is a modified branched-chain glucose polymer prepared from hydroxyethyl starch and is derived from amylopectin. There are two hydroxyethyl starch preparations: hetastarch and pentastarch. Hetastarch (6%) has an average molecular weight of 450,000 and colloid osmotic pressure of 32.7. Pentastarch (10%) has an average molecular weight of 280,000 and colloid osmotic pressure of 40. Because hetastarch is a larger molecular weight compound than pentastarch, it tends to remain in the vasculature and prevent loss of intravascular volume and prevent tissue edema. Other colloids used are dextrans (Dextran 40 and Dextran 70).

Indications and Clinical Uses

Hetastarch is used primarily to treat acute hypovolemia and shock. It is administered IV in acute situations. Hetastarch has a duration of effective volume expansion of 12-48 hours. One of the disadvantages to use of hetastarch is the high cost.

Precautionary Information

Adverse Reactions and Side Effects

Only limited use in veterinary medicine; therefore, adverse effects have not been reported. However, it may cause allergic reactions and hyperosmotic renal dysfunction. Hetastarch suspensions may affect platelet function at clinically relevant doses for up to 24 hours. Do not use in patients with bleeding problems or preexisting coagulopathies.

Contraindications and Precautions

Do not use in animals with bleeding problems (coagulopathies) or active hemorrhage.

Drug Interactions

Hetastarch is available compatible with most fluid solutions.

Instructions for Use

Suspend in saline (0.9%) or 5% dextrose solution for use. Administer in 5-mL/kg increments to small animals, then reassess and increase the dose to rates listed in the dosing section. Hetastarch is used in critical care situations, and it is infused via constant rate infusion (CRI). Hetastarch appears to be more effective and produce fewer side effects than Dextran. Infuse slowly.

Patient Monitoring and Laboratory Tests

Monitor patient's hydration status and blood pressure during administration. Monitor heart rate and rhythm and observe patients for evidence of bleeding. Administration of hetastarch may increase patient's amylase for 2-3 days.

Formulations

Hetastarch is available in 6% injectable solution.

Stability and Storage

Hetastarch is stable in original packaging and is compatible with most fluid administration sets.

Small Animal Dosage

Dogs

- CRI: 10-20 mL/kg/day IV (0.4-0.8 mL/kg/hr).

Cats

- CRI: 5-10 mL/kg/day IV (0.2-0.4 mL/kg/hr).

Large Animal Dosage

Horses

- 8-10 mL/kg bolus dose, or 10 mL/kg/hr or CRI 0.5-1 mL/kg/hr.
No large animal doses have been reported.

Regulatory Information

No regulatory information is available for food animals. Because of low risk of residues, no withdrawal times are suggested.

Hydralazine Hydrochloride

hye-drah-l'ah-zeen hye-droe-klor'ide

Trade and other names: Apresoline

Functional classification: Vasodilator

Pharmacology and Mechanism of Action

Vasodilator. Antihypertensive. Hydralazine relaxes vascular smooth muscle and reduces blood pressure. In arteriolar vascular beds it relaxes vascular smooth muscle to reduce vascular resistance and improves cardiac output. The mechanism of action is not certain. It may generate nitric oxide or act via other smooth muscle-relaxing properties. The peak effect occurs approximately 3-5 hours after administration, and the duration of effect on blood vessels is approximately 12 hours.

Indications and Clinical Uses

Hydralazine is used to dilate arterioles and decrease cardiac afterload. It is primarily used for treatment of CHF, valvular disease of the heart, and other cardiovascular disorders characterized by high peripheral vascular resistance. It may be used with other cardiac drugs. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. However, its use is not as common as other vasodilator drugs, such as the angiotensin-converting enzyme (ACE) inhibitors.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are attributed to excess vasodilation and subsequent hypotension, which results in tachycardia. Hydralazine may dangerously decrease cardiac output. Allergic reactions (lupus-like syndrome) have been reported in people and are related to acetylator status but have not been reported in animals. Repeated use will activate the renin-angiotensin-aldosterone system (RAAS).

Contraindications and Precautions

Do not use in hypotensive animals.

Drug Interactions

No specific drug interactions are reported for animals. However, use cautiously with other drugs that may lower blood pressure.

Instructions for Use

Use of hydralazine in heart failure may accompany other drugs, such as digoxin, pimobendan, and diuretics. Dosage in animals may be adjusted by monitoring blood pressure.

Patient Monitoring and Laboratory Tests

Monitor patients for hypotension. Monitor blood pressure to adjust dose.

Formulations

Hydralazine is available in 10-mg tablets and 20-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Exposure to light may change color and cause decomposition. Hydralazine is

unstable. Mixing with juices, syrups, and flavorings may cause decomposition in as little as 24 hours.

Small Animal Dosage

Dogs

- 0.5 mg/kg (initial dose), titrate to 0.5-2 mg/kg q12h PO.

Cats

- 2.5 mg/cat q12-24h PO.

Large Animal Dosage

Horses

- 1 mg/kg q12h PO or 0.5 mg/kg IV as needed to reduce blood pressure.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Hydrochlorothiazide

hye-droe-klor-oh-thye'ah-zide

Trade and other names: HydroDiuril and generic

Functional classification: Diuretic

Pharmacology and Mechanism of Action

Thiazide diuretic. Like other thiazide diuretics, it inhibits sodium reabsorption in distal renal tubules and causes urinary diuresis. Because thiazide diuretics act in the distal tubules (at the point where most water has already been reabsorbed), their diuretic effects are not as great as compared to loop diuretics such as furosemide.

Indications and Clinical Uses

Like other thiazide diuretics, hydrochlorothiazide is used to increase excretion of sodium, potassium, and water. It also has been used as an antihypertensive. Because thiazide diuretics decrease renal excretion of calcium, they also have been used to treat uroliths containing calcium (calcium oxylate uroliths). Use in animals has been primarily derived from anecdotal experience. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Hydrochlorothiazide may cause electrolyte imbalance such as hypokalemia.

Contraindications and Precautions

Do not use in patient with high serum calcium. Thiazide diuretics will prevent calcium excretion.

Drug Interactions

Use carefully with other diuretics. It may enhance the effects of other diuretics and antihypertensive agents.

Instructions for Use

Hydrochlorothiazide is not as potent as loop diuretics (e.g., furosemide). Clinical efficacy has not been established in veterinary patients.

Patient Monitoring and Laboratory Tests

Monitor hydration status, electrolytes, and renal function.

Formulations

Hydrochlorothiazide is available in 10- and 100-mg/mL oral solution and 25-, 50-, and 100-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 2-4 mg/kg q12h PO.

Cats

- To decrease excretion of calcium in urine: 1 mg/kg q12h, PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Hydrocodone Bitartrate

hye-droe-koe'done bye-tar'trate

Trade and other names: Hycodan

Functional classification: Antitussive, analgesic

Pharmacology and Mechanism of Action

Opioid agonist, analgesic. Like other opioids, hydrocodone is an agonist for mu-opiate and kappa-opiate receptors on nerves and inhibits release of neurotransmitters involved with transmission of pain stimuli (such as Substance P). It has similar properties as morphine, but potency may vary. Central sedative and euphoric effects related to mu-receptor effects in brain. Other opiates used in animals include hydromorphone, codeine, oxymorphone, meperidine, and fentanyl. Hycodan contains homatropine, which is added to decrease abuse by people. Hydrocodone formulations used for antitussive action may also contain guaifenesin or acetaminophen. Hydrocodone may be metabolized to hydromorphone and in some animals (e.g., dogs) the pharmacologic effects may be attributed to hydromorphone.

Indications and Clinical Uses

Hydrocodone is an opiate agonist that has analgesic and sedative properties. However, its use as a sedative or analgesic in small animals is uncommon. The oral

absorption, metabolism, and efficacy have not been studied in animals sufficiently to predict or assess clinical use. However, hydrocodone has been used in animals as an antitussive for symptomatic treatment of airway diseases and many clinicians believe (anecdotally) that it is an effective antitussive. There are no preparations marketed for use in the US that do not contain atropine. (Canadian preparations may contain only hydrocodone.) It may also contain other ingredients for treating cough.

Precautionary Information

Adverse Reactions and Side Effects

Like all opiates, side effects are predictable and unavoidable. Side effects include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses. Paradoxical excitement may occur in some animals.

Contraindications and Precautions

Do not use in patients that may be sensitive to opiate effects or experience dysphoria. Because preparations for oral use contain atropine, do not use in animals in which atropine may be contraindicated.

Drug Interactions

No specific drug interactions are reported for animals.

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Instructions for Use

Hydrocodone is combined with atropine in the product Hycodan. Atropine can decrease respiratory secretions but probably does not exert significant clinical effects at doses in this preparation (1.5 mg homatropine per 5-mg tablet).

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Hydrocodone is available in 5-mg tablets and 1-mg/mL syrup. Homatropine content: 1.5 mg in tablets and 0.3 mg/mL in syrup.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- Antitussive dose: 0.5 mg/kg, q8 hr PO.
- Analgesic dose: 0.5 mg/kg q8-12 hr, PO.

Cats

No dose reported.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Hydrocodone is a Schedule III drug controlled by the DEA.

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Schedule II controlled drug

RCI Classification: 1

Hydrocortisone

hye-droe-kor'tih-sone

Trade and other names: Hydrocortisone, Cortef and generic brands
Hydrocortisone sodium succinate, Solu-Cortef

Functional classification: Corticosteroid

Pharmacology and Mechanism of Action

Glucocorticoid anti-inflammatory drug. Hydrocortisone has weaker anti-inflammatory effects and greater mineralocorticoid effects compared with prednisolone or dexamethasone. Hydrocortisone has properties that most closely resemble natural cortisol in the body. It is about 1/5 the potency of prednisolone and 1/25 the potency of dexamethasone. Anti-inflammatory effects are complex but are primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators.

Indications and Clinical Uses

Hydrocortisone is used for anti-inflammatory effects and for glucocorticoid replacement therapy. Hydrocortisone is not used as commonly as other corticosteroids such as prednisolone or dexamethasone, except when hormone replacement to mimic effects of cortisol are needed. Hydrocortisone sodium succinate is a rapid-acting injectable product that can be used when a prompt response is needed.

Precautionary Information

Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic-pituitary-adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and UTIs. In horses, additional adverse effects include risk of laminitis.

Contraindications and Precautions

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously in diabetic animals, animals with renal failure, or pregnant animals.

Drug Interactions

Glucocorticoids are often synergistic with other anti-inflammatory and immunosuppressive drugs. Administration of corticosteroids with nonsteroidal anti-inflammatory drugs (NSAIDs) will increase the risk of GI injury.

Instructions for Use

Dose requirements are related to severity of disease. Typically for replacement therapy (such as in animals with hypoadrenocorticism) doses start at 1 mg/kg/day.

Patient Monitoring and Laboratory Tests

Monitor electrolytes (sodium and potassium) in animals being treated for hypoadrenocorticism. Monitor liver enzymes, blood glucose, and renal function

during therapy. Monitor patients for signs of secondary infections. Perform adrenocorticotropic hormone (ACTH) stimulation test to monitor adrenal function.

Formulations

Hydrocortisone is available in 5-, 10-, and 20-mg tablets and hydrocortisone sodium succinate is available in various size vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Hydrocortisone is slightly soluble in water and is soluble in alcohol. Degradation occurs at high pH above 7-9. Compounded suspensions have been stable for 30 days. Most compounded topical ointments and lotions are stable for 30 days.

Small Animal Dosage

Dogs and Cats

Hydrocortisone

- Replacement therapy: 1-2 mg/kg q12h PO.
- Anti-inflammatory: 2.5-5 mg/kg q12h PO.

Hydrocortisone Sodium Succinate

- Shock: 50-150 mg/kg IV, for 2 doses, 8 hours apart.
- Anti-inflammatory: 5 mg/kg q12h IV.

Large Animal Dosage

Horses

- Hydrocortisone sodium succinate: 5 mg/kg q12h IV.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Hydromorphone

hye-droe-mor'fone

Trade and other names: Dilaudid, Hydrostat, and generic brands

Functional classification: Analgesic, Opiate

Pharmacology and Mechanism of Action

Opioid agonist, analgesic. Like other opiates, it binds to mu-opiate and kappa-opiate receptors on nerves and inhibits release of neurotransmitters involved with transmission of pain stimuli (such as Substance P). Opiates also may inhibit release of some inflammatory mediators. Central sedative and euphoric effects are related to mu-receptor effects in brain. Hydromorphone has similar qualitative properties as morphine but is six or seven times more potent than morphine. In dogs, the half-life after IV administration was 70-80 minutes. Other opiates used in animals include morphine, codeine, oxymorphone, meperidine, and fentanyl.

Indications and Clinical Uses

Hydromorphone is used in animals for analgesia and sedation and as an adjunct for anesthesia. In dogs and cats it is used as a single agent or in combination with other agents. Hydromorphone is an opiate agonist, with effects similar to morphine.

However, it is more potent than morphine and should be used at lower doses. Because hydromorphone is less expensive than other opiates (e.g., oxymorphone), it is sometimes used instead of other drugs without evidence of superior efficacy. Hydromorphone is approximately half as potent as oxymorphone and five to seven times as potent as morphine and doses should be adjusted accordingly. Studies in dogs indicate that hydromorphone at equivalent doses is equal to oxymorphone for producing sedation in dogs. In cats, duration of effect (0.1 mg/kg) has been 6-7.5 hours.

Precautionary Information

Adverse Reactions and Side Effects

Like all opiates, side effects from hydromorphone are predictable and unavoidable. Side effects from administration include sedation, panting, constipation, urinary retention, and bradycardia. In cats, the most common adverse effects are dysphoria, hypersalivation, and vomiting. Hyperthermia also has been observed in cats, but the mechanism is not known. In dogs, hydromorphone produces less histamine release than morphine administration and therefore may produce fewer histamine-related side effects.

Respiratory depression occurs with high doses. As with other opiates, a slight decrease in heart rate is expected. In most cases this decrease does not have to be treated with anticholinergic drugs (e.g., atropine) but should be monitored. Tolerance and dependence occurs with chronic administration. In horses, undesirable and even dangerous behavior actions can follow rapid intravenous opioid administration. Horses should receive a preanesthetic of acepromazine or an α_2 agonist.

Contraindications and Precautions

Cats and horses are more sensitive to excitement than other species. Hydromorphone may cause bradycardia and AV block in some patients.

Drug Interactions

No significant interactions. Hydromorphone may be used with other anesthetics. If butorphanol is used, it may diminish the effects of hydromorphone by antagonizing mu-opiate receptors.

Instructions for Use

Hydromorphone may be used interchangeably with morphine, provided that doses are adjusted for potency differences. Administration to cats has been more effective when injected IV, rather than IM or SQ, and resulted in faster onset with fewer adverse effects. Oral tablets and solution are available for human use, but use has not been reported for animals.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, if necessary atropine or glycopyrrolate can be administered. If serious respiratory depression occurs, the opioid can be reversed with naloxone. Monitor body temperature in cats. Hyperthermia has been observed in patients postanesthesia.

Formulations

Hydromorphone is available in 1-mg/mL oral solution; 1-, 2-, 3-, 4-, 8-mg tablets; and 1-, 2-, 4-, and 10-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Hydromorphone is soluble in water. Compounded solutions in fluids have been stable for 30 days. It is a Schedule II drug and should be stored in a locked compartment.

Small Animal Dosage

Dogs

- 0.22 mg/kg IM or SQ. Repeat every 4-6 hours or as needed for pain treatment.
- 0.1-0.2 mg/kg IV, repeated every 2 hours or as necessary. A dose of 0.1 mg/kg may be used with acepromazine.

Cats

- 0.1-0.2 mg/kg SQ, IM or 0.05-0.1 mg/kg IV, q2-6h (as needed).
- Epidural dose: 0.05 mg/kg, diluted in saline to 0.2 mL/kg (1 mL per cat).

Large Animal Dosage

Horses

- Epidural: 0.04 mg/kg diluted in 0.9% saline to 20 mL.
No systemic doses have been reported.

Regulatory Information

Hydromorphone is a Schedule II drug controlled by the DEA. Withdrawal times have not been established for food animals, but the elimination rate is rapid and a brief withdrawal time is suggested. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 1

Hydroxyurea

hye-droks'ih-yoo-ree-ah

Trade and other names: Droxia and Hydrea (Canada)

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Antineoplastic agent. Hydroxyurea is a cell-cycle-dependent agent, acting primarily at the S-phase of mitosis. Exact mechanism of action is uncertain, but it may interfere with DNA synthesis in cancer cells. The specific effects on red blood cells (RBCs) occur because of the activity on hemoglobin.

Indications and Clinical Uses

In people, hydroxyurea is used for treatment of sickle cell anemia and occasionally other carcinomas. In animals it has been used in combination with other anticancer modalities for treatment of certain tumors. In animals one of the uses has been treatment of polycythemia vera.

Precautionary Information

Adverse Reactions and Side Effects

Because of only limited use in veterinary medicine, no adverse effects have been reported. In people, hydroxyurea causes leukopenia, anemia, and thrombocytopenia.

Contraindications and Precautions

Avoid use in pregnant animals.

Drug Interactions

No specific drug interactions are reported for animals.

Instructions for Use

Hydroxyurea has been used on a limited basis in veterinary medicine. Most of the use is empirical or extrapolated from human medicine.

Patient Monitoring and Laboratory Tests

Monitor CBC in treated animals.

Formulations

Hydroxyurea is available in 200-, 300-, 400-, and 500-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 50 mg/kg PO once daily, 3 days/week.

Cats

- 25 mg/kg PO once daily, 3 days/week.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Hydroxyzine hydrochloride

hye-droks'ih-zeen

Trade and other names: Atarax, Vistaril

Functional classification: Antihistamine

Pharmacology and Mechanism of Action

Antihistamine (H_1 blocker) of the piperazine class. Like other antihistamines, hydroxyzine acts by blocking the H_1 receptor and suppresses inflammatory reactions caused by histamine. The H_1 blockers have been used to control pruritus and skin inflammation, rhinorrhea, and airway inflammation. Hydroxyzine also has sedative properties and other calming effects on the central nervous system that are not related to the antihistamine effects.

Another antihistamine, cetirizine, is an active metabolite of hydroxyzine. In dogs, most of the antihistamine effect of the administration of hydroxyzine is from the formation of cetirizine, which occurs readily after IV and oral administration.

Indications and Clinical Uses

In animals it has been used to treat pruritus. Efficacy in animals for treating pruritus is low. Although it has been shown in experimental animals to suppress histamine response, it has not been consistently effective relieving pruritus in dogs with atopic dermatitis. Other uses include allergic airway disease and rhinitis. However, efficacy is not established for these uses. In people, additional uses include treatment of anxiety and psychoneurosis and as a sedative before and after general anesthesia.

Precautionary Information

Adverse Reactions and Side Effects

Sedation is the most common side effect. Sedation is the result of inhibition of histamine N-methyltransferase. Sedation may also be attributed to block of other CNS receptors such as those for serotonin, acetylcholine, and alpha-receptors. Antimuscarinic effects (atropine-like effects), such as dry mouth and decreased GI secretions, also are common.

Contraindications and Precautions

No contraindications reported in animals.

Drug Interactions

No specific drug interactions are reported for animals.

Instructions for Use

Clinical studies have shown hydroxyzine to be somewhat effective for treatment of pruritus in dogs, but efficacy rates are low.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Hydroxyzine hydrochloride is available in 10-, 25-, 50-, and 100-mg tablets; 2-mg/mL oral syrup; and 25-mg/mL injection. It is also available in a pamoate form (Vistaril) in 25-, 50-, and 100-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Hydroxyzine is soluble in water. Compounded formulation with syrups was stable for 14 days.

Small Animal Dosage

Dogs

- 2 mg/kg q8-12h IM or PO.

Cats

Effective doses have not been established.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available for food animals. Because of low risk of residues, no withdrawal times are suggested.

RCI Classification: 2

Hyoscyamine

hye-oh-sye'ah-meen

Trade and other names: Levsin

Functional classification: Anticholinergic

Pharmacology and Mechanism of Action

Anticholinergic agent (blocks acetylcholine effect at muscarinic receptor), parasympatholytic.

Indications and Clinical Uses

Hyoscyamine is an anticholinergic drug with actions similar to atropine and related drugs. It will produce an antiemetic effect to decrease vomiting associated with motion sickness and some GI diseases. It is indicated in animals for conditions in which it is important to block parasympathetic responses. It has been used to decrease GI motility and secretions, decrease salivation, and increase heart rate (to treat bradycardia).

Precautionary Information

Adverse Reactions and Side Effects

Side effects include xerostomia, ileus, constipation, tachycardia, and urine retention.

Contraindications and Precautions

Do not use in patients with glaucoma, intestinal ileus, gastroparesis, or tachycardia.

Drug Interactions

Do not mix with alkaline solutions. Hyoscyamine will antagonize the effects of any cholinergic drugs administered (e.g., metoclopramide).

Instructions for Use

Hyoscyamine is used primarily in dogs for cardiovascular and GI diseases.

Patient Monitoring and Laboratory Tests

Monitor heart rate and intestinal motility during treatment.

Formulations

Hyoscyamine is available in 0.125-mg tablets, 0.375-mg extended-release tablets, and 0.025-mg/mL solution.

Stability and Storage

Store in a tightly sealed container at room temperature.

Small Animal Dosage

Dogs

- 0.003-0.006 mg/kg q8h PO.

Cats

No doses have been established for cats.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not use in animals that produce food.

Withdrawal time: None established in US (manufacturer of large animal products lists 0 days milk and meat), but listed as 14 days for meat and 3 days for milk in the UK.

Ibuprofen

eye-byoo-proe'fen

Trade and Other Names: Motrin, Advil, and Nuprin

Functional Classification: Nonsteroidal anti-inflammatory drug (NSAID)

Pharmacology and Mechanism of Action

Like other NSAIDs in this class, ibuprofen produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the cyclo-oxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations and COX-2 activity is important for some biological effects. Ibuprofen is not selective for either COX-1 or COX-2. Ibuprofen is registered for human use, and experience with this drug in veterinary medicine is limited.

Pharmacokinetics have been studied in a variety of animals. In horses, the half-life is approximately 60-90 minutes. Oral absorption is high in horses (80%-90%) regardless of the dose form used, including a compounded paste. Ibuprofen was 90%-100% absorbed when administered orally to dairy goats.

Indications and Clinical Uses

Ibuprofen is not registered for any animals in veterinary medicine. There are drugs in small animals that have been safer for the GI tract and are preferred. Use of ibuprofen in dogs is discouraged because of high risk of GI ulceration. It has been used for musculoskeletal inflammation in horses and ruminants. Administration of 25 mg/kg IV to cows reduced some systemic variables in endotoxin-induced mastitis.

In horses, doses of 10-25 mg/kg have been used, but clinical trials of efficacy have not been reported.

Precautionary Information

Adverse Reactions and Side Effects

Vomiting, severe gastrointestinal ulceration, and hemorrhage have been reported in dogs. Like other NSAIDs, renal injury caused by decrease renal perfusion has occurred with ibuprofen. Ibuprofen may inhibit platelets in animals.

Contraindications and Precautions

Safe doses have not been established for dogs and cats. Do not administer to animals prone to GI ulcers. Do not administer with other ulcerogenic drugs such as corticosteroids.

Drug Interactions

No specific drug interactions are reported. However, like other NSAIDs, ulcerogenic effects are potentiated when administered with corticosteroids. Ibuprofen, like other NSAIDs, may interfere with the action of diuretics, such as furosemide and angiotensin-converting enzyme (ACE) inhibitors.

Instructions for Use

Avoid use in dogs. Safe dosages for other species have not been established, although there has been some off-label use in ruminants and horses.

Patient Monitoring and Laboratory Tests

Monitor for signs of GI ulcers. Monitor renal function during therapy.

Formulations

Ibuprofen is available in 200-, 400-, 600-, and 800-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It has been compounded in alcohol (ethanol) and propylene glycol solutions without loss of stability. It is poorly soluble in water. It has been compounded as an oral paste for horses without compromising the oral absorption.

Small Animal Dosage

Dogs and Cats

Safe dose not established.

Large Animal Dosage

Horses

- 25 mg/kg q8h PO, up to 6 days.

Ruminants

- 14-25 mg/kg/day.

Regulatory Information

No withdrawal times are established for animals intended for food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Imidocarb Hydrochloride

im-id'oh-carb hye-droe-klor'ide

Trade and Other Names: Imizol

Functional Classification: Antiprotozoal

Pharmacology and Mechanism of Action

Imidocarb is an aromatic diamidine. It inhibits nucleic acid metabolism in susceptible organisms and produces anticholinergic effects. Antimicrobial activity against protozoal organisms accounts for its clinical use.

Indications and Clinical Uses

Imidocarb has been used in animals to treat intracellular tickborne pathogens. It has been used to treat *Babesia* infections. In addition, it has been used to treat haemobartonellosis in cats caused by the organisms *Mycoplasma haemofelis* and *Mycoplasma haemominutum*. It also has been used to treat *Cytauxzoon felis* infections in cats and ehrlichial infections in dogs and cats.

Precautionary Information

Adverse Reactions and Side Effects

No toxic reactions were observed in trials with experimental cats. Transient pain or discomfort may occur at the site of injection.

Contraindications and Precautions

No specific contraindications are reported.

Drug Interactions

No drug interactions have been reported.

Instructions for Use

Use of imidocarb has been limited in animals. Most protocols are established from small clinical trials or extrapolation from human use.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Imidocarb compounded formulations are available from some pharmacies.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Cats

- 5 mg/kg IM twice, q14d.

Dogs

- (*Ehrlichia canis*): 6.6 mg/kg IM, twice, q14d.

Large Animal Dosage

No large animal doses are available.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Imipenem + Cilastatin

ih-mih-pen'em + sye-lah-stat'in

Trade and Other Names: Primaxin

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Imipenem + cilastatin is a beta-lactam antibiotic of the carbapenems class with a broad spectrum of activity. Action on the cell wall is similar to other beta-lactams, which is to bind penicillin-binding proteins (PBP) that weaken or interfere with cell wall formation. The carbapenems are capable of binding to a specific PBP (PBP-1) that results in more rapid lysis compared to other beta-lactams. This results in greater bactericidal activity and a longer postantibiotic effect. Carbapenems have a broad spectrum of activity and are among the most active of all antibiotics. Spectrum includes gram-negative bacilli, including *Enterobacteriaceae* and

Pseudomonas aeruginosa. It also is active against most gram-positive bacteria, except methicillin-resistant strains of *Staphylococcus* and *Enterococcus*. Compared to imipenem, meropenem and doripenem are slightly more active. Cilastatin has no antibacterial activity, but it is a specific inhibitor of renal dipeptidase, dehydropeptidase (DHP-I). Therefore, cilastatin blocks renal tubular metabolism of imipenem and improves urinary recovery of imipenem.

Indications and Clinical Uses

Imipenem is used primarily for infections caused by bacteria resistant to other drugs. Imipenem is especially valuable for treating resistant infections caused by *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*. Although active against gram-positive bacteria such as staphylococci (but not methicillin-resistant strains), other less expensive drugs should be used for gram-positive infections. Meropenem and doripenem are newer drugs in the class of carbapenems and have some advantages with respect to activity and convenience of administration.

Precautionary Information

Adverse Reactions and Side Effects

Allergic reactions may occur with beta-lactam antibiotics. With rapid infusion or in patients with renal insufficiency neurotoxicity may occur. Neurotoxicity in animals has included tremors, nystagmus, and seizures. Nephrotoxicity is possible, but imipenem is combined with cilastatin to decrease renal metabolism. Vomiting and nausea are possible. Intramuscular injections can cause painful reactions.

Contraindications and Precautions

Use cautiously in patients prone to seizures. Seizures may be more likely in patients with renal failure.

Drug Interactions

No known drug interactions. Do not mix with other drugs in vial.

Instructions for Use

Doses and efficacy studies have not been determined in animals. Recommendations are based on extrapolation of studies performed in humans. Reserve the use of this drug for resistant, refractory infections. Observe manufacturer's instructions carefully for proper administration. When the vial is initially reconstituted, it should not be given IV. It first must be diluted in a suitable intravenous fluid solution (at least 100 mL). For intravenous administration, add to intravenous fluids. After reconstitution in vial, 250 or 500 mg should be added to not less than 100 mL of fluids and given IV over 30-60 minutes. Intravenous fluid solutions are stable for 48 hours if refrigerated or 8 hours at room temperature. For intramuscular administration, add 2 mL lidocaine (1%). The suspension is stable for only 1 hour. In some hospitals, the intravenous solution has been diluted in fluids and administered SQ without any sign of injection-site reactions (usually 8-14 mL per injection in dogs).

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are ≤ 1 mcg/mL. Most veterinary pathogens have minimum inhibitory concentration (MIC) values less than 1.0 mcg/mL.

Formulations

Imipenem + cilastatin is available in 250- and 500-mg vials for injection. Intramuscular suspension is available in 500- and 750-mg vials.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. After reconstitution it is stable for 4 hours at room temperature and 24 hours refrigerated. Do not freeze intravenous fluid solutions. Slight yellow discoloration is acceptable, but discard if color turns brown.

Small Animal Dosage

Dogs and Cats

- 3-10 mg/kg q6-8h IV or IM. Generally, 5 mg/kg q6-8h IV, IM, or SQ.

Large Animal Dosage

Horses

- 10-20 mg/kg q6h by slow IV infusion.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Imipramine Hydrochloride

im-ip'rah-meen hye-droe-klor'ide

Trade and Other Names: Tofranil and generic brand

Functional Classification: Behavior modification

Pharmacology and Mechanism of Action

Tricyclic antidepressant drug (TCA). Imipramine, like others in this class, is used in people to treat anxiety and depression. Action is via inhibition of uptake of serotonin and norepinephrine at presynaptic nerve terminals. Other TCA drugs used in animals include clomipramine and amitriptyline.

Indications and Clinical Uses

Like other TCAs, imipramine is used in animals to treat a variety of behavioral disorders, including obsessive-compulsive disorders, separation anxiety, and inappropriate urination. There have been fewer studies of efficacy with imipramine than with clomipramine or amitriptyline. Generally, other behavior-modifying drugs such as SSRIs (eg, fluoxetine) or other TCAs (clomipramine) are preferred by behavior experts for treating small animals.

Precautionary Information

Adverse Reactions and Side Effects

Multiple side effects are associated with TCAs, such as antimuscarinic effects (dry mouth and rapid heart rate) and antihistamine effects (sedation). Overdoses can produce life-threatening cardiotoxicity.

Contraindications and Precautions

Use cautiously in patients with heart disease.

Drug Interactions

Do not use with other behavior-modifying drugs, such as serotonin reuptake inhibitors. Do not use with monoamine oxidase inhibitors (MAOIs) such as selegiline.

Instructions for Use

Doses are primarily based on empiricism. There are few controlled efficacy trials available for animals to compare with other drugs in this class. There may be a 2- to 4-week delay after initiation of therapy before beneficial effects are seen.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm in treated animals. Like other TCAs, imipramine may decrease total T4 and free-T4 concentrations in dogs.

Formulations

Imipramine is available in 10-, 25-, and 50-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Although imipramine has been compounded for veterinary use, the potency and stability has not been evaluated for compounded products.

Small Animal Dosage**Dogs**

- 2-4 mg/kg q12-24h PO.

Cats

- 0.5-1 mg/kg q12-24h PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 2

Indomethacin

in-doe-meth'ah-sin

Trade and Other Names: Indocin

Functional Classification: Nonsteroidal anti-inflammatory drug (NSAID)

Pharmacology and Mechanism of Action

NSAID and analgesic. Like other NSAIDs, indomethacin produces potent analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the cyclo-oxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain,

382 Indomethacin

inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations and COX-2 activity is important for some biological effects. Indomethacin is considered a prototype for a nonselective drug because it inhibits equally both COX-1 and COX-2. Indomethacin is registered for human use and experience with this drug in veterinary medicine is limited. Indomethacin acts to inhibit COX that synthesizes prostaglandins. Other anti-inflammatory effects may occur (such as effects on leukocytes) but have not been well characterized. It is used primarily for short-term treatment of moderate pain and inflammation.

Indications and Clinical Uses

Indomethacin, like other NSAIDs, has been used to treat pain and inflammation in people. However, indomethacin has not been used often in clinical veterinary medicine because other safer, registered drugs are available. Indomethacin is used as a prototypical nonselective COX-1 and COX-2 blocker in research. In dogs, the high risk of GI ulceration prohibits its routine use.

Precautionary Information

Adverse Reactions and Side Effects

Indomethacin has produced severe GI ulceration and hemorrhage in dogs. Indomethacin, like other NSAIDs, may cause renal injury via inhibition of renal prostaglandins.

Contraindications and Precautions

Do not use in dogs or cats.

Drug Interactions

Like other NSAIDs, there are several drug interactions possible. NSAIDs have the potential to interfere with the action of diuretics, such as furosemide, and angiotensin-converting enzyme (ACE) inhibitors, such as enalapril. Corticosteroids, when used with NSAIDs, will increase the risk of ulceration.

Instructions for Use

Use cautiously, if at all, because safe doses have not been determined for clinical use in animals.

Patient Monitoring and Laboratory Tests

Monitor for signs of GI toxicity (hemorrhage, ulcers, and perforation).

Formulations

Indomethacin is available in 25- and 50-mg capsules and 5-mg/mL oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Indomethacin is practically insoluble in water but is soluble in ethanol. It decomposes in alkaline conditions and is maximally stable at pH 3.75.

Small Animal Dosage

Dogs and Cats

Safe dose has not been established.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Insulin

in'syoo-lin

Trade and Other Names: ProZinc, Lente insulin, Ultralente insulin, Regular insulin, Glargine insulin, NPH insulin, Caninsulin, Protamine zinc insulin (PZI), Humulin (human insulin; discontinued), Vetsulin is porcine insulin zinc suspension (veterinary), and PZI Vet (veterinary protamine zinc insulin)

Functional Classification: Hormone

Pharmacology and Mechanism of Action

Insulin has multiple effects associated with utilization of glucose. Dog insulin is identical to pork insulin, and cat insulin is similar to beef insulin with only one amino acid difference. Most beef-pork insulin combinations for humans have been discontinued and are not usually available for veterinary use. Human-recombinant insulins can be used in dogs and cats with the same effects as natural insulin. Insulin is available in several preparations:

1. **Regular insulin:** Short acting. Peak is 1-5 hours and duration is 4-10 hours.
2. **Neutral Protamine Hagedorn** (isophane, also called NPH, and Humulin or Novolin): A human-recombinant insulin of crystalline suspension with protamine zinc that is intermediate acting. Peak is 2-10 hours in dogs and 2-8 hours in cats with a duration of action of 4-24 hours in dogs and 4-12 hours in cats (but usually 2-3 hours in cats).
3. **Lente insulin.** Peak is 2-10 hours in dogs and 2-8 hours in cats with a duration of action of 4-24 hours in dogs and 4-12 hours in cats. Addition of protamine or zinc to insulin will produce a crystallized insulin in suspension that has a longer absorption rate than dissolved insulin. The lente forms of insulin control their duration by the size of the crystal. For example, semilente is practically amorphous, whereas ultralente has large crystals, and lente is a combination of ultralente and semilente.
4. **Ultralente insulin:** Peak is 4-16 hours in dogs and 2-14 hours in cats and has a duration of 8-28 hours in dogs and 12-24 hours in cats. It is poorly absorbed in cats and usually not recommended.
5. **Vetsulin:** Also known as Caninsulin. Vetsulin is a U-40 porcine insulin, identical to canine insulin in amino acid content, and is a lente insulin of aqueous zinc suspension of crystalline and noncrystalline insulins. It produces a shorter peak of activity (4 hours) and duration than PZI insulin. This product has been temporarily suspended by some sources.
6. **Protamine-zinc insulin (PZI):** Developed from recombinant human insulin and long acting. Veterinary form is called ProZinc in a 40 unit/mL form for cats. The forms used in animals are identical to the forms marketed for people. Peak is 4-14 hours in dogs and 5-7 hours in cats, with a duration of 6-28 hours in dogs and cats. PZI insulin of animal origin (90% bovine and 10% porcine) has been unavailable.

7. **Glargine insulin:** A human insulin analogue made from recombinant technology. It has a slow onset of 4-18 hours and a duration of 24 hours or greater. This analogue is produced by the substitution of glycine for asparagine and addition of two arginine molecules. These changes shift the isoelectric point toward neutral, which reduces solubility at the pH of SQ tissue and causes it to be released slowly from the injection site, without a peak. It produces consistent concentrations without large fluctuation in peak and trough. It has four amino acid differences from feline insulin. The glucose-lowering properties are shorter in cats than in people, with a peak at 16 hours and duration of 24 hours. However, it produces greater glycemic control in cats than other insulins. Remission rates are highest with glargine insulin in cats. Despite the long-lasting effect, optimum control is achieved with twice-daily dosing in cats with Glargine insulin.
8. **Insulin detemir (Levemir):** Long-acting insulin. Insulin detemir has a 14 carbon fatty acid chain, which decreases absorption, and is highly bound to albumin. Duration is 6-24 hours in people, with peak at 6-8 hours, but has not been established for animals.
9. **Insulin glulisine (Apidra), insulin lispro (Humalog), and insulin aspart (NovoLog):** Rapidly acting insulins used in people. They are used for their rapid onset and short duration of action. In people, they are typically used with a meal and combined with a longer-acting form. These rapid-acting insulin analogues have not been evaluated for animals.

Indications and Clinical Uses

Insulin, in the various forms, is used to treat diabetes mellitus in dogs and cats. It is used to replace insulin that is deficient. In some cats (approximately 50%) some oral hypoglycemic drugs have been used to reduce use of insulin. However, diabetic dogs are more insulin dependent. Regular insulin is short acting and more useful for emergencies such as diabetic ketoacidosis or acute nonketotic syndromes.

Intermediate or long-acting insulin preparations are used for maintenance and are available in a variety of forms (see previous). Most of the animal sources of insulin (beef and pork) have been discontinued and human recombinant insulin formulations have been substituted without differences in efficacy. In cats, glargine insulin has shown better efficacy than other forms and has been associated with a better remission rate. In addition to diabetes mellitus, insulin is occasionally used to treat severe cases of hyperkalemia.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects primarily related to overdoses that result in hypoglycemia.

Glargine insulin has a low pH (4) and may sting from injection. Other insulins are more neutral.

Contraindications and Precautions

Do not use without the ability to monitor glucose in animals because of the risk of hypoglycemia. Mixing regular insulin and insulins containing zinc in the same syringe will prolong absorption of the regular insulin. Do not mix isophane insulin or phosphate-buffered insulin with zinc insulins (lente, ultralente, semilente).

Drug Interactions

Administration of corticosteroids (prednisolone, dexamethasone, etc.) will interfere with action of insulin.

Instructions for Use

Dietary management is essential for optimal glucose control. Feed cats a high-protein, low-carbohydrate diet. Feed dogs a high-fiber, low-fat diet. Doses should be carefully adjusted in each patient depending on response.

For cats with ketoacidosis, alternative dosing regimen has used 0.2 units/kg IM initially, then 0.1 units/kg IM every hour until the glucose level is less than 300, then 0.25-0.4 units/kg q6h SQ. With most forms of insulin (including protamine zinc insulin and Gargine insulin) in cats, twice-daily dosing usually is required. However, consider once-daily dosing in cats if blood glucose nadir develops 10 hours or longer after administration. Pet owners are instructed to use appropriate syringe types for administration (e.g., U-40 vs. U-100). Many cats, if properly managed, may go into remission and not require lifelong insulin treatment.

Patient Monitoring and Laboratory Tests

Monitor blood glucose, glycosylated hemoglobin, and/or fructosamine concentrations. When treating diabetes, it is desirable to maintain glucose concentrations between 100 and 300 mg/dL, with the nadir (lowest point) being 80-150 mg/dL. Serum fructosamine concentrations also can be monitored with the following guidance: ≤ 450 $\mu\text{mol/L}$ good control; 450-500 $\mu\text{mol/L}$ moderate control; > 500 $\mu\text{mol/L}$ poor control.

Formulations

Insulin is usually available in 100 units/mL injection (U-100), with some products available in smaller concentration of 40 units/mL (U-40, e.g., ProZinc or Vetsulin). Protamine zinc beef-pork (PZI VET) insulin also may be available as 40 units/mL injection (U-40). Some previously available insulin products have been discontinued, such as Iletin II Pork Insulin (Regular and NPH formulations), Humulin U Ultralente, and Humulin L Lente (Humulin U and Humulin L).

Stability and Storage

Proper storage is critical for proper action of insulin: Keep refrigerated. Warm gently and roll vial prior to injection to ensure proper mixing of vial contents. Do *not* freeze vials of insulin. Do *not* allow vials of insulin exposure to heat. Do not mix types of insulin in the same vial or syringe. Veterinarians should not use formulations of insulin that are compounded in unreliable conditions. Dilution of insulin should only be done by a pharmacist because specific diluents must be used.

Small Animal Dosage

Dogs

- Ketoacidosis for dogs < 3 kg: 1 unit/animal initially, then 1 unit/animal q1h; for dogs 3-10 kg: 2 units/animal initially, then 1 unit/animal q1h; and for dogs > 10 kg: 0.25 unit/kg initially, then 0.1 unit/kg q1h IM.
- NPH for dogs < 15 kg: 1 unit/kg q12-24h SQ (adjust dose with monitoring); dogs > 25 kg: 0.5 unit/kg q12-24h SQ (adjust dose with monitoring).
- Vetsulin: Initial dose 0.5 U/kg, once or twice daily, SQ. Adjust dose (increase or decrease of 25% of dose) by monitoring.

Cats

- Ketoacidosis: 0.2 unit/kg IM initially, then 0.1 unit/kg IM every hour until glucose level is less than 300 mg/dL and then continue with 0.25-0.4 unit/kg SQ q6h.
- NPH not recommended for cats.

386 Interferon

- Ultralente and PZI insulin: Initial dose is 0.5 unit/kg SQ and then once or twice daily (usually twice is needed) with subsequent doses adjusted to produce desirable glucose levels, usually no higher than 3 units per cat. Final adjusted dose for most cats is 0.9 (\pm 0.4) unit/kg.
- Glargine insulin: Start with 0.5 U/kg q12h, SQ. Some cats can be managed with once-daily dosing. Adjust dose via monitoring.

Regulatory Information

No regulatory information is available for animals intended for food. Because of low risk of residues, no withdrawal times are suggested.

Interferon

in-ter-feer'on

Trade and Other Names: Virbagen omega

Functional Classification: Immunostimulant

Pharmacology and Mechanism of Action

Recombinant omega interferon contained in Virbagen omega is produced by silkworms previously inoculated with interferon-recombinant baculovirus. It allows the production of pure interferon. Omega interferon of feline origin, produced by genetic engineering, is a Type 1 interferon closely related to alpha interferon. The exact mechanism of action of interferon omega is not understood, but it may enhance nonspecific defenses in dogs and cats. Interferon does not act directly and specifically on the pathogenic virus but exerts its effect by inhibition of the internal synthesis mechanisms of the infected cells. After injection it has a half-life of 1.4 hours in dogs and 1.7 hours in cats. It is bound to receptors in cells infected by virus.

There are multiple interferons available for human use (e.g., treatment of AIDS-related diseases and cancer-associated diseases). These interferons may be alpha-2a, alpha 2b, n-1, and n-3. These types of interferons are not interchangeable.

Indications and Clinical Uses

Interferon is used to stimulate the immune system in patients. It has been used to stimulate immune cells in dogs with parvovirus and in cats with feline retrovirus (feline leukemia virus [FeLV] and feline immunodeficiency virus [FIV]). It has not been effective for FIP in cats. Human interferon alpha, orally, has improved clinical signs in cats with FIV.

Precautionary Information

Adverse Reactions and Side Effects

It may induce vomiting and nausea. In some animals it may induce hyperthermia 3-6 hours after injection. In cats, it may produce soft feces to mild diarrhea. A slight decrease in white blood cells, platelets, and red blood cells and an increase in the concentration of alanine aminotransferase may be observed. These parameters usually return to normal in the week following the last injection. In cats, it may induce transient fatigue during the treatment.

In people, injections of interferon alpha have been associated with influenza-like symptoms. Other effects, such as bone marrow suppression, also have been reported in people.

Contraindications and Precautions

Do not vaccinate dogs or cats receiving interferon.

Drug Interactions

Do not mix with any other vaccine/immunological product, except the solvent supplied for use with the product.

Instructions for Use

Doses and indications for animals have primarily been based on extrapolation of human recommendations, experimental studies, or specific studies in cats with viral infections.

Patient Monitoring and Laboratory Tests

Monitor CBC during treatment.

Formulations Available

Interferon is available in 5- and 10-million units/vial. The freeze-dried fraction must be reconstituted with 1 mL of the specific diluent to obtain, depending on the presentation, a solution containing 5 million units or 10 million units of recombinant interferon.

Stability and Storage

Interferon has a shelf life of 2 years. The product should be used immediately after reconstitution and should be stored in its original carton. Store and transport at $4^{\circ}\text{C} \pm 2^{\circ}\text{C}$. Do not freeze.

Small Animal Dosage

Dogs

- 2.5 million units/kg IV once daily for 3 consecutive days.

Cats

- 1 million units/kg IV once daily for 5 consecutive days. Three separate 5-day treatments must be performed at day 0, day 14, and day 60.
- 10 units/kg human interferon alpha on an alternate-week schedule, oral.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not administer to animals intended for food.

Iodide

eye'-oh-dyde

Trade and Other Names: Potassium iodide, EDDI, ethylenediamine dihydroiodide.

Functional Classification: Iodine supplement

Pharmacology and Mechanism of Action

Iodide is administered as a supplement. Although its action for treating disease is not well established, it is administered as an adjunctive for zygomycosis, conidiobolomycosis, and fungal granuloma. The mechanism of action against fungal organisms is not known. Iodide is also important for thyroid gland function and has been used to treat some thyroid disorders.

Indications and Clinical Uses

Ethylenediamine dihydroiodide is used as a nutritional source of iodine in cattle. Iodide has been used to treat fungal granulomatous disease and infections associated with zygomycetes. The antifungal treatment has been questioned for animals because the efficacy is not established. Because it may increase respiratory secretions, it has been used as an expectorant, but the efficacy has not been established. In people, iodide has been used to treat hyperthyroidism, but effectiveness for this use in cats has not been established. Potassium iodide is also used to protect the thyroid gland from radiation injury in the event of a radiation emergency (accidental exposure to radiation) or following administration of radioactive iodide. In cattle, in addition to a feed supplement, EDDI is used as an expectorant and as an aid in the treatment of bovine infertility. EDDI is sometimes added to the feed of cattle for the purpose of decreasing foot rot infections, lumpy jaw (*Actinomyces bovis*), woody tongue (*Actinobacillus lignieresii*), and bronchitis. There is a lack of published scientific evidence for a beneficial effect. In horses iodine is used to treat sporotrichosis, and occasionally other fungal infections such as basidiobolomycosis and conidiobolomycosis (Zygomycosis). For horses, treatment is initiated with doses listed in the dosing section below, and to prevent relapse treatment is continued for 4 weeks beyond resolution of clinical signs.

Precautionary Information

Adverse Reactions and Side Effects

Iodide adverse reactions (iodism) include excess lacrimation, swelling of eyelids, nonproductive cough, increased respiratory secretions, and dermatitis. Its use may cause abortion in horses or limb deformities in foals.

Contraindications and Precautions

Do not use in pregnant animals.

Drug Interactions

No drug interactions have been reported for small animals.

Instructions for Use

Iodide has been administered as a 1-g/mL potassium iodine solution (SSKI) or as a 65-mg/mL solution. It also has been administered as a 10% potassium iodide/5% iodine solution given orally with food.

In cattle, EDDI is administered in the feed or mixed with feed, salt, or mineral mixture or in the drinking water.

Patient Monitoring and Laboratory Tests

Monitor serum thyroid concentrations with prolonged use.

Formulations

Available for food animals as EDDI: equivalent to 4.6% EDDI or 46 mg/g of EDDI. Also available as potassium iodide as 1 g/mL potassium iodide solution (SSKI) or a 65-mg/mL oral solution or 10% potassium iodide/5% iodine solution.

Inorganic potassium iodide has been used in horses orally but must be obtained as the chemical grade and compounded for horses.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze solutions. Inorganic potassium iodide is unstable in light, heat, and excess humidity.

Small Animal Dosage

Dogs and Cats

- Fungal infections: Start with 5 mg/kg q8h, PO, and increase gradually to 25 mg/kg q8h, PO.
- Emergency treatment after radiation exposure: 2 mg/kg PO per day.
- Expectorant: 5 mg/kg q8h, PO

Large Animal Dosage

Cattle

- Feed supplement: 50-217 mg EDDI per head per day (mix with feed).
- Expectorant and other indications: 650-1300 mg EDDI per head twice daily PO for 7 days.

Horses (treatment of fungal granuloma)

- 20-40 mg/kg per day, IV for 7-10 days (using 20% sodium iodide).
- 10-40 mg/kg per day, PO (using inorganic potassium iodide).
- 0.86-1.72 mg/kg of EDDI, or use 20-40 mg/kg per day of the 4.6% organic iodine dextrose base of EDDI, PO.

Regulatory Information

Withdrawal times in food-producing animals has not been established.

Ipecac

ih'peh-kak

Trade and Other Names: Ipecac and Syrup of ipecac

Functional Classification: Emetic

Pharmacology and Mechanism of Action

Emetic drug. Ipecac contains two alkaloids: cephalin and emetine. These alkaloids stimulate gastric receptors linked to the chemoreceptor trigger zone (CRTZ) to stimulate vomiting.

Indications and Clinical Uses

Ipecac is indicated for emergency treatment of poisoning. When used in animals, it should be administered promptly after poisoning. Inducing vomiting with ipecac is not effective beyond 30-60 minutes after poisoning. After successful administration, it is estimated that vomiting removes only 10%-60% of ingested toxicant. Therefore, other systemic antidotes and/or activated charcoal should also be considered.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects with acute therapy for poisoning. Chronic administration can lead to myocardial toxicity.

Contraindications and Precautions

Do not induce vomiting if the patient has ingested caustic chemicals or if there is a risk of aspiration pneumonia.

Drug Interactions

Ipecac is not as effective if drugs that act as antiemetics have been administered. Such drugs include tranquilizers (e.g., acepromazine), anticholinergics (e.g., atropine), antihistamines, and prokinetic agents (e.g., metoclopramide).

Instructions for Use

Ipecac is available as nonprescription drug. Onset of vomiting may require 20-30 minutes.

Patient Monitoring and Laboratory Tests

Poisoned animals should be monitored closely because ipecac may not entirely eliminate ingested toxicant.

Formulations

Ipecac is available in a 30-mL bottle oral solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 3-6 mL/dog PO.

Cat

- 2-6 mL/cat PO.

Large Animal Dosage

Not recommended for large animals.

Regulatory Information

No regulatory information is available for animals intended for food. Because of low risk of residues, no withdrawal times are suggested.

Iodate, Iopanoic Acid

ih'poe-date and i-oh-pa-noe'-ik as-id

Trade and Other Names: Orografin, Calcium iodate, Iodopanoic acid

Functional Classification: Antithyroid agent

Pharmacology and Mechanism of Action

Cholecystographic agent. This drug is an iodinated biliary radiocontrast dye. Iodate inhibits deiodinases responsible for conversion of thyroid hormone T₄ to T₃. It also blocks T₃ receptors. It lowers the T₃ level but not the T₄ levels.

Indications and Clinical Uses

Iodate is used as treatment for hyperthyroidism in cats. Reduction of T₃ levels should occur within 1 week. The use is not as common as other treatments, but it has been administered as an alternative to methimazole, radiation therapy, or surgery. Response rate may be as high as 66%. Iodate formulations may not be

available to veterinarians and iopanoic acid has been used as a substitute. If iopanoic acid (Telepaque) is used as a substitute, it may be less effective.

Precautionary Information

Adverse Reactions and Side Effects

Iodate can cause hypothyroidism. No significant adverse effects have been reported in cats, but compounds containing iodide have caused hypersensitivity reactions in people. In humans, chronic high doses of compounds containing iodide can cause sore mouth, swollen tissues, skin reactions, or GI upset.

Contraindications and Precautions

Monitor for reduction of thyroid levels in animals or clinical signs. Relapses have occurred in cats after 10 weeks to 6 months of treatment.

Drug Interactions

No drug interactions have been reported for small animals.

Instructions for Use

Use of iodate has been experimental, and precise doses have not been evaluated. In one study, two thirds of treated cats responded. More experience is needed to determine if response to treatment is transient.

Patient Monitoring and Laboratory Tests

Monitor serum thyroid T3 concentrations. Iodate lowers the T-3 level but the T-4 levels may be unchanged or may increase because of decreased conversion of T4 to T3.

Formulations

Iodate has been available as either calcium or sodium iodate. Orografin 500-mg capsules have been formulated into 50-mg capsules by pharmacists. (These may have to be specifically formulated for cats.) Availability of Orografin has become a problem for veterinarians and iopanoic acid (Telepaque) has been used as a substitute. It is formulated into capsules for cats.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Cats

- Iodate: 15 mg/kg q12h PO. Most common dose has been 50 mg/cat twice daily. Dose is equivalent regardless of whether sodium or calcium iodate is used.
- Iopanoic Acid: 50 mg per cat, q12h, PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not administer to animals intended for food.

Irbesartan

er-beh-sar'tan

Trade and Other Names: Avapro

Functional Classification: Vasodilator

Pharmacology and Mechanism of Action

Vasodilator. Angiotensin receptor blocker (ARB). Irbesartan has been shown to block angiotensin II receptors and prevent the effects associated with angiotensin II. It has been used in people who cannot tolerate angiotensin-converting enzyme (ACE) inhibitors. The metabolism in dogs and cats is uncertain and it is not known if doses extrapolated from human use have equivalent activity in dogs and cats. Losartan, another ARB, is used as an alternative in people but is reportedly not effective in dogs because they do not produce the active metabolite.

Indications and Clinical Uses

Angiotensin II blockers, such as irbesartan, are used in people as alternatives to ACE inhibitors. However, they are rarely used in animals because most animals tolerate ACE inhibitors well. Use of ARB in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects have been reported in animals. Hypotension is a potential problem from overdosing.

Contraindications and Precautions

Do not administer to hypotensive or dehydrated animals. No other contraindications have been reported for animals.

Drug Interactions

No drug interactions have been reported for small animals. Use cautiously with other vasodilators.

Instructions for Use

In dogs, irbesartan is preferred over losartan because losartan is not converted to active products in dogs.

Patient Monitoring and Laboratory Tests

Monitor blood pressure and heart rate in treated animals. Monitor electrolytes if it is administered long term.

Formulations

Irbesartan is available in 75-, 150-, and 300-mg tablets. One product (Avalide) contains irbesartan in combination with hydrochlorothiazide.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 30-60 mg/kg q12h PO. Start with 30 mg/kg to avoid prerenal azotemia and hypotension.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Iron Dextran

Trade and Other Names: AmTech Iron Dextran, Ferrodex, and HemaJect

Functional Classification: Mineral supplement

Pharmacology and Mechanism of Action

Iron supplement. Iron dextran is injected in animals (most commonly pigs) for prevention of iron-deficiency anemia. Iron dextran injection contains either 100 mg elemental iron per mL or 200 mg per mL. Ferric hydroxide is complexed with a low-molecular-weight dextran in this formulation.

Indications and Clinical Uses

Use in animals, primarily young pigs, for treatment and prevention of iron-deficiency anemia. Injections are usually made IM at 1 to 4 days of age.

Precautionary Information

Adverse Reactions and Side Effects

Injections may produce transient myositis and muscle weakness.

Contraindications and Precautions

No specific contraindications.

Drug Interactions

No drug interactions are reported.

Instructions for Use

Inject in midportion of rear thigh muscle in pigs.

Patient Monitoring and Laboratory Tests

Monitor iron concentrations in treated animals and CBC to monitor effectiveness.

Formulations

Iron dextran is 100 or 200 elemental iron per mL.

Stability and Storage

Store in a tightly sealed container, at room temperature, protected from light. Do not mix with other solutions.

Small Animal Dosage

No dose is reported for small animals.

Large Animal Dosage

Pigs

- 100 mg (1 mL) IM to 2 to 4 day-old pigs and repeat in 10 days.
- 200 mg (1 mL of higher concentration) IM to pigs at 1-3 days of age.

Regulatory Information

No withdrawal time is necessary.

Isoflupredone Acetate

eye-soe-floo'preh-done ass'ih-tate

Trade and Other Names: Predef 2X

Functional Classification: Corticosteroid

Pharmacology and Mechanism of Action

Corticosteroid. Anti-inflammatory and immunosuppressive effects are approximately 17 times more potent than cortisol and 4 times more potent than prednisolone. Anti-inflammatory effects are complex but primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. Use is for treatment of inflammatory and immune-mediated disease.

Indications and Clinical Uses

Isoflupredone acetate is used for treating various musculoskeletal, allergic, and systemic inflammatory diseases. Large animal uses include inflammatory disorders, especially musculoskeletal inflammation, and recurrent airway disease (RAO) (formerly called chronic obstructive pulmonary disease [COPD]) in horses. Isoflupredone acetate, like other corticosteroids, has been used to treat ketosis in cattle. In large animals, it also has been used to treat septic shock. However, efficacy for using corticosteroids to treat septic shock is not supported by evidence.

Precautionary Information

Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic-pituitary adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and UTIs. In horses, additional adverse effects include risk of laminitis, although a clear association between laminitis and corticosteroids has not been established.

Contraindications and Precautions

Use with caution in patients prone to infection or GI ulcers. Administration of isoflupredone may induce hepatopathy, diabetes mellitus, or hyperlipidemia. Use cautiously in pregnant animals or in young, rapidly growing animals. Use of corticosteroids may impair healing.

Drug Interactions

Corticosteroids will increase risk of GI ulceration when administered with nonsteroidal anti-inflammatory drugs (NSAIDs).

Instructions for Use

When administered to treat primary ketosis in cattle, it is advised to also administer intravenous glucose.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform adrenocorticotrophic (ACTH) stimulation test to monitor adrenal function.

Formulations

Isoflupredone is available in a 2-mg injection in 10- and 100-mL vials.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- No doses are listed for isoflupredone because it is generally not administered to small animals. However, based on anti-inflammatory potency, doses of 0.125-0.25 mg/kg/day IM can be considered.

Large Animal Dosage**Cattle**

- 10-20 mg total dose per animal q12-24h IM.
- Ketosis: 10-20 mg as a total single dose per animal q12-24h IM.

Horses

- 5-20 mg total dose per animal q12-24h IM.
- Pulmonary disease: 0.02-0.03 mg/kg q24h.
- Intraarticular: 5-20 mg per joint.

Pigs

- 0.036 mg/kg/day IM.

Regulatory Information

Cattle and pig withdrawal time (meat): 7 days.

No milk withdrawal time is listed for US labeling. In Canada, withdrawal times are listed as 5 days for meat and 72 hours for milk.

For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Isoflurane

eye-soe-floo'rane

Trade and Other Names: Aerrane

Functional Classification: Anesthetic

Pharmacology and Mechanism of Action

Inhalant anesthetic. Like other inhalant anesthetics, the mechanism of action is uncertain. Isoflurane produces a generalized, reversible depression of the CNS. Inhalant anesthetics vary in their solubility in blood, their potency, and the rate of induction and recovery. Those with low blood/gas partition coefficients are associated with the most rapid rates of induction and recovery. Isoflurane has a vapor pressure of 250 mm Hg (at 20°C), a blood/gas partition coefficient of 1.4, and a fat/blood coefficient of 45.

Indications and Clinical Uses

Isoflurane, like other inhalant anesthetics, is used for general anesthesia in animals. It is associated with rapid induction of anesthesia and rapid recovery rates. It is metabolized to only a small percent (<1%) and has minimal effects on other organs. It has a minimum alveolar concentration (MAC) value of 1.63%, 1.3%, and 1.31% in cats, dogs, and horses, respectively.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are related to anesthetic effects (e.g., cardiovascular and respiratory depression).

Contraindications and Precautions

Do not administer unless it is possible to control ventilation and monitor heart rate and rhythm.

Drug Interactions

No drug interactions are reported. However, like other inhalant anesthetics, other anesthetic agents act synergistically and will lower dose requirement.

Instructions for Use

Use of inhalant anesthetics requires careful monitoring. Dose is determined by depth of anesthesia.

Patient Monitoring and Laboratory Tests

Monitor respiratory rate, heart rate, and rhythm during administration.

Formulations

Isoflurane is available in a 100-mL bottle.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- Induction: 5%, maintenance: 1.5%-2.5%.

Large Animal Dosage

- MAC value: 1.5%-2%.

Regulatory Information

Withdrawal times are not established for animals that produce food. Clearance is rapid, and short withdrawal times are suggested.

For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Isoniazid

eye-soe-nye'-a-zid

Trade and Other Names: INH, Isonicotinic Acid Hydrazide

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Antibacterial agent. Mechanism of action is via interference with lipid and nucleic acid biosynthesis in actively growing tubercle bacilli.

Indications and Clinical Uses

Isoniazid is used in people to treat tuberculosis. In animals it is used to treat atypical bacteria infections, such as those caused by *Mycobacterium*.

Precautionary Information

Adverse Reactions and Side Effects

The use is uncommon in animals and adverse effects have not been well-documented. Hepatic toxicity is the most serious concern when isoniazid is used in people. Other reported adverse effects include rash and peripheral neuropathy.

Contraindications and Precautions

No specific contraindications have been reported for animals. However, it should not be used in animals with evidence of hepatic disease.

Drug Interactions

Isoniazid metabolism may be decreased by itraconazole and increased by rifampin.

Instructions for Use

Isoniazid administration in animals is limited to indications where other drugs are not effective.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes. Monitor patients for signs of neurologic toxicity.

Formulations

Isoniazid is available in 100-, 300-, and 500-mg tablets; 10-mg/mL syrup; or 100-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- 5 mg/kg per day, (up to 10-15 mg/kg/day) PO, IM, IV. It also is administered as 15 mg/kg 2 to 3 times per week.

Large Animal Dosage

- No dose reported.

Regulatory Information

No withdrawal time has been established for large animals. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Isoproterenol Hydrochloride

eye-soe-proe-teer'eh-nole hye-droe-klor'ide

Trade and Other Names: Isuprel and Isoprenaline hydrochloride

Functional Classification: Beta-agonist

Pharmacology and Mechanism of Action

Adrenergic agonist. Isoproterenol stimulates both beta₁- and beta₂-adrenergic receptors. Like other beta-agonists, it stimulates activity of adenylyl cyclase. In cardiac tissue, isoproterenol is one of the most potent agonists and will increase rate, conduction, and contractility. Beta-agonists will also relax bronchial smooth muscle and arterial smooth muscle. It has a rapid onset of activity, with rapid systemic clearance and short duration of action.

Indications and Clinical Uses

Isoproterenol is administered when it is necessary for prompt stimulation of the heart (inotropic and chronotropic) or to relieve acute bronchoconstriction. It is short acting and must be administered IV or via inhalation.

Precautionary Information

Adverse Reactions and Side Effects

Isoproterenol causes adverse effects related to excessive adrenergic stimulation, seen primarily as tachycardia and tachyarrhythmias. High doses can cause calcium accumulation in myocardium and tissue injury. Adrenergic agonists can produce potassium imbalance in animals.

Contraindications and Precautions

Do not use if formulation turns pink or a dark color.

Drug Interactions

Isoproterenol will potentiate other adrenergic agonists. Treatment will potentiate cardiac arrhythmias and should be used cautiously with other arrhythmogenic drugs.

Instructions for Use

Because of a short half-life, isoproterenol must be infused via constant rate infusion (CRI) or repeated if administered IM or SQ. It is recommended for short-term use only because repeated treatment will cause cardiac injury.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during treatment. Monitor serum potassium with repeated use.

Formulations

Isoproterenol is available in 0.2-mg/mL ampules for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water with good aqueous stability. It is susceptible to light, and if a dark color is observed, it should be discarded (pink to brownish color). Solutions above pH 6.0 may decompose more rapidly. In 5% dextrose solutions it is stable for 24 hours. It has been added to ultrasonic nebulizers in distilled water for respiratory

therapy and was stable in solution for 24 hours. It also is stable if mixed with cromolyn sodium.

Small Animal Dosage

Dogs and Cats

- 10 mcg/kg q6h IM or SQ.
- Dilute 1 mg in 500 mL of 5% dextrose or lactated Ringer's solution and infuse IV 0.5-1 mL/min (1-2 mcg/min) or to effect.
- CRI: Administer to effect at 0.01-0.1 mcg/kg/min.

Large Animal Dosage

- 1 mcg/kg q15min IV, until desired response.

Regulatory Information

No regulatory information is available for animals intended for food. Because of low risk of residues, no withdrawal times are suggested.

RCI Classification: 2

Isosorbide Dinitrate, Isosorbide Mononitrate

eye-soe-sor'bide dye-nye'trate, eye-soe-sor'bide mahn-oh-neye'trate

Trade and Other Names: Isosorbide dinitrate: Isordil, Isorbid, and Sorbitrate and Isosorbide mononitrate: Monoket

Functional Classification: Vasodilator

Pharmacology and Mechanism of Action

Nitrate vasodilator. Like other nitrovasodilators, it produces vasodilation via generation of nitric oxide. It relaxes vascular smooth muscle, especially venous. Isosorbide mononitrate is a biologically active form of isosorbide dinitrate. Compared to isosorbide dinitrate, it does not undergo first-pass metabolism and is completely absorbed orally.

Indications and Clinical Uses

Isosorbide dinitrate is used to reduce preload in patients with CHF. In people, it is primarily used to treat angina. The use in animals has not been established, and nitroglycerin is used more frequently (topically) or infusions of nitroprusside IV are used in critical care situations. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are primarily related to overdoses that produce excess vasodilation and hypotension. Tolerance may develop with repeated doses.

Contraindications and Precautions

Do not administer to patients with hypovolemia. Use cautiously in animals with low cardiac reserve.

Drug Interactions

No drug interactions are reported.

400 Isotretinoin

Instructions for Use

Generally, doses are titrated to individuals depending on response. Isosorbide mononitrate is absorbed better than isosorbide dinitrate and may be preferred in clinical situations.

Patient Monitoring and Laboratory Tests

Monitor patient's cardiovascular status during treatment.

Formulations

Isosorbide dinitrate is available in 2.5-, 5-, 10-, 20-, 30-, and 40-mg tablets and 40-mg capsules.

Isosorbide mononitrate is available in 10- and 20-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- Isosorbide dinitrate: 2.5-5 mg/animal q12h PO or 0.22-1.1 mg/kg q12h PO.
- Isosorbide mononitrate: 5 mg/dog; administer two doses per day 7 hours apart PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

There is a low risk of residue potential.

RCI Classification: 4

Isotretinoin

eye-soe-tret'ih-noe-in

Trade and Other Names: Accutane

Functional Classification: Dermatologic agent

Pharmacology and Mechanism of Action

Isotretinoin is a keratinization-stabilizing drug. Isotretinoin reduces sebaceous gland size, inhibits sebaceous gland activity, and decreases sebum secretion. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Indications and Clinical Uses

In people, it is primarily used to treat acne. In animals it has been used to treat sebaceous adenitis.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects not reported for animals, although experimental studies have demonstrated that it can cause focal calcification (such as in myocardium and vessels).

Contraindications and Precautions

Isotretinoin is absolutely contraindicated in pregnant animals because of fetal abnormalities.

Drug Interactions

No drug interactions are reported.

Instructions for Use

Use in veterinary medicine is confined to limited clinical experience and extrapolation from human reports. High expense of this medication has limited veterinary use.

Patient Monitoring and Laboratory Tests

No monitoring is necessary for animal use.

Formulations

Isotretinoin is available in 10-, 20-, and 40-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage**Dogs**

- 1-3 mg/kg/day (up to a maximum recommended dose of 3-4 mg/kg/day PO).

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not use in animals intended for food.

Isoxsuprine

eye-soks'yoo-preen

Trade and Other Names: Vasodilan and generic brands

Functional Classification: Vasodilator

Pharmacology and Mechanism of Action

Vasodilator. The mechanism of action for isoxsuprine has not been identified. It has been suggested to act as a beta₂-agonist (for which experimental evidence is not supportive) or by increasing concentrations of nitric oxide. It also may inhibit mechanisms that are calcium dependent. It relaxes vessels in digits of horses.

Indications and Clinical Uses

Isoxsuprine is used in horses for navicular disease and other diseases of the foot, such as laminitis. The efficacy has not been established for these indications, even though the use has persisted for many years. There are no reports of its use in other animals.

Precautionary Information

Adverse Reactions and Side Effects

Hypotension is the primary adverse effect. It lowers arterial pressure. In horses, side effects may also include rubbing noses on objects, hyperexcitability, sweating, tachycardia, and restlessness.

Contraindications and Precautions

Do not use in hypotensive or dehydrated animals.

Drug Interactions

No drug interactions are reported.

Instructions for Use

When used in horses, it often is used with other vasodilators and anti-inflammatory drugs. It is not known if it acts synergistically with these other medications.

Patient Monitoring and Laboratory Tests

Monitor heart rate in treated animals.

Formulations

Isoxsuprine is available in 10- and 20-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Although isoxsuprine is compounded for equine use, stability of compounded formulations has not been evaluated.

Small Animal Dosage

No small animal doses are reported.

Large Animal Dosage

Horses

- Navicular disease and laminitis: 0.6 mg/kg q12h PO, for 6 to 14 weeks. In some dosing protocols, if 0.6 mg/kg q12h has not improved horse's condition within 3 weeks, the dose has been doubled.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Itraconazole

it-rah-kahn'ah-zole

Trade and Other Names: Sporanox and Itrafungol (available in Europe for cats)

Functional Classification: Antifungal

Pharmacology and Mechanism of Action

Azole (triazole) antifungal drug. Itraconazole inhibits ergosterol synthesis in fungal cell membrane. Fungistatic. It is active against dermatophytes and systemic fungi, such as *Blastomyces*, *Histoplasma*, and *Coccidioides*. It is more potent against these

fungi than ketoconazole. Itraconazole can be incorporated into sebum and stratum corneum and can be detected in skin for 3-4 weeks after treatment.

Experience in dogs and cats has shown it to be absorbed orally and doses have been established for treating systemic fungal infections and dermatophytes. In horses, the oral solution is better absorbed than the capsules (65% vs. 12%). The half-life for the solution is 11 hours.

Indications and Clinical Uses

Itraconazole is used to treat dermatophytes and systemic fungi, such as *Blastomyces*, *Histoplasma*, and *Coccidioides*. It also has been shown effective for treatment of *Malassezia* dermatitis, but doses are lower than for other infections (see dosing section). Although it has been used to treat infections caused by aspergillosis, efficacy has not been as good as with other antifungal drugs such as voriconazole or amphotericin B. Itraconazole is often considered the first choice for dermatophyte infections in cats.

Precautionary Information

Adverse Reactions and Side Effects

Itraconazole is better tolerated than ketoconazole. Ketoconazole inhibits hormone synthesis and can lower concentrations of cortisol, testosterone, and other hormones in animals. However, itraconazole has little effect on these enzymes and will not produce endocrine effects. However, vomiting and hepatotoxicity are possible, especially at high doses. In one study, hepatotoxicity was more likely at high doses. Some 10%-15% of dogs will develop high liver enzyme levels. Itraconazole has produced skin lesions in dogs, consisting of vasculitis, sterile suppurative skin lesions, and ulcerative skin lesions. High doses in cats caused vomiting and anorexia.

Contraindications and Precautions

Dose with food for best oral absorption. Compounded formulations may not be bioequivalent to proprietary forms. Use cautiously in any animal with signs of liver disease. Use cautiously in pregnant animals. At high doses in laboratory animals, it has caused fetal abnormalities.

Drug Interactions

Antacid drugs (proton pump inhibitors or H₂-receptor blockers) will decrease oral absorption. Itraconazole is a cytochrome P450 enzyme inhibitor. It may cause drug interactions because of inhibition of P450 enzymes. The extent of cytochrome P450 inhibition is not as high as for ketoconazole but may be important for some of the low therapeutic index drugs (see Appendix).

Instructions for Use

Administer with food for best absorption, unless the oral solution is used. Doses are based on studies in animals in which itraconazole has been used to treat blastomycosis in dogs. Lower doses may be used in cats and dogs for dermatophytes and in dogs for treating *Malassezia* dermatitis. Doses in horses are based on specific pharmacokinetic studies. Other uses or doses are based on empiricism or extrapolation from human literature.

Patient Monitoring and Laboratory Tests

Monitor liver enzyme concentrations.

Formulations Available

Itraconazole is available in 100-mg capsules and 10-mg/mL oral liquid. Itrafungol for cats is 10-mg/mL oral liquid (available in Europe).

Stability and Storage

Itraconazole is practically insoluble in water but is soluble in ethanol. It is unstable and may lose potency if not maintained in manufacturer's original formulation (capsules and solution). Compounded formulations are highly unstable and insoluble. Oral absorption of extemporaneously compounded itraconazole suspensions and capsules has been poor and is not recommended. Oral commercial formulation (in cyclodextran) has a pH of approximately 2.0 and the pH should be maintained to ensure optimal absorption. Do not freeze.

Small Animal Dosage

Dogs

- 2.5 mg/kg q12h or 5 mg/kg q24h PO.
- Dermatophytes: 3 mg/kg/day for 15 days.
- *Malassezia* dermatitis: 5 mg/kg q24h PO for 2 days, repeated each week for 3 weeks.

Cats

- 5 mg/kg q12h PO (25-50 mg per cat).
- Dermatophytes: 1.5-3 mg/kg (up to 5 mg/kg) q24h PO for 15 days (although some cats needed an additional 15-day course of therapy).
- 5-10 mg/kg q24h PO for 7 days, then alternating with 1 week on and 1 week off.

Large Animal Dosage

Horses

- 5 mg/kg/day (2.5 mg/kg q12h) PO. In horses, the capsules are absorbed poorly and inconsistently. Use the oral solution (Sporanox) for optimum oral absorption.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Ivermectin

eye-ver-mek'tin

Trade and Other Names: Heartguard, Ivomec, Eqvalan liquid, Equimectrin, IverEase, Zimecterin, Privermectin, Ultramectin, Ivercide, Ivercare, and Ivermax. Acarexx is a topical form for cats.

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic drug. Avermectins (ivermectin-like drugs) and milbemycins (milbemycin and moxidectin) are macrocyclic lactones and share similarities, including mechanism of action. These drugs are neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in parasites. Paralysis and death of the parasite are caused by increased permeability to chloride ions and hyperpolarization of nerve cells. These drugs also potentiate other chloride channels, including ones gated by GABA. Mammals ordinarily are not affected because they lack glutamate-gated chloride

channels, and there is a lower affinity for other mammalian chloride channels. Because these drugs ordinarily do not penetrate the blood–brain barrier, GABA-gated channels in the CNS of mammals are not affected. Ivermectin is active against intestinal parasites, mites, bots, heartworm microfilaria, and developing larvae. Ivermectin can also produce heartworm adulticide effects when administered long-term. Ivermectin has no effect on trematode or cestode parasites.

Indications and Clinical Uses

Ivermectin is used in horses for the treatment and control of large strongyles (adult) (*Strongylus vulgaris*, *Strongylus edentatus*, and *Triodontophorus* species), small strongyles (adult and fourth stage larvae) (*Cyathostomum* species, *Cylicocycclus* species, *Cylicostephanus* species), pinworms (adult and fourth-stage larvae) (*Oxyuris equi*), large roundworms (adult) (*Parascaris equorum*), hairworms (adult) (*Trichostrongylus axei*), large mouth stomach worms (adult) (*Habronema muscae*), neck threadworms (microfilariae) (*Onchocerca* species), and stomach bots (*Gastrophilus* species). In cattle it is used for treatment and control of GI nematodes (adults and fourth-stage larvae) (*Haemonchus placei*, *Ostertagia ostertagi*) (including inhibited larvae), *O. lyrata*, *Trichostrongylus axei*, *T. colubriformis*, *Cooperia oncophora*, *C. punctata*, *C. pectinata*, *Oesophagostomum radiatum*, *Nematodirus helvetianus* (adults only), *N. spathiger* (adults only), *Bunostomum phlebotomum*; lungworms (adults and fourth-stage larvae) (*Dictyocaulus viviparus*); grubs (parasitic stages) (*Hypoderma bovis*, *H. lineatum*); sucking lice (*Linognathus vituli*, *Haematopinus euryesternus*, *Solenopotes capillatus*); and mites (scabies) (*Psoroptes ovis* [syn. *P. communis* var. *bovis*], *Sarcoptes scabiei* var. *bovis*).

In pigs it is used for treatment and control of GI roundworms (adults and fourth-stage larvae) (large roundworm, *Ascaris suum*; red stomach worm, *Hyostromylylus rubidus*; nodular worm, *Oesophagostomum* species; threadworm, *Strongyloides ransomi* (adults only); somatic roundworm larvae (threadworm, *Strongyloides ransomi* [somatic larvae]); lungworms (*Metastrongylus* species [adults only]); lice (*Haematopinus suis*); and mites (*Sarcoptes scabiei* var. *suis*).

In small animals (dogs and cats) it is used as a heartworm preventative (low dose) or to treat external parasites (mites) and intestinal parasites at higher doses. The benefit for heartworm prophylaxis in animals is the ability to kill young larvae, older larvae, and immature or young adults and adult filariae. Ivermectin is an effective microfilaricide after adulticide therapy. Ivermectin has been recommended by the America Heartworm Society to treat heartworm positive dogs for 2-3 months prior to adulticide therapy. This allows immature worms to reach full maturity that are more susceptible to melarsomine, as well as preventing new infection. Ivermectin can also reduce numbers of adult heartworms when administered long-term at preventative doses. For optimal heartworm adulticide effect, it is often administered with oral doxycycline (10 mg/kg per day) for several months. Treatment of *Demodex* infections is effective but requires higher doses than for any other indication.

Precautionary Information

Adverse Reactions and Side Effects

Toxicity may occur at high doses and in breeds in which ivermectin crosses the blood–brain barrier. Sensitive breeds include Collies, Australian shepherds, Old English sheepdogs, Longhaired Whippets, and Shetland sheepdogs. Toxicity is neurotoxic and signs include hypersalivation, depression, ataxia, difficulty with vision, coma, and death. Sensitivity to ivermectin occurs in certain breeds because of a mutation in the multidrug resistance gene (MDR1) that codes for the membrane pump p-glycoprotein (p-gp). This mutation affects the efflux pump in the blood–brain barrier. Therefore, ivermectin can accumulate in the brain of

susceptible animals. High doses in normal animals may also produce similar toxicosis. Most nonsusceptible dogs can tolerate doses of 100-400 mcg/kg. But sensitive breeds (dogs with MDR mutation) may exhibit toxicity at doses of 150-340 mcg/kg. Ivermectin at doses of 400 mcg/kg has produced neurological toxicosis in Siamese kittens, and doses as low as 300 mcg/kg have been lethal in kittens. Retinopathy has also been observed in dogs administered high doses. In affected animals, a sudden onset of blindness and/or mydriasis may occur, but dogs recover if the drug is discontinued. In horses, adverse reactions may include itching because of effects on microfilariae.

Contraindications and Precautions

Do not administer to animals younger than 6 weeks of age. Animals with high numbers of microfilaremia may show adverse reactions to high doses. If dogs are sensitive to ivermectin (see earlier list of breeds), they may be sensitive to other drugs in this class (avermectins). Ivermectin at approved clinical doses for treatment of endoparasites or heartworm prevention has been safe in pregnant animals. At high doses used for treating demodicosis, safety is not known, but there have been no reports of teratogenic effects. In the most sensitive laboratory animal (mouse) the lowest dose that is teratogenic is 400 mcg/kg. Dogs with MDR mutation may also be sensitive to other drugs such as loperamide, milbemycin, moxidectin, and anticancer drugs. Ivermectin is excreted in milk.

Drug Interactions

Do not administer with drugs that could potentially increase the penetration of ivermectin across the blood-brain barrier. Such drugs include ketoconazole, itraconazole, cyclosporine, and calcium-channel blockers.

Instructions for Use

Ivermectin is used in a wide range of animals for internal and external parasites. Dosage regimens vary, depending on the species and parasite treated. Heartworm prevention is the lowest dose; other parasites require higher doses. Heartguard and a topical form are the only forms approved for small animals; for other indications, large animal injectable products are often administered PO, IM, or SQ to small animals. Do not administer IV. Injections in pigs should be made in the neck only. Because some dogs may be sensitive to ivermectin, if a dog has not previously received ivermectin and high doses are needed (e.g., to treat *Demodex*), start with a low dose (50-100 mcg/kg), then increase by increments of 50-100 mcg/kg/day on subsequent doses every day. During this increase the dog should be observed for signs of CNS toxicity (ataxia, tremors, sedation). Once the maintenance dose is achieved, it should be administered once daily until 4 weeks after the second consecutive negative monthly skin scraping.

Patient Monitoring and Laboratory Tests

Monitor for microfilaremia prior to administration in small animals. For other parasitic infections, confirm successful treatment with fecal examinations or skin scrapings.

Formulations

Ivermectin is available in 1% (10 mg/mL) and 0.27% (2.7 mg/mL) injectable solution; 10-mg/mL oral solution; 0.8-mg/mL oral sheep drench; 18.7-mg/mL oral paste; 68-, 136-, and 272-mcg tablets; and 55- and 165-mg feline tablets. A water-soluble topical is 0.01% (0.1 mg/mL), available in ampules in foil pouches for treating ear mites in cats.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Heartworm preventative: 6 mcg/kg q30day PO.
- Prior to adulticide treatment: Administer preventative dose for up to three months prior to adulticide treatment.
- Microfilaricide: 50 mcg/kg PO 2 weeks after adulticide therapy.
- Heartworm adulticide: Ivermectin administered at preventive doses, combined with doxycycline at 10 mg/kg, PO, per day, periodically (4 weeks at a time) for several months.
- Ectoparasite therapy: 200-400 mcg/kg (0.2-0.4 mg/kg) IM, SQ, or PO.
- Endoparasites: 200-400 mcg/kg (0.2-0.4 mg/kg) weekly SQ or PO.
- Demodicosis therapy: Start with 100 mcg/kg/day (0.1 mg/kg) and increase dose by 100 mcg/kg/day to 600 mcg/kg/day (0.6 mg/kg) for 60-120 days, PO. (Successful treatment is confirmed with negative skin scrapings.)
- Sarcoptic mange and Cheyletiellosis therapy: 200-400 mcg/kg q7days PO or q14 days SQ for 4-6 weeks.

Cats

- Heartworm preventative: 24 mcg/kg q30 days PO.
- Ectoparasite therapy: 200-400 mcg/kg (0.2-0.4 mg/kg) IM, SQ, or PO.
- Endoparasite therapy: 200-400 mcg/kg (0.2-0.4 mg/kg) weekly SQ or PO.
- Topical: 0.5 mL per ear (0.1 mg/mL) for treating ear mites.

Large Animal Dosage

Horses

- 200 mcg/kg (0.2 mg/kg) IM, oral paste, or oral solution.

Calves

- Slow-release bolus: 5.7-13.8 mg/kg, as a single dose, which has a duration of 135 days.

Cattle and Goats

- Injection solution: 200 mcg (0.2 mg) per kg as a single dose SQ.

Pigs

- 300 mcg (0.3 mg) per kg, SQ as a single dose.

Sheep

- Injection solution: 200 mcg (0.2 mg) per kg as a single dose SQ.
- 200 mcg/kg PO.

Regulatory Information

Pigs withdrawal time (meat): 18 days for SQ injection.

Cattle and calves withdrawal time (meat): 35 days cattle for SQ injection or 180 days for slow-release bolus. 48 days for topical (pour-on).

Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age.

Sheep withdrawal time (meat): 11 days.

Goats withdrawal time: 11-14 days (meat) and 6-9 hours (milk). When administering SQ to goats use 35 hours for meat and 40 hours for milk.

Ivermectin + Praziquantel

eye-ver-mek'tin + pray-zih-kwon'tel

Trade and Other Names: Equimax

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic drug. Ivermectin + praziquantel are indicated for use in horses for treatment and control of tapeworms, large strongyles (including *Strongylus vulgaris*, *S. edentatus*, *S. equines*), and small strongyles, pinworms, ascarids, hairworms, stomach worms, bots, *Habronema* spp., and other parasites.

Indications and Clinical Uses

Ivermectin has properties as described in the Ivermectin monograph. Praziquantel is added to this formulation to increase the spectrum.

Precautionary Information

Adverse Reactions and Side Effects

Toxicity may occur at high doses. Ivermectin appears to be safe for pregnant animals.

Contraindications and Precautions

Ivermectin can be administered to breeding, pregnant, and lactating animals without adverse effects.

Drug Interactions

Use cautiously with other drugs that may affect penetration across the blood-brain barrier.

Instructions for Use

Use of this drug is similar to individual drugs ivermectin and praziquantel.

Patient Monitoring and Laboratory Tests

Fecal samples should be examined for parasites to monitor effectiveness.

Formulations

Ivermectin + praziquantel is available in a paste composed of 1.87% ivermectin and 14.03% praziquantel.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

No dose available for small animals.

Large Animal Dosage

Horses

- 200 mcg/kg ivermectin and 1 mg/kg praziquantel PO.

Regulatory Information

No withdrawal times are available for animals intended for food (extralabel use).

Kanamycin Sulfate

kan-ah-mye'sin sul'fate

Trade and Other Names: Kantrim

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Aminoglycoside antibiotic. Bactericidal. Like other aminoglycosides, kanamycin acts to inhibit bacteria protein synthesis via binding to 30S ribosome. Kanamycin has a broad spectrum of activity that includes *Staphylococcus* spp. and gram-negative bacilli. It has weak activity against streptococci and anaerobic bacteria. Kanamycin is not as active against most bacteria as gentamicin or amikacin.

Indications and Clinical Uses

Kanamycin is a broad-spectrum antibiotic used to treat gram-negative infections. It is less active than gentamicin, amikacin, or tobramycin. Therefore, there is little advantage for using kanamycin over the other drugs in this class.

Precautionary Information

Adverse Reactions and Side Effects

Nephrotoxicity is the most dose-limiting toxicity. Ensure that patients have adequate fluid and electrolyte balance during therapy. Ototoxicity and vestibulotoxicity also are possible.

Contraindications and Precautions

Do not use in animals with renal disease. Do not use in dehydrated animals.

Drug Interactions

When used with anesthetic agents, neuromuscular blockade is possible with high doses. Do not mix in vial or syringe with other antibiotics. Ototoxicity and nephrotoxicity are potentiated by loop diuretics such as furosemide.

Instructions for Use

Kanamycin is not as active as other aminoglycosides. For serious infections consider gentamicin or amikacin.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI minimum inhibitory concentration (MIC) value break point for susceptibility is less than or equal to 16 mcg/mL. Monitor BUN, creatinine, and urine for evidence of renal toxicity.

Formulations

Kanamycin is available in 200- and 500-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water but is not stable in compounded formulations. Do not mix with other drugs. Do not freeze.

Small Animal Dosage

Dogs and Cats

- 10 mg/kg q12h IV or IM.
- 20 mg/kg q24h IV or IM.

Large Animal Dosage

Horses

- 10 mg/kg q24h IV.

Regulatory Information

Avoid use in food-producing animals. Extended withdrawal times (as long as 18 months) may be needed for withdrawal time in cattle. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Kaolin + Pectin

kay'oh-lin + pek'tin

Trade and Other Names: Generic brands only

Functional Classification: Antidiarrheal

Pharmacology and Mechanism of Action

Antidiarrheal compound. Kaolin is a form of aluminum silicate and pectin is a carbohydrate that is extracted from the rinds of citrus fruits. This product has a claim to act as a demulcent and adsorbent in the treatment of diarrhea. The action of kaolin-pectin is believed to be related to binding of bacterial toxins (endotoxins and enterotoxins) in the GI tract. However, experimental studies have shown that kaolin-pectin has been an ineffective binder of *E. coli* enterotoxin and clinical studies have failed to show a benefit from the administration of kaolin-pectin. This product may change the consistency of stools, but it will not decrease fluid or electrolyte loss, nor will it shorten the duration of illness. Kao-Pectate formulations contain salicylate as one of the active ingredients.

Indications and Clinical Uses

Kaolin and pectin combinations are used for the symptomatic treatment of acute diarrhea. Despite the lack of clinical evidence of efficacy, some veterinarians administer this drug for short-term treatment. Commercial forms that contain salicylate (8.68 mg/mL) may have anti-inflammatory effects to decrease secretory diarrhea caused by bacteria.

Precautionary Information

Adverse Reactions and Side Effects

Side effects are uncommon. There is 8.7-mg/mL salicylate in the regular strength and 16 mg/mL in the extra-strength formulation. Because some animals may be sensitive to salicylates, this ingredient in the formulation should be considered before administering to animals.

Contraindications and Precautions

No specific contraindications in animals.

Drug Interactions

No drug interactions are reported. However, the kaolin component may prevent absorption of other drugs. Administer other oral drugs 30 minutes prior to kaolin-pectin to avoid drug interaction.

Instructions for Use

Kaolin-pectin may not change the course of diarrhea but may change the character of the feces.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Kaolin-pectin is no longer found in the product Kao Pectate (previously available in a 12 oz. oral suspension). All formulations for Kao-Pectate contain bismuth subsalicylate. Salicylate (8.68 mg/mL) is present in Kao-Pectate.

Veterinary formulations of kaolin-pectin are available under various generic names in 1-quart and 1-gallon containers containing 5.8 g of kaolin and 0.139 g of pectin per 30 mL (one ounce).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 1-2 mL/kg q2-6h PO.

Large Animal Dosage

Horses and Cattle

- 180-300 mL q2-3h PO.

Calves and Foals

- 90-120 mL q2-3h PO.

Regulatory Information

There is little risk of residues in animals that produce food. No withdrawal times are necessary.

Ketamine Hydrochloride

ket'ah-meen hye-droe-klor'ide

Trade and Other Names: Ketalar, Ketavet, and Vetalar

Functional Classification: Anesthetic

Pharmacology and Mechanism of Action

Anesthetic agent. Exact mechanism of action is not known, but most evidence supports its action as a centrally acting dissociative agent. Ketamine produces mild analgesia and modulates pain via its ability to act as a noncompetitive antagonist for n-methyl D-aspartate (NMDA) receptors. Ketamine is an equal concentration of two isomers (R-ketamine and S-ketamine). S-ketamine is more active and eliminated faster. Ketamine is rapidly metabolized in most animals (60-90 minute half-life in dogs); however, metabolite (norketamine) may produce more prolonged NMDA antagonistic effects.

Indications and Clinical Uses

Ketamine is used for short-term anesthetic procedures. Duration of action is generally 30 minutes or less. Ketamine has some analgesic properties via its effects on NMDA receptors and has been administered as an adjunct to other analgesic medications, usually with opiates, sometimes as a slow continuous rate infusion

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(CRI). Ketamine is often combined in use with other anesthetics and sedatives such as benzodiazepines (diazepam) or α_2 agonists (medetomidine, dexmedetomidine, and xylazine). Such combinations have been synergistic and allowed lower doses of each individual component. One example of a combination is MLK, which is morphine (or fentanyl), lidocaine, and ketamine.

Although ordinarily contraindicated in patients with epilepsy, it has been used to treat cases of refractory status epilepticus through its NMDA receptor effects.

Precautionary Information

Adverse Reactions and Side Effects

Ketamine causes pain with intramuscular injection (pH of solution is 3.5). Tremors, muscle spasticity, and convulsive seizures have been reported. Spontaneous movements, salivation, and increased body temperature are more common in dogs when high doses are used. Ketamine will increase heart rate and blood pressure as a result of an increase in sympathetic tone. It will produce an increased cardiac output compared to other anesthetic agents. Salivation, mydriasis, and regurgitation are increased in animals that receive ketamine, which may be reduced by premedication within atropine. Apnea may develop in some animals, and oxygen supplementation should be provided.

Contraindications and Precautions

Do not use in animals with head injury because it may elevate cerebral spinal fluid (CSF) pressure. Use cautiously, if at all, in animals with glaucoma (increases intraocular pressure). Do not use in animals prone to seizures (although some animals with seizures have been successfully treated with ketamine).

Drug Interactions

Ketamine hydrochloride is maintained at an acidic pH for stability and solubility. If mixed with alkalinizing solutions, instability or precipitation can result.

Instructions for Use

Ketamine is often used in combination with other anesthetics and anesthetic adjuncts, such as xylazine, dexmedetomidine, medetomidine, acepromazine, opiates, and benzodiazepines (e.g., diazepam). Constant rate infusions (CRI) may be used to maintain a plane of anesthesia and analgesia. To prepare CRI, 0.6 mL (60 mg) may be added to 1 L of fluids and infuse at a rate of 10 mL/kg for analgesia. For use in cats, a sedative such as acepromazine (0.1 mg/kg) or a benzodiazepine is recommended prior to administration of ketamine. Intravenous doses are generally less than intramuscular doses. In cats, ketamine may be sprayed into the mouth (10 mg/kg) and produces similar effects as IM injection. Animals receiving ketamine will have open eyelids, and artificial tears should be applied to prevent corneal injury.

Patient Monitoring and Laboratory Tests

Monitor heart rate and breathing in patients anesthetized with ketamine.

Formulations

Ketamine is available in 100-mg/mL injection solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Ketamine is soluble in water and ethanol. Ketamine hydrochloride has been successfully administered when combined in a syringe immediately prior to injection with drugs such as α_2 agonists and acepromazine. Ketamine has been added to

IV saline solution for horses at a concentration of 3 mg/mL (30 mg in a 1 L bag) and infused for 8 hours, or to maintenance fluids.

Small Animal Dosage

For all animals: Lower doses listed for intravenous use; higher doses listed for intramuscular use.

Dogs

- 5.5-22 mg/kg IV or IM. (Generally, the lower dose range is given IV compared to IM.) It is recommended to use adjunctive sedative or tranquilizer treatment.
- Constant rate infusion (CRI) for perioperative use: Loading dose of 0.3-0.5 mg/kg IV, followed by 0.3-0.6 mg/kg/hr (5-10 mcg/kg/min), followed by 0.12 mg/kg/hr after surgery (18 hours). The rate during surgery may be increased to 1 mg/kg/hr if needed.
- CRI for light sedation: 1-2 mg/kg/hr, which may be combined with other sedatives.

Cats

- 2-25 mg/kg IV or IM. (Generally, the lower dose range is given IV compared to IM.) It is recommended to use adjunctive sedative or tranquilizer treatment. (In cats it also can be sprayed into the mouth and produce similar effect as IM 10 mg/kg.)
- Short-term procedures: 5 mg/kg ketamine + 2.5 mcg/kg dexmedetomidine (or 5 mcg/kg medetomidine), mixed together, and administered IM.
- CRI: Loading dose of 0.3-0.5 mg/kg IV, followed by 0.3-0.6 mg/kg/hr (5-10 mcg/kg/min). This rate may be increased to 1 mg/kg/hr (15 mcg/kg/min) if needed, or lowered to 2-5 mcg/kg/min when combined with other drugs (e.g., opiates).

Large Animal Dosage

Horses, Cattle, Sheep, and Swine

- 2 mg/kg IV.
- CRI: Loading dose of 0.6 mg/kg IV, followed by CRI of 0.4-0.8 mg/kg/hr.
- 10 mg/kg IM. Often used in combination with other agents, such as xylazine.
- Foals, treatment of seizures: 0.02 mg/kg/min CRI.

Regulatory Information

Extralabel use: Withdrawal time of at least 3 days for meat and 48 hours for milk.

Schedule III controlled drug

RCI Classification: 2

Ketoconazole

kee-toe-kah'nah-zole

Trade and Other Names: Nizoral

Functional Classification: Antifungal

Pharmacology and Mechanism of Action

Azole (imidazole) antifungal drug. Ketoconazole has a similar mechanism of action as other azole antifungal agents (itraconazole and fluconazole). It inhibits a P450 enzyme in fungi and inhibits ergosterol synthesis in fungal cell membrane.

414 Ketoconazole

Fungistatic. It has antifungal activity against dermatophytes and a variety of systemic fungi, such as *Histoplasma*, *Blastomyces*, and *Coccidioides* and *Malassezia* yeast. Other azole antifungal drugs include voriconazole, itraconazole, and fluconazole.

Indications and Clinical Uses

Ketoconazole is used in dogs, cats, and some exotic animals to treat dermatophytes and systemic fungi, such as *Blastomyces*, *Histoplasma*, and *Coccidioides*. It also has been shown effective for treatment of *Malassezia* dermatitis. It does not have good activity against *Aspergillus*. Ketoconazole should not be used in horses because oral absorption is poor unless administered with a highly acidic vehicle. In dogs, it has a profound effect on cytochrome P450 enzymes and will inhibit metabolism of many drugs. This property has been used to reduce doses of cyclosporine (ketoconazole dose of 5-10 mg/kg). It is also via the inhibition of steroid P450 biosynthesis that ketoconazole has been used as a treatment for canine hyperadrenocorticism (canine Cushing's disease).

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects in animals include dose-related vomiting, diarrhea, hepatic injury, and rare thrombocytopenia in dogs. Liver enzyme elevations are common. Ketoconazole inhibits hormone synthesis and can lower concentrations of cortisol, testosterone, and other hormones in animals. Ketoconazole may produce a lighter hair coat color in some animals. Ketoconazole has been associated with cataract formation in dogs.

Contraindications and Precautions

Do not administer to pregnant animals. At high doses in laboratory animals, it has caused embryotoxicity and fetal abnormalities. Some of these effects on pregnancy may be because of the inhibition of estrogen synthesis by ketoconazole.

Drug Interactions

Ketoconazole is a potent inhibitor of hepatic and intestinal cytochrome P450 enzymes and will inhibit metabolism of other drugs (anticonvulsants, cyclosporine, warfarin, and cisapride).

Instructions for Use

Oral absorption depends on acidity in the stomach. Do not administer with antisecretory drugs or antacids. Because of endocrine effects, ketoconazole has been used for short-term treatment of hyperadrenocorticism. However, many experts believe that ketoconazole is not an effective long-term treatment for canine Cushing's disease.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes (ALT, ALP) for evidence of toxicity. Ketoconazole will lower serum cortisol levels.

Formulations

Ketoconazole is available in 200-mg tablets and 100-mg/mL oral suspension (Canada).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Ketoconazole is practically insoluble in water but is soluble in ethanol. When

ketoconazole was compounded extemporaneously from tablets with syrups and flavorings, it was stable for 60 days. However, ketoconazole requires acidity for solubility and may not be absorbed from these formulations. If compounded in alkaline conditions, it may precipitate.

Small Animal Dosage

Dogs

- 10-15 mg/kg q8-12h PO.
- *Malassezia* infection: 5 mg/kg q24h PO × 3 weeks.
- Hyperadrenocorticism: Start with 5 mg/kg q12h initially, then increase after 7 days to 12-15 mg/kg q12h PO.

Cats

- 5-10 mg/kg q8-12h PO.

Large Animal Dosage

Horses

Poorly absorbed. Fluconazole, itraconazole, or voriconazole is more completely absorbed.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

K

Ketoprofen

kee-toe-proe'fen

Trade and Other Names: Orudis-KT (human OTC tablet), Ketofen (veterinary injection), and Anafen (outside the US.)

Functional Classification: Nonsteroidal anti-inflammatory drug (NSAID)

Pharmacology and Mechanism of Action

Ketoprofen, like other NSAIDs, produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the cyclo-oxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Ketoprofen is a nonselective inhibitor of COX-1 and COX-2. There is weak evidence of its ability to inhibit lipoxygenase.

Indications and Clinical Uses

Ketoprofen is an NSAID and is used for treatment of moderate pain and inflammation. It has a half-life in most animals of less than 2 hours, but it has a duration of action for up to 24 hours. Ketoprofen is not registered in the US for small animals but has been labeled for dogs and cats in other countries. It has been

given by injection for acute treatment and by tablet for long-term use. In dogs and cats, it has been shown effective for treating pyrexia. In horses, ketoprofen is used for musculoskeletal inflammation and pain, abdominal pain, and other inflammatory conditions. Ketoprofen also has been used in cattle, goats, sheep, and pigs. In cattle, it has been effective for fever, pain, and inflammation associated with mastitis. It is registered for use in cattle in Canada but not in the US.

Precautionary Information

Adverse Reactions and Side Effects

All NSAIDs share the similar adverse effect of GI toxicity. The most common side effect is vomiting. GI ulceration is possible in some animals. Ketoprofen has been administered for 5 consecutive days in dogs without serious adverse effects, but longer treatment should be avoided. Dogs that received ketoprofen for 30 consecutive days (0.25 mg/kg per day) induced pyloric lesions and fecal occult blood. In horses, ketoprofen has been less ulcerogenic than phenylbutazone or flunixin meglumine in one study. Bleeding problems can occur if ketoprofen is administered before or after surgery.

Contraindications and Precautions

Do not administer to animals prone to GI ulcers. Do not administer with other ulcerogenic drugs such as corticosteroids. Do not use extended-release formulations of ketoprofen.

Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors.

Instructions for Use

Although not approved in the US, ketoprofen is approved for small animals in other countries. Doses listed are based on approved use in those countries. It is available as an OTC drug for humans in the US. In the US if it is used in small animals, either the large animal injectable formulation or the human oral OTC tablets are used.

Patient Monitoring and Laboratory Tests

Monitor patient for signs of GI intoxication (vomiting and diarrhea). Monitor renal function during chronic treatment.

Formulations

Ketoprofen is available in 12.5-mg tablets (OTC); 25, 50, and 75 mg (human preparation); and 100-mg/mL injection for horses. It is available in 10 mg/mL outside the US.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Ketoprofen is insoluble in water, but it is soluble in ethanol. Stability of oral compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 1 mg/kg q24h PO for up to 5 days. Initial dose can be given via injection at up to 2 mg/kg SQ, IM, or IV.

Large Animal Dosage

Horses

- 2.2-3.3 mg/kg/day IV or IM.

Pigs

- 3 mg/kg/day, PO, IV or IM.

Cattle and Small Ruminants

- 3 mg/kg/day IV or IM for up to 3 days.

Regulatory Information

Extralabel use in US: Withdrawal time of at least 7 days for meat and 24 hours for milk at a dose of 3.3 mg/kg q24h, IM or IV.

Registered in Canada for swine and cattle with a meat withdrawal time of 1 day.

Withdrawal time: None established, but at least 7 days for meat and 48 hours for milk is recommended.

RCI Classification: 4

Ketorolac Tromethamine

kee-toe'role-ak troe-meth'eh-meen

Trade and Other Names: Toradol

Functional Classification: Nonsteroidal anti-inflammatory drug (NSAID)

K

Pharmacology and Mechanism of Action

Ketorolac, like other NSAIDs, produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the cyclo-oxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Ketorolac is a nonselective inhibitor of COX.

Indications and Clinical Uses

Ketorolac is infrequently used in veterinary medicine. There are only limited data on safety and efficacy for veterinary uses. It has occasionally been used to treat pain and inflammation in dogs.

Precautionary Information

Adverse Reactions and Side Effects

Like other NSAIDs, it may cause GI ulceration and renal ischemia. Ketorolac may cause GI lesions if administered more frequently than every 8 hours.

Contraindications and Precautions

Do not administer more than two doses. Do not administer to animals prone to GI ulcers. Do not administer with other ulcerogenic drugs such as corticosteroids.

Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors.

Instructions for Use

Limited clinical studies in dogs have been conducted. However, it may be effective in some patients for short-term use. Long-term administration is discouraged.

Patient Monitoring and Laboratory Tests

Monitor for signs of GI ulceration.

Formulations

Ketorolac is available in 10-mg tablets and 15- and 30-mg/mL injection in 10% alcohol.

Stability and Storage

Store in a tightly sealed container, protected from light, protected from humidity, and at room temperature. Ketorolac tromethamine is soluble in water and slightly soluble in ethanol. Stability of oral compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 0.5 mg/kg q8-12h PO, IM, or IV.

Cats

No safe dose is established.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

Withdrawal times are not established for animals that produce animals. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Lactated Ringer's Solution

Trade and Other Names: LRS

Functional Classification: Fluid replacement

Pharmacology and Mechanism of Action

Lactated Ringer's solution is a fluid solution for replacement intended for intravenous administration. Lactated Ringer's solution contains a balanced combination of electrolytes and an alkalinizing buffer. This solution contains 28 mEq/L of lactate.

Indications and Clinical Uses

Lactated Ringer's solution is indicated as a replacement or maintenance fluid. It also is used as a vehicle to deliver intravenous medications via constant rate infusion (CRI). It has been administered SQ, intraosseous (in bone medullary cavity), and intraperitoneal (IP) in animals when intravenous access is not possible. It contains lactate, a metabolizable base, but will not correct acidosis as quickly as bicarbonate. Severely acidemic animals may already have high lactate serum levels.

Precautionary Information

Adverse Reactions and Side Effects

No significant adverse effects.

Contraindications and Precautions

Administer intravenous fluids only in patients monitored carefully.

Drug Interactions

Lactated Ringer's solution has a pH of 6-7.5. Do not add medications to this solution if they are unstable at this pH. Lactated Ringer's contains calcium. Do not add drugs to this solution that may bind (chelate) to calcium.

Instructions for Use

Fluid requirements vary depending on animal's needs (replacement vs. maintenance). For shock therapy, administer one-half the calculated dose in the first 30 minutes and in 10-mL/kg increments every 15 minutes, followed by a CRI. For severe acidemia, consider fluids supplemented with bicarbonate instead of lactate.

Patient Monitoring and Laboratory Tests

Monitor patient's hydration status and electrolyte balance. With high administration rates, monitor patient for signs of pulmonary edema.

Formulations

Lactated Ringer's solution is available in 250-, 500-, and 1000-mL fluid bags.

Stability and Storage

Store in a tightly sealed container. If container has been punctured or transferred to another container, sterility cannot be assured.

Small Animal Dosage

Dogs and Cats

- Moderate dehydration: 15-30 mL/kg/hr IV.
- Severe dehydration: 50 mL/kg/hr IV

420 Lactulose

- Maintenance: 55-65 mL/kg/day IV, SQ, or IP (2.5 mL/kg/hr).
- During anesthesia: 10-15 mL/kg/hr IV.
- Shock therapy: (for dogs) 90 mL/kg IV and (for cats) 60-70 mL/kg IV.

Large Animal Dosage

Cattle, Horses, and Pigs

- Maintenance: 40-50 mL/kg/day IV.
- Moderate dehydration: 15-30 mL/kg/hr IV.
- Severe dehydration: 50 mL/kg/hr IV.

Calves and Foals

- Moderate dehydration: 45 mL/kg at a rate of 30-40 mL/kg/hr IV.
- Severe dehydration: 80-90 mL/kg at a rate of 30-40 mL/kg/hr IV. In severe cases it may be given as rapidly as 80 mL/kg/hr.

Regulatory Information

There is no risk of harmful residues in animals intended for food. No withdrawal times are necessary.

Lactulose

lak'tyoo-lose

Trade and Other Names: Chronulac and generic brands

Functional Classification: Laxative

Pharmacology and Mechanism of Action

Laxative. Lactulose is a disaccharide sugar containing one molecule of fructose and one molecule of galactose. Lactulose produces a laxative effect by osmotic effect in the colon. It is a nonabsorbed sugar and retains water in the intestine after oral administration via an osmotic effect. Lactulose also will decrease the pH of the intestinal lumen.

Indications and Clinical Uses

Lactulose is administered orally for treatment of hyperammonemia (hepatic encephalopathy) because it decreases blood ammonia concentrations via lowering the pH of the colon; thus ammonia in the colon is not as readily absorbed. Lactulose also is administered orally to produce a laxative effect for treatment of constipation.

Precautionary Information

Adverse Reactions and Side Effects

Excessive use may cause fluid and electrolyte loss.

Contraindications and Precautions

Use lactulose with caution in animals with diabetes because it contains lactose and galactose.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

In veterinary medicine, clinical studies to establish efficacy are not available. In addition to doses cited, 20-30 mL/kg of 30% solution retention enema has been used in cats.

Patient Monitoring and Laboratory Tests

When used for treating hepatic encephalopathy, monitor the patient's hepatic status.

Formulations

Lactulose is available in 10 g/15 mL liquid solution (3.3 g per 5 mL).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water. Darkening of the solution may occur without affecting stability. Avoid freezing.

Small Animal Dosage

Dogs

- Constipation: 1 mL/4.5 kg q8h (to effect) PO.
- Hepatic encephalopathy: 0.5 mL/kg q8h PO.

Cats

- Constipation: 1 mL/4.5 kg q8h (to effect) PO.
- Hepatic encephalopathy: 2.5-5 mL/cat q8h PO.

Large Animal Dosage

Horses and Cattle

- 0.25-0.5 mL/kg/day PO.

Regulatory Information

There is little risk of residues in animals intended for food. No withdrawal times are necessary.

Leflunomide

le-FLOO-noe-mide, or leh-FLEW-nah-mide

Trade and Other Names: Arava and generic

Functional Classification: Immunosuppressive drug

Pharmacology and Mechanism of Action

Leflunomide is an isoxazole immunosuppressive drug. Leflunomide is not active as the parent drug, but it is converted to an active metabolite A77 1726 (also known as M1 and Teriflunomide), which inhibits T-cell and B-cell proliferation and is responsible for clinical immunosuppressive effects. It inhibits the synthesis of pyrimidine via inhibition of the enzyme dihydroorotate dehydrogenase. This enzyme is important for the de novo pyrimidine synthesis, which is critical for function of activated and stimulated lymphocytes. It also may produce anti-inflammatory effects by inhibiting proinflammatory cytokines.

After oral absorption, the plasma levels of leflunomide are low or undetectable. Therapeutic effects are produced from the metabolite A77 1726 (M1) for the immunosuppressive action. If monitoring is performed, the measurement should

focus on the metabolite concentrations. In people, the metabolite M1 has a very long half-life of approximately 2 weeks. But, in limited studies in dogs, the half-life was only 21 hours, and the peak concentrations were much lower than in people. In people the long half-life requires several days to accumulate to steady-state levels and to decline from a peak level. Loading doses are often administered in people. However, because of the shorter half-life, loading doses are not needed in dogs and steady-state concentrations will be attained in approximately 5 days.

Indications and Clinical Uses

This drug is used in people primarily for rheumatoid arthritis. In dogs it has been used for a variety of immune-mediated diseases as a substitute for other drugs such as azathioprine or mycophenolate. These diseases include myasthenia gravis, Evan's syndrome, immune-mediated hemolytic anemia and thrombocytopenia, and polymyositis/polyarthritis. Efficacy has not been studied in controlled clinical studies but are reported anecdotal observations.

Precautionary Information

Adverse Reactions and Side Effects

The most common adverse effects in dogs have been decreased appetite and diarrhea. Mild anemia and lethargy also have been observed. Although rare, leukopenia is possible and periodic CBC to monitor patients is recommended.

Contraindications and Precautions

Do not administer to pregnant animals. This drug can be toxic to a developing fetus.

Drug Interactions

No interactions are reported.

Instructions for Use

Leflunomide is used most often in dogs for immunosuppressive treatment when other drugs have failed or when the patient has become refractory to other drugs and a substitute is considered. The dosing protocols used currently are derived from extrapolation and some anecdotal reports. Most veterinarians start with 4 mg/kg per day, then lower the dose as the patient responds. Pharmacokinetic studies in dogs suggest that the dose of 4 mg/kg per day may not produce drug levels that are considered therapeutic. Therefore, in patients that have not responded, there should be consideration for higher doses.

Patient Monitoring and Laboratory Tests

Monitor CBC and platelet counts in treated animals. Anemia has been reported as a consequence of treatment. If blood monitoring is pursued, plasma samples may be collected and measured for A77 1726 (the active metabolite). This metabolite is stable in serum for up to 5 months under refrigerated conditions. Drug concentrations at 12 hours (trough) are considered effective if greater than 20 mcg/mL.

Formulations

Available in 5-, 10-, and 20-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 4 mg/kg per day, usually in divided doses of 2 mg/kg q12h, tapered to 2 mg/kg q24h, PO. After an induction period, the dose may be decreased by 25% increments until the patient is stabilized or until the disease resolves. Some patients may require higher starting doses.

Cats

- No dose has been reported for cats.

Large Animal Dosage

No large animal doses are available.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Leucovorin Calcium

loo-koe-vor'in kal'see-um

Trade and Other Names: Wellcovorin and generic brands

Functional Classification: Antidote

Pharmacology and Mechanism of Action

Leucovorin is a reduced form of folic acid that is converted to active folic acid derivatives for purine and thymidine synthesis.

Indications and Clinical Uses

Use of leucovorin is uncommon in animals. It may be used as an antidote for folic acid antagonists. In humans it is primarily used as rescue for overdoses of folic acid antagonists (methotrexate) and treatment of adverse reactions from methotrexate but also may be considered for reactions caused by pyrimethamine and trimethoprim.

Precautionary Information

Adverse Reactions and Side Effects

No adverse reactions reported for animals, but allergic reactions have been reported in people.

Contraindications and Precautions

No contraindications reported for animals.

Drug Interactions

Leucovorin will interfere with action of trimethoprim and pyrimethamine.

Instructions for Use

Clinical studies have not been reported in veterinary medicine. Although leucovorin may prevent toxicity from trimethoprim, it will not prevent toxic reactions that may be caused by sulfonamides in animals.

424 Levamisole Hydrochloride

Patient Monitoring and Laboratory Tests

Monitor CBC if this drug is used to treat overdose of folic acid antagonists.

Formulations Available

Leucovorin is available in 5-, 10-, 15-, and 25-mg tablets and 3- and 5-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water but is insoluble in ethanol. Reconstituted solutions have stability for 7 days at room temperature or refrigerated.

Small Animal Dosage

Dogs and Cats

- With methotrexate administration: 3 mg/m² IV, IM, or PO.
- As antidote for pyrimethamine toxicosis: 1 mg/kg q24h PO.

Large Animal Dosage

No large animal doses are reported. However, if pyrimethamine toxicosis is suspected in horses, doses listed for small animals may be considered.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Levamisole Hydrochloride

leh-vam'ih-sole hye-droe-klor'ide

Trade and Other Names: Levasole, Ripercol, Tramisol, and Ergamisol

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Levamisole is an antiparasitic drug of the imidazothiazole class. It eliminates a variety of parasites via neuromuscular toxicity. Levamisole has an immunorestorative effect in animals, but the mechanism of action on the immune system is unknown. It may activate and stimulate proliferation of T-cells; augment monocyte activation; and stimulate macrophages, including phagocytosis and chemotaxis. It may increase neutrophil mobility. However, it is not cytotoxic to neutrophils or immune cells.

Indications and Clinical Uses

In cattle and sheep, it is used to treat a variety of nematodes, including stomach worms (*Haemonchus*, *Trichostrongylus*, and *Ostertagia species*), intestinal worms (*Trichostrongylus*, *Cooperia*, *Nematodirus*, *Bunostomum*, *Oesophagostomum*, and *Chabertia species*), and lungworms (*Dictyocaulus species*). In pigs it is used to treat nematodes such as large roundworms (*Ascaris suum*), nodular worms (*Oesophagostomum species*), intestinal thread worms (*Strongyloides ransomi*), and lungworms (*Metastrongylus species*). Levamisole has been used for treatment of endoparasites in dogs and as a microfilaricide. Macrocytic lactones (e.g., milbemycin oxime or ivermectin) are considered a preferred heartworm microfilaricide. In people, levamisole is used as an immunostimulant to aid in treatment of colorectal carcinoma and malignant melanoma. In animals, levamisole also is used as an immunostimulant, but reports of efficacy are lacking.

Precautionary Information

Adverse Reactions and Side Effects

Levamisole may produce cholinergic toxicity. It has produced vomiting in some dogs. The injectable formulation has caused some swelling at the site of injection. In humans, when used as an immunostimulant, it has caused stomatitis, agranulocytosis, and thrombocytopenia.

Contraindications and Precautions

Use cautiously in animals with high heartworm microfilaria burdens. Reactions are possible from heavy kill rate of microfilaria. There are no adverse reactions on fertility and no effects on pregnancy. In rats and rabbits there was no evidence of teratogenicity or embryotoxicity at doses of 180 mg/kg. Levamisole is abused in people and often mixed with cocaine to either potentiate the effects to produce additional CNS stimulation, or is added as a marker compound. When used in this form in people, it has produced agranulocytosis in some individuals. Levamisole may potentially be converted to Aminorex, a CNS stimulant in horses, with amphetamine properties, which may affect performance.

Drug Interactions

Do not use with pyrantel because they share the same mechanism of toxicity.

L

Instructions for Use

In heartworm-positive dogs, it may sterilize female adult heartworms. Levamisole has also been used as an immunostimulant; however, clinical reports of its efficacy are not available. Because of the possibility of contamination at the injection site, use a clean needle with each animal and clean the injection site.

Patient Monitoring and Laboratory Tests

Monitor for microfilaria before treatment because of risk of reaction with a high heartworm burden.

Formulations

Levamisole is available in 0.184-g bolus; 2.19-g bolus; 9-, 11.7-, and 18.15-g per packet; 136.5-mg/mL and 182-mg/mL injection (levamisole phosphate); and 50-mg tablet (Ergamisol).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Endoparasites: 5-8 mg/kg once PO (up to 10 mg/kg PO for 2 days).
- Hookworms: 10 mg/kg/day for 2 days.
- Microfilaricide: 10 mg/kg q24h PO for 6-10 days (recommended to use macrocyclic lactones instead).
- Immunostimulant: 0.5-2 mg/kg 3 times/week PO. (In humans the immunostimulant dose is given q8h for 3 days.)

Cats

- Endoparasites: 4.4 mg/kg once PO.
- Lungworms: 20-40 mg/kg q48h for 5 treatments PO.

Large Animal Dosage

Cattle and Sheep

- 8 mg/kg once PO, or approximately one 2.19 g bolus per 450-750 pounds (200-340 kg).
- Levamisole injection (for cattle): 8 mg/kg SQ into mid neck area, once, or approximately 2 mL per 100 pounds (45 kg).

Pigs

- 8 mg/kg in drinking water.

Regulatory Information

Cattle withdrawal time (meat): 2 days (PO) and 7 days (SQ injection).

Sheep withdrawal time (meat): 3 days.

Pig withdrawal time (meat): 3 days.

Horses: There are some reports that levamisole can be converted to Aminorex in horses, which is a CNS stimulant and a banned substance in racing horses.

Levetiracetam

lev-eh-teer-ass'eh-tam

Trade and Other Names: Keppra

Functional Classification: Anticonvulsant

Pharmacology and Mechanism of Action

Anticonvulsant. The mechanism of action is not certain, but it does not involve inhibitory neurotransmitters. It inhibits burst firing of neurons without affecting normal neuronal excitement. It does not undergo hepatic metabolism but may undergo metabolism that does not include cytochrome P450 enzymes. Elimination relies on renal clearance.

Indications and Clinical Uses

In dogs, levetiracetam has been used to treat seizures, especially those refractory to other anticonvulsants. In dogs, it has been considered a drug of choice as an add-on medication when patients are refractory to phenobarbital and bromide therapy. It often is used in combination with other anticonvulsants. Levetiracetam has been used to treat seizure disorders in cats at a dose of 20 mg/kg every 8 hours and found to be effective in some cases. In dogs the oral absorption is 100%, the half-life is 3-4 hours, and the volume of distribution is 0.4-0.5 L/kg. In cats the oral absorption is also 100%, with a half-life of 3 hours and a volume of distribution similar to dogs.

Precautionary Information

Adverse Reactions and Side Effects

Weakness, lethargy, and dizziness have been reported in people. Adverse effects have been rare in animals, except for occasional lethargy and decreased appetite.

Contraindications and Precautions

No known contraindications.

Drug Interactions

Ordinarily, there are no direct interactions with drugs that inhibit or induce cytochrome P450 enzymes. However, studies in dogs and people have confirmed that phenobarbital can enhance the clearance of levetiracetam. For example, the half-life is shorter and clearance is more rapid when dogs are administered phenobarbital simultaneously. The mechanism for the interaction is unknown. Interactions with other concurrently used anticonvulsants have not been reported.

Instructions for Use

It is rapidly and completely absorbed, and absorption is not affected by feeding. An injectable formulation is available but not used often in veterinary medicine. However the injectable solution has been administered at a dose of 20 mg/kg IV bolus increments to a maximum of 60 mg/kg in emergency situations.

Patient Monitoring and Laboratory Tests

Monitor seizure frequency. Currently no clinical monitoring test for serum exists in routine laboratories. However, some laboratories have this capability. Therapeutic plasma/serum concentrations in people are in the range of 5-45 mcg/mL.

Formulations

Levetiracetam is available in 250-, 500-, and 750-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. It is soluble in water, and it may be acceptable to mix with other foods, syrups, or flavorings immediately prior to oral administration.

Small Animal Dosage

Dogs

- 20 mg/kg q8h, PO. More frequent administration or higher doses may be necessary with concurrent phenobarbital treatment.
- Intravenous use (emergency situations): 20 mg/kg IV bolus, repeated if necessary up to 60 mg/kg.

Cats

- 20-mg/kg q8h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Levodopa

lee'voe-doe'pah

Trade and Other Names: Larodopa and L-dopa

Functional Classification: Dopamine agonist

Pharmacology and Mechanism of Action

Dopamine, when administered systemically, does not cross the blood–brain barrier. However, levodopa crosses more easily via a carrier-mediated process and is converted to dopamine after crossing the blood–brain barrier. Dopamine is used in neurodegenerative disorders to stimulate CNS dopamine receptors.

Indications and Clinical Uses

In people, levodopa is used for treating Parkinson's disease, and it is used in combination with carbidopa (a peripheral decarboxylase inhibitor) and entacapone (an o-methyltransferase inhibitor) to potentiate therapy. In animals, it has been used for treating hepatic encephalopathy.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects in animals have not been reported. In people, dizziness, mental changes, difficult urination, and hypotension are among the reported adverse effects.

Contraindications and Precautions

There are no specific contraindications for use in animals.

Drug Interactions

Antidopamine drugs will interfere with action. Such drugs include metoclopramide, phenothiazines (e.g., acepromazine), and risperidone.

Instructions for Use

Clinical studies have not been reported in veterinary medicine. Titrate dose for each patient.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations Available

Levodopa is available in 100-, 250-, and 500-mg tablets or capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Levodopa is slightly soluble in water but more soluble in acid solutions. It will be rapidly oxidized with exposure to air, which will be indicated by a darkening of the formulation. Injectable solutions have been prepared extemporaneously and found to be stable for 96 hours.

Small Animal Dosage

Dogs and Cats

- Hepatic encephalopathy: 6.8 mg/kg initially, PO, then 1.4 mg/kg q6h, PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available for animals intended for food. Because of low risk of residues, no withdrawal times are suggested.

Levothyroxine Sodium

lee-voe-thye-roks'een soe'dee-um

Trade and Other Names: T4, L-thyroxine, Soloxine, Thyro-Tabs, Synthroid, ThyroMed. Leventa and equine powders include Equisyn-T4, Levo-Powder, Thyroid Powder, and Thyro-L

Functional Classification: Hormone

Pharmacology and Mechanism of Action

Thyroid hormone. Levothyroxine is used as replacement therapy for treating patients with hypothyroidism. Levothyroxine is T4, which is converted in most patients to the active T3. Requirements and pharmacokinetics vary among animals and doses are adjusted on the basis of thyroid monitoring. Levothyroxine has a half-life of approximately 20 hours in dogs.

Indications and Clinical Uses

Levothyroxine is used for replacement therapy in animals with thyroid hormone deficiency (hypothyroidism). It has been used in many species, including dogs, cats, and horses. Although it has been suggested for use in treating dogs with von Willebrand's disease, clinical studies failed to show an effect on clotting factors, bleeding times, or von Willebrand's factor (vWf) from levothyroxine treatment (0.04 mg/kg).

Intravenous levothyroxine sodium may be used in dogs for acute treatment of hypothyroid dogs with myxedema coma (4-5 mcg/kg IV).

Precautionary Information

Adverse Reactions and Side Effects

High doses may produce thyrotoxicosis, but is uncommon. Potential adverse effects from IV treatment include arrhythmias or pneumonia.

Contraindications and Precautions

No specific contraindications are reported for small animals. When switching from one brand to another, it is advised to follow up by testing to ensure that brands are therapeutically equivalent.

Drug Interactions

Patients receiving corticosteroids may have decreased ability to convert T4 to the active T3. The following drugs may lower thyroid concentrations when administered to otherwise healthy animals: nonsteroidal anti-inflammatory drugs (NSAIDs), sulfonamides, and phenobarbital, although results in some dogs may not be clinically significant. Although not reported in animals, in people administration of estrogens increases thyroid binding globulin and may decrease the active form of thyroid hormone (T4) in patients receiving thyroid supplementation. Monitor T4 levels in these patients and increase dose of thyroxine if necessary. Feeding may decrease oral absorption.

Instructions for Use

Thyroid supplementation should be guided by testing to confirm diagnosis and postmedication monitoring to adjust dose. The brands Soloxine and Synthroid have been equivalent according to studies in dogs, but the oral liquid (Leventa) is absorbed 150%-200% more than the oral tablets and dose adjustments should be

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considered when switching from oral tablets to oral liquid. For tablets, bioavailability is only 37% (average). When using the liquid formulation (Leventa), use the specially designed syringes for dosing. The starting dose listed in the dosing section for tablets in dogs (22 mcg/kg q12) may not be high enough for some dogs, and monitoring is recommended to adjust dose appropriately.

Patient Monitoring and Laboratory Tests

Monitor serum T4 concentrations to guide therapy. Normal thyroxine (T4) baseline levels are 20-55 nmol/L (1.5 to 4.3 mcg/dL). Thyrotropin-releasing hormone (TRH) injection should result in at least 1.5-fold increase in T4. To monitor postpill adequacy of therapy, some feel that the most valuable sample to collect is immediately prior to the next scheduled dose (trough level). Alternatively, some clinicians take a peak concentration by collecting a blood sample 4-6 hours after administering the pill, and the T4 should be between 30 and 60 nmol/L (2.3-4.6 mcg/dL). If administering the oral liquid, the peak concentration occurs at 2-2.5 hours. In horses, postpill peak occurs at 1-2 hours.

Formulations

Levothyroxine is available in a range of sizes from 0.025- to 0.8-mg tablets (in 0.1-mg increments), 0.1 to 0.8-mg chewable tablets, 1.0-mg/mL oral solution for dogs, and 1 g per 453.6 of oral powder (1 gram per pound) used for horses.

Stability and Storage

Levothyroxine is inherently unstable and can be markedly affected by heat, light, and humidity. Store in a tightly sealed container, protected from light, and at room temperature. Thyroxine is only slightly soluble in water or ethanol. It is more soluble at pH <2 or >8. It has been unstable in some compounded formulations. However, it may be added to food products if administered immediately. Powder may be mixed with water and added to horse's grain every day. When it was mixed with ethanol followed by mixing with a syrup, it was stable for 15 days at room temperature and 47 days refrigerated. However, other compounded preparations have been stable for only 15 days (refrigerated) or 11 days (room temperature). Therefore, use of compounded formulations should probably be limited to a storage time of 10-15 days.

The oral solution (Leventa) has an 18-month shelf-life when stored refrigerated, but once opened it can be stored for 2 months at room temperature, protected from light, and for 6 months refrigerated.

Small Animal Dosage

Dogs

- 18-22 mcg/kg (0.018-0.022 mg/kg) q12h PO (adjust dose via monitoring); an alternative dose is 0.5 mg per square meter (0.5 mg/m²).
- Liquid (1 mg/mL): 20 mcg/kg PO, q24h, but doses may range from 12-42 mcg/kg q24h after adjusting. Maximum dose is 30 mcg/kg.
- IV therapy for acute treatment: 4-5 mcg/kg IV.

Cats

- 10-20 mcg/kg/day (0.01-0.02 mg/kg) PO (adjust dose via monitoring).

Large Animal Dosage

Horses

- 10-60 mcg/kg (0.01 to 0.06 mg/kg) q24h or 5-30 mcg/kg (0.005-0.03 mg/kg) q12h PO. When using the oral powder for dosing in horses, 1 level teaspoon

contains 12 mg of levothyroxine (T4), and 1 tablespoon contains 36 mg of levothyroxine (T4). This powder may be mixed in with daily ration of grain (e.g., 4 level teaspoons mixed with 30 mL water and added to oats per day).

Regulatory Information

No regulatory information is available for animals intended for food. Because of low risk of residues, no withdrawal times are suggested.

Lidocaine Hydrochloride

lye'doe-kane hye-droe-klor'ide

Trade and Other Names: Xylocaine and generic brands

Functional Classification: Local anesthetic, antiarrhythmic

Pharmacology and Mechanism of Action

Local anesthetic. Lidocaine inhibits nerve conduction via sodium channel blockade. Class-1 antiarrhythmic. Decreases Phase 0 depolarization without affecting conduction. After systemic administration lidocaine is metabolized to monoethylglycinexylidide (MEGX), which also has antiarrhythmic properties. Lidocaine also has analgesic properties after systemic administration. During intravenous infusion, it may decrease pain response. In horses, infusions of lidocaine have decreased postoperative ileus either through a direct effect, via suppression of painful stimuli, or through anti-inflammatory effects on neutrophils. Pharmacokinetics in dogs and cats are similar; however, cats have increased sensitivity to the cardiac effects. In horses, half-life ranges from 40 min to 80 min, with a high, but variable, clearance rate.

Indications and Clinical Uses

Lidocaine is used commonly as a local anesthetic and for acute treatment of ventricular arrhythmias. Lidocaine should be used cautiously for treating supraventricular arrhythmias because it may increase cardiac conduction. Lidocaine also is used for pain management. It has been administered as a constant rate infusion (CRI) in animals, especially in postsurgical patients. Lidocaine has been combined with other analgesics, which may be synergistic and allow lower doses of each individual component. One example of a combination is MLK, which is morphine (or fentanyl), lidocaine, and ketamine. Lidocaine has been used, on a limited basis, to treat seizures that are refractory to other drugs. In horses, studies have confirmed that a lidocaine CRI may help to restore intestinal motility and is used to treat intestinal ileus.

Precautionary Information

Adverse Reactions and Side Effects

High doses cause CNS effects (tremors, twitches, and seizures) and vomiting, but risk of lidocaine-induced seizures is low. Lidocaine can produce cardiac arrhythmias, but it has greater effect on abnormal cardiac tissue than normal tissue. Intravenous doses of lidocaine in cats have resulted in death. In cats under anesthesia, lidocaine administration has caused decreased cardiac output, cardiovascular depression, and decreased oxygen delivery to tissues. In cats, lidocaine has also produced methemoglobinemia and hemolysis. Intravenous and

CRIs in horses have caused muscle fasciculations, rapid eye blinking, anxiety, ataxia, weakness, and seizures.

Contraindications and Precautions

Cats are more susceptible to adverse effects, and lower doses should be used for cats. Absorption from lidocaine patches in cats is only 6.3% and not expected to present a problem. In animals with decreased blood flow to liver (e.g., animals under anesthesia) clearance may be reduced. CRI in cats is lower than rate in dogs.

Drug Interactions

Lidocaine hydrochloride is maintained as an acidic solution for solubility. Although short-term mixing with alkaline solutions may not interfere with stability (i.e., immediately prior to administration), storage in alkalinizing solutions can cause precipitation. If mixed with alkalinizing solutions, it should be administered promptly.

Instructions for Use

When used for local infiltration, many formulations contain epinephrine to prolong activity at the injection site. Avoid using formulations that contain epinephrine in patients with cardiac arrhythmias. Note that human formulations may contain epinephrine, but no veterinary formulations contain epinephrine. To increase pH, speed onset of action, and decrease pain from injection, one may add 1 mEq sodium bicarbonate to 10 mL lidocaine (use immediately after mixing). To prepare solutions for infusion in horses, mix 10 g of 2% lidocaine in 3 L of LRS (0.33% solution).

Patient Monitoring and Laboratory Tests

Monitor for signs of neurotoxicity (e.g., depression, muscle twitching, and seizures). Monitor ECG during treatment for cardiac rate and rhythm in treated animals.

Formulations

Lidocaine is available in 5-, 10-, 15-, and 20-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Topical preparations have been prepared and found to be stable for several weeks.

Small Animal Dosage

Dogs

- Antiarrhythmic: 2-4 mg/kg IV (to a maximum dose of 8 mg/kg over 10-minute period).
- Antiarrhythmic: 25-75 mcg/kg/min IV, CRI.
- Antiarrhythmic: 6 mg/kg q1.5h IM.
- Epidural: 4.4 mg/kg of 2% solution.

Cats

- Antiarrhythmic: Start with 0.1 to 0.4 mg/kg initially, and then increase to 0.25-0.75 mg/kg IV slowly if there has been no response.
- Antiarrhythmic: Loading dose of 0.5-1 mg/kg IV, followed by 10-20 mcg/kg/min, (0.6-1.2 mg/kg/hr), IV, CRI.
- Epidural: 4.4 mg/kg of 2% solution.

Large Animal Dosage

Horses

- Antiarrhythmic: 0.25-0.5 mg/kg q5-15 min IV, for a total of 1.5 mg/kg, then as a CRI of 0.05 mg/kg/min (50 mcg/kg/min).

- Postoperative ileus: 1.3 mg/kg IV bolus administered over 15 min, followed by 0.05 mg/kg/min (50 mcg/kg/min) CRI.
- Analgesia: 2 mg/kg IV, followed by 50 mcg/kg/min, CRI.

Regulatory Information

Extralabel use withdrawal time: 1 day for meat and 24 hours for milk.

Horses: Clearance prior to racing, approximately 2.5 days.

RCI Classification: 2

Lincomycin Hydrochloride, Lincomycin Hydrochloride Monohydrate

lin-koe-mye'sin hye-droe-klor'ide, lin-koe-mye'sin hye-droe-klor'ide mono-hye'drate

Trade and Other Names: Lincocin and Lincomix

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Lincosamide antibiotic. Lincomycin is similar in mechanism to clindamycin. Mechanism of action is also similar to macrolides, such as erythromycin, and there may be cross resistance among these drugs. Like the other related drugs, the site of action is the 50S ribosomal subunit. By inhibiting this ribosome, it decreases protein synthesis. In most bacteria it is bacteriostatic. The spectrum includes primarily gram-positive bacteria and atypical bacteria such as *Mycoplasma*.

Indications and Clinical Uses

Lincomycin has a gram-positive spectrum and has limited use for other infections. In small animals it is used for pyoderma and other soft tissue infections caused by susceptible gram-positive bacteria. It is also active against *Mycoplasma*, *Erysipelothrix*, and *Leptospira* species. In pigs and birds, it is used primarily for treatment of infections caused by *Mycoplasma*. Although it has been injected IM in cattle and sheep for treatment of septic arthritis, laryngeal abscesses, and mastitis, this treatment is not currently recommended. Compared to lincomycin, clindamycin has better activity against anaerobic bacteria.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are uncommon. Lincomycin has caused vomiting and diarrhea in animals. Severe, and even fatal, enteritis can be caused from oral administration to ruminants.

Contraindications and Precautions

Do not administer orally to rodents, horses, ruminants, or rabbits. Oral administration to ruminants and horses can cause severe enteritis.

Drug Interactions

No drug interactions reported for animals.

Instructions for Use

Action of lincomycin and clindamycin are similar enough that clindamycin can be substituted for lincomycin.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are less than or equal to 0.25 mcg/mL for streptococci and less than or equal to 0.5 for other organisms.

Formulations

Lincomycin is available in 100-, 200-, and 500-mg tablets; 400 mg/g of powder; 16 g/40 g of soluble powder; 10, 20, and 50 g/lb of premix; 50-mg/mL syrup; and 25-, 100-, and 300-mg/mL solution for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 15-25 mg/kg q12h PO.
- Pyoderma: 10 mg/kg q12h PO.

Large Animal Dosage

Pigs

- Swine dysentery: 250 mg per gallon of drinking water, which is approximately 8.4 mg/kg/day if given as the only source of drinking water for 5-10 days.
- *Mycoplasma* infections: 11 mg/kg q24h or 11 mg/kg q12h IM injection.

Cattle

- Septic arthritis, mastitis, and abscesses: 5 mg/kg q24h IM for 5-7 days.
- Refractory infections: 10 mg/kg q12h IM.

Sheep

- Septic arthritis: 5 mg/kg q24h for 3-5 days IM.

Regulatory Information

Withdrawal time for pigs: 0, 1, 2, or 6 days, depending on product and route of administration. (For most products, allow 6 days for oral administration and 2 days for IM administration.) For extra-label use in cattle, FARAD recommends 7 days for meat and 96 hours for milk, at a dose of 5 mg/kg.

Linezolid

lih-neh-zoe'lide

Trade and Other Names: Zyvox and Zyvoxam (Canada)

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Linezolid is an antibiotic in the oxazolidinone class (synthetic drugs). It is bacteriostatic with a unique mechanism of action. It inhibits protein synthesis by binding to a site on the bacterial 23S ribosomal RNA of the 50S subunit. This prevents formation of the 70S ribosomal unit; therefore protein synthesis is inhibited. Linezolid has good penetration into cells and extracellular fluid. Urine concentrations are high enough to inhibit urinary tract pathogens. In dogs the pharmacokinetics are similar to humans. The oral absorption is almost 100%, and

the half-life is slightly faster than humans. Linezolid does not undergo hepatic P450 metabolism, and one third of the total clearance relies on the kidneys.

Indications and Clinical Uses

Linezolid is active against streptococci and staphylococci and is indicated for treatment of infections that have become resistant to other drugs, particularly when there is resistance to the beta-lactam antibiotics (penicillins, ampicillin derivatives, and cephalosporins). It is not indicated for gram-negative infections. Linezolid is indicated for treatment of methicillin-resistant and oxacillin-resistant strains of *Staphylococcus* (e.g., MRSA and MRSP) and drug-resistant *Enterococcus* spp. Because of the high cost of linezolid, it is not used for routine infections.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include diarrhea and nausea. Rarely, anemia and leukopenia have been observed in people. Because of limited use in animals, adverse effects have not been reported.

Contraindications and Precautions

No contraindications reported.

Drug Interactions

Linezolid is a Type-A monoamine oxidase inhibitor (MAOI). Possible interactions occur with serotonin reuptake inhibitors such as fluoxetine and selegiline to produce serotonin syndrome. Interactions are also possible if administered with adrenergic drugs such as phenylpropanolamine. However, this effect has not been reported for animals. Linezolid is not expected to affect metabolism of other drugs. Intravenous formulation is physically incompatible with other drugs in IV line. If administered with other drugs IV, flush out administration line first.

Instructions for Use

Linezolid is reserved for infections that are resistant to other drugs, such as *Enterococcus*, *Streptococcus*, or *Staphylococcus* infections.

Patient Monitoring and Laboratory Tests

Choice of drug should be selected on the basis of susceptibility monitoring. CLSI lists the break point for susceptibility as less than or equal to 4.0 mcg/mL for *Staphylococcus* and less than or equal to 2.0 for *Enterococcus*.

Formulations

Linezolid is available in 400- and 600-mg tablets, 20-mg/mL oral suspension powder, and 2-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with other drugs. Oral suspension is stable for 21 days after reconstitution at room temperature.

Small Animal Dosage

Dogs and Cats

- 10 mg/kg q8-12h PO or IV. (Use every 8 hours for serious infections and every 12 hours for less life-threatening infections.)

Large Animal Dosage

No large animal dose is available.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Liothyronine Sodium

lye-oh-thye'roe-neeen soe'dee-um

Trade and Other Names: Cytomel

Functional Classification: Hormone

Pharmacology and Mechanism of Action

Thyroid supplement. Liothyronine is equivalent to T3. T3 is more active than T4, but ordinarily T4 is converted in animals to the active form of T3.

Indications and Clinical Uses

Liothyronine is used for similar indications as levothyroxine (T4), except that in this instance, the active T3 hormone is administered. It may be indicated in cases in which there is failure to convert T4 to the active T3 hormone. In most cases, it is preferred to administer levothyroxine instead of liothyronine.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported.

Contraindications and Precautions

No contraindications reported.

Drug Interactions

No drug interactions reported for animals.

Instructions for Use

Doses of liothyronine should be adjusted on the basis of monitoring T3 concentrations in patients. It is rarely necessary to administer T3 alone for treatment of hypothyroidism. In most patients drugs that contain T4 should be used (e.g., levothyroxine). Liothyronine has been used as a diagnostic test for cats.

Patient Monitoring and Laboratory Tests

Monitor serum T3 concentrations. Used for T3 suppressing test in cats.

Formulations

Liothyronine is available in 5-, 25-, 50-, and 60-mcg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 4.4 mcg/kg q8h PO.
- T3 suppression test in cats: Collect pre-sample for T4 and T3, administer 25 mcg q8h for 7 doses and then collect post-samples for T3 and T4 after last dose.

Large Animal Dosage

No large animal dose is available.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Lisinopril

lye-sin'oh-pril

Trade and Other Names: Prinivil and Zestril

Functional Classification: Vasodilator, angiotensin-converting enzyme (ACE) inhibitor

Pharmacology and Mechanism of Action

Like other ACE inhibitors, lisinopril inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and will also stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. The ability of aldosterone to cause sodium and water retention contributes to congestion. Lisinopril, like other ACE inhibitors, will cause vasodilation and decrease aldosterone-induced congestion. Lisinopril also contributes to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins. Like other ACE inhibitors, lisinopril can reduce renal hypertension and improve renal perfusion, decrease glomerular pressure, and lead to improvement in some patients with renal disease.

Indications and Clinical Uses

Lisinopril, like other ACE inhibitors, is used to treat hypertension and congestive heart failure (CHF). Enalapril has been used more often in animals. Other uses may include primary hypertension. Lisinopril also may be used to treat some forms of renal disease in animals. When glomerular filtration pressures are high, lisinopril may improve some patients with renal disease, but effects on survival have not been established.

Precautionary Information

Adverse Reactions and Side Effects

Like other ACE inhibitors, it may cause azotemia in some patients. Carefully monitor patients receiving high doses of diuretics.

Contraindications and Precautions

Discontinue ACE inhibitors in pregnant animals; they cross the placenta and have caused fetal malformations and death of the fetus.

Drug Interactions

Use cautiously with other hypotensive drugs and diuretics. Nonsteroidal anti-inflammatory drugs (NSAIDs) may decrease vasodilating effects.

Instructions for Use

Clinical studies using lisinopril in animals have not been reported.

Patient Monitoring and Laboratory Tests

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

Formulations

Lisinopril is available in 2.5-, 5-, 10-, 20-, and 40-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Lisinopril has been mixed with syrup for oral administration and found to be stable for 30 days at either room temperature or refrigerated.

Small Animal Dosage

Dogs

- 0.5 mg/kg q24h PO.

Cats

No dose established.

Large Animal Dosage

No large animal dose is available.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Lithium Carbonate

lih'thee-um kar'boe-nate

Trade and Other Names: Lithotabs

Functional Classification: Immunostimulant

Pharmacology and Mechanism of Action

Lithium stimulates granulopoiesis and elevates neutrophil pool in animals. It also affects the CNS because it affects the balance of CNS neurotransmitters.

Indications and Clinical Uses

In people lithium is used for treatment of depression. It has not been used for this purpose in animals. It has also been used experimentally to increase neutrophil counts following cancer therapy and to prevent cytotoxicity caused from anticancer drugs.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include nephrogenic diabetes insipidus, ptyalism, lethargy, and seizures. In people, cardiovascular problems, drowsiness and diarrhea are among the adverse effects.

Contraindications and Precautions

Not recommended in cats.

Drug Interactions

No drug interactions are reported.

Instructions for Use

Use in animals is uncommon, and little dosing information is available.

Patient Monitoring and Laboratory Tests

Monitor neutrophil count.

Formulations

Lithium is available in 150-, 300-, and 600-mg capsules; 300-mg tablets; and 300-mg/5 mL syrup.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 10 mg/kg q12h PO.

Cats

Not recommended.

Large Animal Dosage

No large animal dose is available.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Lomustine

loe-mus'teen

Trade and Other Names: CeeNu and CCNU

Functional Classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. It is one of two nitrosoureas used: lomustine (1-[2-chloroethyl]-3-cyclohexyl-1-chloroethylnitrosourea), known by the abbreviation of CCNU, and carmustine (1,3-bis-2-chloroethyl-1-nitrosourea), known by the abbreviation BCNU. These drugs, in addition to being lipid soluble, are alkylating agents. Both of the nitrosoureas are metabolized spontaneously to alkylating and carbamylating compounds. The binding occurs preferentially at the O-6 of guanine. Bifunctional interstrand cross-links are responsible for the cytotoxicity of nitrosoureas. Oral

absorption and high membrane penetration are attributed to high lipophilicity. Because oral absorption is high, lomustine can be administered effectively as tablets. After absorption, lomustine is metabolized to antitumor metabolites. Both the parent drug and the metabolites are lipid soluble. The CNS penetration of lomustine has been determined from the plasma/cerebrospinal fluid (CSF) ratio, which is 1:3.

Indications and Clinical Uses

Lomustine (CCNU) is used to treat tumors of the CNS, mast cell tumors, and lymphoma in dogs and cats. It has occasionally been used to treat other forms of cancer. Lomustine has been used more often than carmustine.

Precautionary Information

Adverse Reactions and Side Effects

Bone marrow effects are the most serious. In people, lomustine has a delayed nadir of bone marrow toxicity, which is as long as 4-6 weeks with slow recovery, but in dogs the nadir of bone marrow effects generally is seen 6-7 days after dosing. Maximum tolerated dose in dogs is 90 mg/m². At higher doses (100 mg/m²) myelosuppression has been reported. Thrombocytopenia also has been reported from lomustine administration as a cumulative effect.

In cats, neutropenia is the most dose-limiting effect of treatment. Cats resemble people in that bone marrow nadir of toxicity occurs at 3-4 weeks. Nitrosoureas also can be toxic to the rapidly dividing cells of mucosa. In people, nitrosoureas also have caused pulmonary fibrosis and hepatotoxicity. Hepatotoxicity may be a delayed reaction. The hepatic damage, when observed in dogs, has been irreversible. In people, carmustine (BCNU) has been associated with a higher rate of hepatic injury than lomustine.

Contraindications and Precautions

Consider risks to bone marrow with use in small animals.

Drug Interactions

Use with caution with any drugs that may cause bone marrow suppression.

Instructions for Use

The nitrosourea drugs are used to treat CNS tumors and other forms of cancer. Protocols used in small animals are different from those given to people, which are as much as 150-200 mg/m². Oral treatment should be given on an empty stomach if possible.

Patient Monitoring and Laboratory Tests

Monitor CBC and liver enzymes in treated patients.

Formulations

Lomustine is available in 10-, 40-, and 100-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 70-90 mg/m² q4wk PO.
- Lymphoma: 60 mg/m² q4wk, for four treatments.
- Brain tumors: 60-80 mg/m² q6-8wk PO.

Cats

- 50-60 mg/m² q3-6wk PO. Alternatively, administer 10-20 mg/cat q3-6wk.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not administer to animals that produce food.

Loperamide Hydrochloride

loe-pare'ah-mide hye-droe-klor'ide

Trade and Other Names: Imodium and generic brands

Functional Classification: Analgesic, opioid

Pharmacology and Mechanism of Action

Opiate agonist. Like other opiates, loperamide acts on the mu-opiate receptors of the GI tract. It decreases propulsive intestinal contractions and increases segmentation (an overall constipating effect). It also increases the tone of GI sphincters. In addition to affecting motility, opiates have an antisecretory effect and stimulate absorption of fluid, electrolytes, and glucose. Their effects on secretory diarrhea are probably related to inhibition of calcium influx and decreased calmodulin activity. Action of loperamide is limited to the intestine. CNS effects do not occur because it does not cross the blood-brain barrier.

Indications and Clinical Uses

Loperamide is used for symptomatic treatment of acute nonspecific diarrhea. It has been administered orally to dogs and cats. Long-term use is discouraged because it may lead to constipation. It has been administered to large animals, but this is not recommended.

Precautionary Information**Adverse Reactions and Side Effects**

Loperamide can cause severe constipation with repeated use. In some dogs that have a mutation in the multidrug resistance (MDR) gene, they may lack p-glycoprotein in the blood-brain barrier. In these susceptible animals, loperamide will cross the blood-brain barrier and cause profound sedation. Such cases may be reversed with naloxone. Dogs most susceptible include Collie breeds, Australian shepherds, Old English sheepdogs, Longhaired Whippets, and Shetland sheepdogs.

Contraindications and Precautions

Small dogs and Collie-type dogs may be at higher risk of adverse effects.

Drug Interactions

Do not administer with drugs that may act as MDRI (p-glycoprotein) membrane inhibitors, such as ketoconazole. (Other inhibitors are listed in Appendix.) These inhibitors may increase blood-brain barrier penetration and cause depression.

442 Lorazepam

Instructions for Use

Doses are based primarily on empiricism or extrapolation of human dose. Clinical studies have not been performed in animals.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Loperamide is available in 2-mg tablets, 2-mg capsules, and 1- and 0.2-mg/mL oral liquid (OTC).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Loperamide is slightly soluble in water but only at low pH. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 0.1 mg/kg q8-12h PO.

Cats

- 0.08-0.16 mg/kg q12h PO.

Large Animal Dosage

No large animal doses have been reported. If administered to horses or ruminants, it may induce problems associated with decreased intestinal motility.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Lorazepam

lor-ay'zeh-pam

Trade and Other Names: Ativan and generic brands

Functional Classification: Anticonvulsant

Pharmacology and Mechanism of Action

Benzodiazepine. Central-acting CNS depressant, with action similar to diazepam. Mechanism of action appears to be via potentiation of GABA receptor-mediated effects in CNS. In animals, lorazepam does not undergo extensive hepatic metabolism, but it is glucuronidated before excretion. In dogs, lorazepam had a half-life of 0.9 hours, with systemic clearance less than half that of diazepam. Oral absorption is 60%. Therefore, the oral formulation may be suitable in dogs for some conditions.

Indications and Clinical Uses

Lorazepam, as a benzodiazepine, may be considered for anxiety disorders in animals, but it has not been used as commonly as other drugs such as diazepam. Lorazepam also is effective for treating seizures, but it is not used as often in animals as other anticonvulsants. In controlled studies it has been equally as effective as diazepam in dogs.

Precautionary Information

Adverse Reactions and Side Effects

Sedation is the most common side effect. Lorazepam causes polyphagia. Some animals may experience paradoxical excitement. Chronic administration may lead to dependence and a withdrawal syndrome if discontinued.

Contraindications and Precautions

Oral administration of another benzodiazepine, diazepam, has caused idiosyncratic liver injury in cats, but this is unlikely for lorazepam.

Drug Interactions

Use cautiously with other drugs that may cause sedation. Do not mix with buprenorphine.

Instructions for Use

Doses based on empiricism. There have been no clinical trials in veterinary medicine, although it is expected to produce effects similar to other benzodiazepines. For intravenous use, dilute 50/50 with 0.9% saline or 5% dextrose prior to use.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations Available

Lorazepam is available in 0.5-, 1-, and 2-mg tablets and 2- and 4-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Lorazepam is practically insoluble in water. It is slightly soluble in some infusion solutions (e.g., 0.054 mg/mL in 5% dextrose). Solutions should be discarded if they turn a dark color.

Small Animal Dosage

Dogs

- 0.05 mg/kg q12h PO.
- Seizures: 0.2 mg/kg IV. Repeat every 3-4 hours for seizure control if necessary.

Cats

- 0.05 mg/kg q12-24h PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not administer to animals intended for food.

Schedule IV controlled drug

RCI Classification: 2

Losartan

loe-zar'tan

Trade and Other Names: Cozaar

Functional Classification: Vasodilator

Pharmacology and Mechanism of Action

Vasodilator, Angiotensin II receptor blocker (ARB). It has high affinity and selectivity for the AT1 receptor. The action is similar to that of ACE inhibitors, except that it directly blocks the receptor, rather than inhibits synthesis of angiotensin II. ARBs have the advantage of being less likely to induce hyperkalemia and are more easily tolerated in people. Losartan and other ARBs have been used in people who cannot tolerate angiotensin-converting enzyme (ACE) inhibitors. In people it is metabolized to the active carboxylic acid metabolite, which is 10-40 times more potent than the parent drug and believed to be responsible for most clinical effects. The metabolite is not produced in effective levels in dogs.

Indications and Clinical Uses

In dogs, it is reported that they do not convert losartan to the active metabolite, and therefore it has little activity in dogs. However, a related drug, irbesartan (30 mg/kg q12h), has been shown to block angiotensin II receptors.

Precautionary Information

Adverse Reactions and Side Effects

No adverse reactions have been reported in animals. In people, hypotension may occur.

Contraindications and Precautions

No specific contraindications have been reported for animals. Do not use in pregnant animals.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

In dogs, losartan is not converted to the active metabolite. Therefore it has little bioactivity (*J Pharmacol Exp Ther*, 268:1199-1205, 1999). It is suggested instead to consider irbesartan at a dose of 30 mg/kg q12h PO.

Patient Monitoring and Laboratory Tests

Monitor blood pressure in treated animals.

Formulations

Losartan is available in 25- and 50-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

Not recommended.

Cats

No dose established.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 3

Lufenuron

loo-fen'yoo-rah-n

Trade and Other Names: Program

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic. Lufenuron is a benzoylurea insecticide. This class of insecticides was previously used on fruits to decrease damage by insects. Lufenuron (Program) has been used for prevention of flea infections in dogs and cats because it inhibits chitin synthesis. For this use it has been given to dogs at a dose of 10 mg/kg every 30 days and to cats at a dose of 30 mg/kg every 30 days. It may also have some inhibition on fungal cell membranes because it inhibits the cell wall of fungi, which contain chitin, and other complex polysaccharides. Because of this property on fungal cell membranes there has been interest in using lufenuron to treat dermatophytes in small animals. However, proven efficacy has been controversial.

Indications and Clinical Uses

Lufenuron is used to control flea infestations by preventing hatching of eggs. It has been used as part of flea control, often with other drugs that kill adult fleas. Lufenuron has been combined with milbemycin in formulations for small animals, and additional details may be found in the section on milbemycin. There are clinical reports of the use of lufenuron for treating dermatophyte infections in small animals—particularly cats—at high doses of 80-100 mg/kg orally. However, endorsement of this use has diminished and dermatologists have disputed the efficacy and have observed a high incidence of recurrence. In horses lufenuron was not absorbed orally and is not effective for treating fungal infections. It does not have any in vitro effect on *Aspergillus fumigatus* or *Coccidioides immitis*.

Precautionary Information

Adverse Reactions and Side Effects

Refer to the section on lufenuron or milbemycin for details.

Contraindications and Precautions

No contraindications are reported for animals. Some animals may be sensitive to milbemycin, and additional details are found in that section.

Drug Interactions

No drug interactions reported for animals, except those that may pertain to milbemycin.

Instructions for Use

Lufenuron is a highly lipophilic drug and is absorbed best with a meal. If cats have free access to their food, withhold their food until such time that a meal will be consumed readily before administering the lufenuron oral dose. Lufenuron may control flea development with administration once every 30 days in animals.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Lufenuron is available in 45-, 90-, 135-, 204.9-, and 409.8-mg tablets and 135- and 270-mg suspension per unit pack.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Flea control: 10 mg/kg q30d PO.
- Dermatophytes: 80 mg/kg (efficacy questionable).

Cats

- Flea control: 30 mg/kg q30d PO or injection of 10 mg/kg SQ every 6 months.
- Dermatophytes: 80 mg/kg; 100 mg/kg PO is the minimum dose for treating cats in a cattery. These doses should be repeated initially after the first 2 weeks and possibly once per month in animals that may be re-exposed (efficacy questionable).

Large Animal Dosage

Horses

Not effective.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Lufenuron + Milbemycin Oxime

loo-fen'yoo-rah-n + mil-beh-mye'sin oks'eem

Trade and Other Names: Sentinel tablets and Flavor Tabs

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Combination of two antiparasitic drugs. Refer to sections on lufenuron or milbemycin for details.

Indications and Clinical Uses

Lufenuron + milbemycin is used to protect against fleas, heartworms, roundworms, hookworms, and whipworms.

Precautionary Information

Adverse Reactions and Side Effects

There is a high margin of safety at doses used for flea control or treatment of dermatophytes. Adverse effects have not been reported. Lufenuron appears to be relatively safe in pregnant and young animals.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions reported for animals.

Instructions for Use

See section on lufenuron or milbemycin for details.

Patient Monitoring and Laboratory Tests

Monitor for heartworm status in dogs before initiating treatment with milbemycin.

Formulations

The milbemycin/lufenuron ratio is as follows: 2.3/46-mg tablets and 5.75/115-, 11.5/230-, and 23/460-mg Flavor Tabs.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage**Dogs**

- Administer one tablet every 30 days based on tablet size and weight range listed in product label.

Cats

No dose is reported. Each tablet is formulated for the size of the dog.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Lysine (L-Lysine)

lye'seen

Trade and Other Names: Enisyl-F

Functional Classification: Antiviral

Pharmacology and Mechanism of Action

Lysine is an amino acid–based supplement for treating feline herpes virus Type 1 (FHV-1). It acts by antagonism of the growth-promoting effect of arginine, which is an essential amino acid of FHV-1.

Indications and Clinical Uses

Lysine is a supplement for treating FHV-1 in cats. It is intended to reduce viral shedding in infected cats and may improve some clinical signs associated with FHV. However, it has questionable efficacy for treatment of upper respiratory infections in cats. Dietary lysine did not control upper respiratory or ocular infection in cats.

448 Lysine (L-Lysine)

studied in a shelter environment and actually led to an increase in severity of some infections. For this reason, routine use for viral infections in cats should be re-evaluated.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects have been reported in cats.

Contraindications and Precautions

No contraindications have been reported.

Drug Interactions

No drug interactions have been reported for animals.

Instructions for Use

L-Lysine monohydrate can be supplied as a powder and mixed with a small amount of food.

Patient Monitoring and Laboratory Tests

Monitor patient's CBC during treatment.

Formulations

Paste (Enisyl-F) is distributed in syringes in which each mark on the syringe represents 1 mL (250 mg/mL). It has also been available for cats as a metered dose pump to add to food, 100 gram powder (to be mixed with food), 5 ounce oral gel (Viralyis), 600 mL oral paste, and flavored treats.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Cats

- 400 mg/cat/day PO, daily supplement added to cat food.
- Paste formulation: 1-2 mL to adult cats and 1 mL to kittens.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Magnesium Citrate

Trade and other names: Citroma, CitroNesia, and Citro-Mag (Canada)

Functional classification: Laxative

Pharmacology and Mechanism of Action

Saline cathartic. Acts to draw water into the small intestine via an osmotic effect. Fluid accumulation produces distension, which promotes bowel evacuation.

Indications and Clinical Uses

Magnesium citrate is administered orally for constipation and bowel evacuation prior to certain procedures. It also may be used to promote intestinal clearance of an ingested toxin. It is prompt in its cathartic action.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. However, fluid and electrolyte loss can occur with overuse.

Contraindications and Precautions

Magnesium accumulation may occur in patients with renal impairment. Cathartics containing magnesium decrease oral absorption of ciprofloxacin and other fluoroquinolones.

Drug Interactions

No drug interactions have been reported for animals. However, it may increase clearance of some drugs administered orally.

Instructions for Use

Magnesium citrate is commonly used to evacuate the bowel prior to surgery or diagnostic procedures. Doses are empirical and extrapolated from other species. Onset of action is rapid.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. However, monitor magnesium concentrations in patients if repeated treatments or high doses are administered.

Formulations

Magnesium citrate is available in a 6% oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 2-4 mL/kg/day PO.

Large Animal Dosage

Horses and Cattle

- 2-4 mL/kg once PO.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Magnesium Hydroxide

Trade and other names: Milk of Magnesia, Carmilax, and Magnalax

Functional classification: Laxative

Pharmacology and Mechanism of Action

Saline cathartic. Magnesium hydroxide acts to draw water into the small intestine via an osmotic effect. Fluid accumulation produces distension, which promotes bowel evacuation.

Indications and Clinical Uses

Magnesium hydroxide is used for constipation and bowel evacuation prior to certain procedures. It is commonly used to evacuate the bowel prior to surgery or diagnostic procedures. Onset of action is rapid. Magnesium hydroxide also is used as an oral antacid to neutralize stomach acid. In large animals it is used as an antacid and mild cathartic. In cattle, approximately 1 g/kg as a single dose significantly increases rumen pH and decreases rumen microbial activity.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. However, fluid and electrolyte loss can occur with overuse.

Contraindications and Precautions

Magnesium accumulation may occur in patients with renal impairment.

Drug Interactions

Cathartics containing magnesium decrease oral absorption of ciprofloxacin and other fluoroquinolones.

Instructions for Use

Administer to patients only if they are properly hydrated.

Patient Monitoring and Laboratory Tests

Monitor electrolytes with chronic use.

Formulations

Magnesium hydroxide is available as an oral liquid 400 mg/5 mL (Milk of Magnesia) OTC. Milk of Magnesia is approximately 400 mg per 1 teaspoon. It is also available as a 27-g bolus for cattle and sheep and as a powder 310-360 g/lb (approximately 745 g/kg). As a powder, 1.0 pounds of powder is equivalent to 1 gallon of Milk of Magnesia and three 27-g boluses are equal to 1 quart of Milk of Magnesia.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- Antacid: 5-10 mL/dog q4-6h PO.
- Cathartic: 15-50 mL/dog q24h PO.

Cats

- Antacid: 5-10 mL/cat q4-6h PO.
- Cathartic: 2-6 mL/cat q24h.

Large Animal Dosage

Sheep and Cattle

- 1 g/kg or 1 bolus per 27 kg (60 pounds) PO, once (3-4 boluses for adult cattle).
- For the powder, mix 1 lb with 1 gallon water and administer 500 mL/45 kg (500 mL per 100 pounds).

Regulatory Information

Withdrawal time for animals intended for food: 12-24 hours (milk) depending on the product.

Magnesium Sulfate

Trade and other names: Epsom salts

Functional classification: Laxative, antiarrhythmic

Pharmacology and Mechanism of Action

Saline cathartic and antiarrhythmic. Magnesium sulfate when administered orally acts to draw water into the small intestine via an osmotic effect. Fluid accumulation produces distension, which promotes bowel evacuation. It is used as a replacement for magnesium in patients who are deficient. When used as an antiarrhythmic it serves as a source of magnesium for treating refractory arrhythmias because in animals with hypomagnesemia it acts as a cofactor for the Na/K ATPase pump. It also may block calcium channels.

Indications and Clinical Uses

Magnesium sulfate is used for constipation and bowel evacuation prior to certain procedures. An injectable solution of magnesium sulfate is used to treat refractory arrhythmias in patients who are critically ill. In horses magnesium sulfate is administered for ventricular tachycardia that is not responsive to other drugs. In cattle, magnesium sulfate is used to treat hypomagnesemia, especially in dairy cattle.

Precautionary Information

Adverse Reactions and Side Effects

High doses may cause muscle weakness and respiratory paralysis. With repeated administration, fluid and electrolyte loss can occur with overuse. When treating arrhythmias it has been administered at doses of 0.1-0.2 mEq/kg safely.

Contraindications and Precautions

Magnesium accumulation may occur in patients with renal impairment.

Drug Interactions

Cathartics containing magnesium decrease oral absorption of ciprofloxacin and other fluoroquinolones. Magnesium sulfate is incompatible with alkaline solutions. Some metal ions (e.g., calcium) may form insoluble sulfates.

Instructions for Use

Magnesium sulfate when used as a laxative is administered for its prompt action to evacuate bowel prior to surgery or diagnostic procedures. Onset of action is rapid. For use in cattle (hypomagnesemia) an initial dose can be administered IV, followed

452 Mannitol

by an SQ dose to produce a sustained effect. Monitor animals for hypocalcemia, which can occur simultaneously.

Patient Monitoring and Laboratory Tests

Monitor magnesium and calcium concentrations. Normal magnesium concentrations in animals are 1.32-2.46 mEq/L. Many cattle also have hypocalcemia.

Formulations

Magnesium sulfate is available as solid crystals in generic preparations. Solution for injection is 12.5% mEq/mL. Intravenous and subcutaneous solutions for cattle are usually 1.5-4 g/L.

Stability and Storage

Crystals are stable if stored in a dry container. Store injectable solutions at room temperature, in a tightly sealed vial, protected from light.

Small Animal Dosage

Dogs

- 1-2 mEq/kg/day, PO. (or 8-25 g/dog q24h PO).

Cats

- 2-5 g/cat q24h PO.

Dogs and Cats

- Constant rate infusion (CRI) for treating arrhythmias: 0.15-0.3 mEq/kg slowly over 5-15 minutes, followed by 0.75-1.0 mEq/kg/day.
- Use during fluid therapy: Supplement fluid solutions with 0.75-1 mEq/kg/day.

Large Animal Dosage

Cattle

- 2-3 g per cow IV over 10 minutes. This may be followed by 200-400 mL per cow of 25% magnesium sulfate, SQ to supply 50-100 g per cow.

Horses

- 1 g/horse q12-24h PO or 2-4 mg/kg IV. For ventricular tachycardia an infusion of 1 g/min, up to a maximum of 25 g, can be administered IV.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Mannitol

man'ih-tole

Trade and other names: Osmitrol

Functional classification: Diuretic

Pharmacology and Mechanism of Action

Hyperosmotic diuretic. Mannitol occurs naturally as a sugar in fruits and vegetables. As an osmotic diuretic, mannitol is freely filtered by the glomerulus, but it is not reabsorbed by the renal tubule. Therefore it increases osmolality of the urine. The osmotic effect inhibits reabsorption of fluid from the renal tubules, and this produces a natriuretic effect and strong diuresis. Reabsorption of sodium chloride

and solutes also is inhibited. Mannitol, compared to other diuretic drugs, produces a more profound diuretic effect, which can potentially cause excessive fluid loss in a patient. After intravenous administration, mannitol increases the plasma osmolality, which draws fluid from tissues to plasma, which is helpful for treating tissue edema (e.g., cerebral edema). It reduces intracranial pressure. It is also used as an antiglaucoma agent because it lowers intraocular pressure when administered IV.

Indications and Clinical Uses

Mannitol is administered IV for treatment of cerebral edema, acute glaucoma, and conditions associated with tissue edema. Mannitol also has been used to promote urinary excretion of certain toxins and in the management of anuric or oliguric renal failure.

Precautionary Information

Adverse Reactions and Side Effects

Mannitol produces a profound diuresis and can cause significant fluid loss and electrolyte imbalance. An administration rate that is too rapid may expand the extracellular volume excessively.

Contraindications and Precautions

Do not use in patients who are dehydrated. Use cautiously when intracranial bleeding is suspected because it may increase bleeding. (This effect is controversial when dealing with intracranial hemorrhage.)

Drug Interactions

Do not administer simultaneously with blood replacement. If blood is administered simultaneously, sodium chloride must be added to each liter of mannitol (20 mEq/L). Mannitol may increase renal clearance of some drugs.

Instructions for Use

Use only in animals in which fluid and electrolyte balance can be monitored.

Patient Monitoring and Laboratory Tests

Monitor hydration and electrolyte balance in treated animals. Monitor intraocular pressure when treating acute glaucoma.

Formulations

Mannitol is available in a 5%, 10%, 15%, 20%, and 25% solution for injection. The 25% solution is equivalent to 1 g in 4-mL vials.

Stability and Storage

Once solutions are prepared, discard unused portions. If solutions are chilled, crystals may form.

Small Animal Dosage

Dogs

- Diuretic: 1 g/kg of 5%-25% solution IV to maintain urine flow.
- Fluid expansion: 0.5-2 g/kg IV (or 0.1 g/kg/hr)
- Glaucoma or CNS edema: 0.25-2 g/kg of 15%-25% solution over 30-60 min IV (repeat in 6 hours if necessary)

Cats

- Fluid expansion: 0.5 g/kg to 0.8 g/kg IV over 5 minutes, followed by constant rate infusion of 1 mg/kg/min.

Large Animal Dosage

- 0.25-1 g/kg (20% solution) IV administered over 1 hour.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Marbofloxacin

mar-boe-floks'ah-sin

Trade and other names: Zeniquin and Marbocyl (European name)

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Fluoroquinolone antimicrobial. Marbofloxacin acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. Marbofloxacin is a bactericidal with a broad spectrum of activity. Sensitive bacteria include *Staphylococcus*, *Escherichia coli*, *Proteus*, *Klebsiella*, and *Pasteurella*. *Pseudomonas aeruginosa* is moderately sensitive but requires higher concentrations. Some methicillin-resistant *Staphylococcus* also may be resistant to fluoroquinolones. Marbofloxacin has poor activity against streptococci and anaerobic bacteria.

Indications and Clinical Uses

Marbofloxacin, like other fluoroquinolones, is used to treat susceptible bacteria in a variety of species. Marbofloxacin is registered for use in dogs and cats. Infections treated with marbofloxacin include skin and soft tissue infections, bone infections, UTIs, pneumonia, and infections caused by intracellular organisms. Marbofloxacin has been effective for some bloodborne pathogens such as *Mycoplasma haemofelis*, in cats at a dose of 2.75 mg/kg q24h PO for 14 days. Marbofloxacin also has been used in horses to treat infections caused by susceptible bacteria. In dogs the half-life is 7-9 hours, but it has been longer in some studies. In horses the half-life has varied from 4.7 to 7.6 hours, depending on the study. Volume of distribution in these species is 1.2 to 2 L/kg. Oral absorption is close to 100% in small animals and approximately 60% in horses.

Precautionary Information

Adverse Reactions and Side Effects

High concentrations may cause CNS toxicity. Like other fluoroquinolones, it may cause some nausea, vomiting, and diarrhea at high doses. When administered IV to anesthetized patients, it did not alter cardiovascular parameters. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4-28 weeks of age. Large, rapidly growing dogs are the most susceptible. Marbofloxacin at a dose of twice the upper limit caused articular damage in dogs that were 4-5 months old. In cats 8 months old at doses of 17 and 28 mg/kg for 42 days articular, cartilage injury was observed. Blindness in cats has been reported from some quinolones such as enrofloxacin and nalidixic acid. There are no known clinical reports of this reaction with marbofloxacin, and toxicity studies by the manufacturer showed that it did not cause ocular lesions or vision problems in cats. At doses of 17 mg/kg and 28 mg/kg (three times

and five times the upper limit of dosing) it did not produce ocular changes. Marbofloxacin has been administered to horses orally without producing adverse effects in the GI tract.

Contraindications and Precautions

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures.

Drug Interactions

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, and calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur. Marbofloxacin may be administered with other antibiotics and anesthetic agents without evidence of drug interaction.

Instructions for Use

At the low range of the approved label dose, marbofloxacin is active against most susceptible bacteria. Within the approved dose range, higher doses are needed for organisms with higher minimum inhibitory concentration (MIC) values. Doses published for European use are lower than US approved doses, but there is no evidence that this has affected efficacy. For example, successful treatment of pyoderma in European studies has been accomplished with doses of 2.0 mg/kg once daily, but in the US the lowest dose is 2.75 mg/kg once daily.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms in dogs and cats are ≤ 1.0 mcg/mL. If other fluoroquinolones are used to test susceptibility to marbofloxacin, results will be similar. However, marbofloxacin is slightly more active than other veterinary quinolones against *Pseudomonas aeruginosa*, and the human drug ciprofloxacin is more active.

Formulations

Marbofloxacin is available in 25-, 50-, 100-, and 200-mg tablets. Injectable marbofloxacin (Marbocyl) is approved in other countries but not in the US.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not compound with ingredients that may chelate with quinolones, such as iron or calcium.

Small Animal Dosage

Dogs

- 2.75-5.5 mg/kg once-daily PO.

Cats

- 2.75-5.5 mg/kg once-daily PO.

Large Animal Dosage

Horses

- 2 mg/kg once-daily IV or PO for treatment of susceptible gram-negative bacteria. (IV formulation not available in the US.) An oral dose of 2 mg/kg may not be sufficient for treating other bacteria that cause infections in horses, including gram-positive cocci. However, higher doses have not been tested.

Regulatory Information

Marbofloxacin is prohibited from use in animals intended for food. There are no withdrawal times established because it should not be administered to animals that produce food.

Maropitant citrate

mar-op'-i-tent

Trade and other names: Cerenia

Functional classification: Antiemetic

Pharmacology and Mechanism of Action

Maropitant is an antiemetic from the same group as the human drug aprepitant (Emend). These drugs act as an antiemetic by blocking the neurokinin-1 (NK₁) receptor (also known as Substance P). It has less affinity for other neurokinin receptors (NK₂ and NK₃). Although NK₁ receptors are involved in other physiologic and behavioral responses, at doses used to control vomiting there were no adverse effects associated with blockade of other receptors. Neurokinin-1 is a neurotransmitter to stimulate vomiting from the emetic center. Maropitant can inhibit vomiting that is stimulated from both central and peripheral sources mediated by other neurotransmitters such as acetylcholine, histamine, dopamine, and serotonin. In dogs, the half-life was 4 to 8 hours, depending on the dose. Dose-dependent pharmacokinetics occur with the clearance decreasing and half-life increasing with doses above 2 mg/kg. Because of nonlinear pharmacokinetics, accumulation is possible with repeated dosing. Oral absorption is 24% at 2 mg/kg and 37% at 8 mg/kg in dogs. Pharmacokinetics are not affected by feeding. In cats the clearance is much lower than in dogs, and the half-life is longer than in dogs at 13-17 hours. In cats, it has nearly complete SQ absorption and 50% oral absorption.

Indications and Clinical Uses

Maropitant is approved for use as an antiemetic in dogs to inhibit vomiting from both central and peripheral sources. It has been effective to inhibit vomiting from chemotherapy, gastrointestinal disease, toxins, renal disease, vestibular stimuli (motion sickness), and circulating stimuli via the chemoreceptor trigger zone. After SQ injection it has a rapid onset and a duration of 24 hours. Although not approved for cats, it has been used safely and effectively in cats to treat vomiting from a variety of sources, such as motion sickness and stimulation by emetogenic agents, with a duration of action of 24 hours.

Precautionary Information

Adverse Reactions and Side Effects

Maropitant may cause slight pain or irritation from SQ injection. It has been recognized that the pain is caused by alteration of the formulation, which may occur when the injectable formulation is stored at room temperature. The cyclodextrin complex of maropitant is preserved at cold temperatures and is more stable and intact when the formulation is refrigerated. Therefore, the adverse event associated with a painful injection can be reduced if injectable maropitant is

stored in the refrigerator before use. Safety studies have been conducted with maropitant in both preclinical and clinical trials. In experimental dogs it was safe at 3× and 5× the labeled dose. Adverse effects observed in trials included excess salivation and muscle tremors. In cats it has been well-tolerated at high doses (of a factor of 10×) and was safe at 5 mg/kg for 15 consecutive days.

Contraindications and Precautions

There is accumulation after repeated doses and decreased clearance with higher doses. Therefore, because of accumulation, it should not be administered for more than 5 consecutive days. Allow a 2-day washout period before instituting another course of treatment. Take care to identify any underlying disease whenever possible instead of relying on maropitant to control the clinical signs. Maropitant effects and pharmacokinetics are not affected by renal disease.

Drug Interactions

Single doses have been administered in an IV line, but precipitation may be observed if mixed with alkalinizing solutions. Maropitant is an NK₁ inhibitor. Other neurokinin receptors are affected by a lesser degree. Because of the unique mechanism of action, drug interactions have not been identified. Maropitant has been used safely with other drugs, including anesthetics and anticancer agents. Maropitant is highly protein bound, but it is not known if there are protein-binding interactions with other drugs.

Instructions for Use

Clinical trials in dogs have outlined the appropriate protocols for use of maropitant. It has been effective for a wide range of causes of vomiting in dogs. In cats, although not approved, it has been effective for a variety of causes of vomiting, including motion sickness and stimulation from emetogenic agents. The effective dose in cats is 1 mg/kg regardless of cause.

Patient Monitoring and Laboratory Tests

Monitor for clinical signs and disease that may be a cause for the vomiting. Other specific monitoring and tests are not needed to use maropitant safely.

Formulations

Maropitant is available in 16-, 24-, 60-, or 160-mg tablets and a 10-mg/mL injectable solution.

Stability and Storage

Store in a tightly sealed container, protected from light. The injectable formulation can be stored at room temperature and in the refrigerator, but as noted earlier, pain from injection can be reduced if formulation is stored in the refrigerator. Discard vial after 28 days of first use.

Small Animal Dosage

Dogs

- 1 mg/kg SQ, or 2 mg/kg PO, once daily for no more than 5 consecutive days.
- Motion sickness: 8 mg/kg PO, once daily for up to 2 consecutive days.

Cats

- 1 mg/kg, once daily, IV, SQ, or PO (same dose for all causes of vomiting, including motion sickness).

Large Animal Dosage

No large animal doses have been identified.

Regulatory Information

No regulatory information is available for food animals. There are no withdrawal times established, and it is not recommended to be administered to animals that produce food.

MCT Oil

Trade and other names: Medium chain triglycerides (MCT) oil

Functional classification: Nutritional supplement

Pharmacology and Mechanism of Action

MCT oil supplements triglycerides in animals.

Indications and Clinical Uses

MCT oil is used to treat lymphangiectasia and as a component of enteral feeding formulas.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects not reported in veterinary medicine. It may cause diarrhea in some patients.

Contraindications and Precautions

No contraindications reported.

Drug Interactions

No drug interactions reported.

Instructions for Use

Results of clinical trials using MCT oil have not been reported. Many enteral feeding formulas contain MCT oil (many polymeric formulations).

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

MCT is available as an oral liquid.

Stability and Storage

Store in a tightly sealed container, protected from light, at room temperature, and in a cool place. Do not store in a plastic container. It may be mixed with fruit juices or food products prior to administration.

Small Animal Dosage

- 1-2 mL/kg daily in food.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Mebendazole

meh-ben'dah-zole

Trade and other names: Telmintic, Telmin, Vermox (human preparation), and generic brands

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Benzimidazole antiparasitic drug. Like other benzimidazoles, mebendazole produces a degeneration of the parasite microtubule and irreversibly blocks glucose uptake in parasites. Inhibition of glucose uptake causes depletion of energy stores in the parasite, eventually resulting in death. However, there is no effect on glucose metabolism in mammals.

Indications and Clinical Uses

Mebendazole is used in horses for treatment of infections caused by large roundworms (*Parascaris equorum*), large strongyles (*Strongylus edentatus*, *S. equinus*, and *S. vulgaris*), small strongyles, and mature and immature (fourth larval stage pinworms [*Oxyuris equi*]). In dogs it has been used for treatment of infections of roundworms (*Toxocara canis*), hookworms (*Ancylostoma caninum* and *Uncinaria stenocephala*), whipworms (*Trichuris vulpis*), and tapeworms (*Taenia pisiformis*).

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are rare. Mebendazole causes occasional vomiting and diarrhea in dogs. Some reports suggest idiosyncratic hepatic reactions in dogs.

Contraindications and Precautions

No contraindications have been reported.

Drug Interactions

No drug interactions have been reported for animals.

Instructions for Use

The powder for horses may be sprinkled directly on the horse's grain or dissolved in 1 L of water and administered via stomach tube. For dogs, it may be added directly to its food.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Mebendazole is available in 40- or 166.7-mg/g powder, 200-mg/g equine paste, 33.3-mg/mL solution, and 100-mg chewable tablets (human preparation). Some equine formulations contain 83.3 mg mebendazole plus 375 mg trichlorfon in each gram of powder.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 22 mg/kg (mixed with food) q24h for 3 days. May be repeated in 3 weeks.

Large Animal Dosage

Horses

- 8.8 mg/kg PO.

Regulatory Information

Do not administer to horses intended for food.

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Meclizine

mek'lih-zeen

Trade and other names: Antivert, Bonine, Meclozine (British name), and generic brands

Functional classification: Antiemetic

Pharmacology and Mechanism of Action

Antiemetic. Antihistamine. Like other antihistamines, it blocks the effect of histamine on the H₁ receptor. However, it also has central anticholinergic actions, which may be responsible for the central-acting antiemetic properties.

Indications and Clinical Uses

Meclizine is used to treat vomiting. It may suppress the chemoreceptor trigger zone. It also is used for treatment of motion sickness. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Other drugs with proven efficacy (e.g., maropitant) are often used instead of meclizine for vomiting.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. Anticholinergic (atropine-like) effects may cause side effects.

Contraindications and Precautions

Use cautiously in animals with GI obstruction or glaucoma.

Drug Interactions

No drug interactions have been reported for animals.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals is based on experience in people or anecdotal experiences in animals.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Mecizine is available in 12.5-, 25-, and 50-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 25 mg per dog q24h PO (for motion sickness, administer 1 hour prior to traveling).

Cats

- 12.5 mg per cat q24h PO (for motion sickness, administer 1 hour prior to traveling).

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

M

Meclofenamate Sodium, Meclofenamic Acid

mek'loe-fen'am-ate soe-dee'um, mek'loe-fen-am'ik ass'id

Trade and other names: Arquel and Meclofen

Functional classification: Nonsteroidal anti-inflammatory drug (NSAID)

Pharmacology and Mechanism of Action

Meclofenamate is also known as meclofenamic acid and is related to tolfenamic acid, which is approved in some countries for animals. Meclofenamate and other NSAIDs have produced analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the cyclo-oxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. Meclofenamic acid is a balanced COX-1/COX-2 inhibitor.

Indications and Clinical Uses

Meclofenamate is used in animals for treatment of pain and inflammation.

The most common use has been musculoskeletal inflammation. Use in animals has diminished because of decreased availability and increased popularity of other drugs.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals, but adverse effects common to other NSAIDs are possible. These side effects are generally GI in nature (e.g., gastritis, gastric ulcers).

Contraindications and Precautions

Do not administer to animals prone to GI ulcers. Do not administer with other ulcerogenic drugs such as corticosteroids. The original labeling for animals suggests that duration is limited to 5-7 days.

Drug Interactions

Like other NSAIDs, ulcerogenic effects are potentiated when administered with corticosteroids. Meclofenamic acid, like other NSAIDs, may interfere with the action of diuretics, such as furosemide, and angiotensin-converting enzyme (ACE) inhibitors.

Instructions for Use

Most of the experience with meclufenamate has been with horses. Commercial formulations are no longer marketed for animals. Administer with food.

Patient Monitoring and Laboratory Tests

Monitor for signs of GI ulceration during use.

Formulations

Meclofenamate is available in 50- and 100-mg capsules (rarely available commercially any longer), 10- and 20-mg tablets (formulation for dogs), and granules for horses (5% meclufenamic acid).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 1.1 mg/kg/day for up to 5 days PO.

Large Animal Dosage

Horses

- 2.2 mg/kg q24h PO.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Medetomidine Hydrochloride

meh-deh-toe'mih-deen hye-droe-klor'ide

Trade and other names: Domitor

Functional classification: Analgesic, Alpha₂ agonist

Pharmacology and Mechanism of Action

Alpha₂-adrenergic agonist. Alpha₂-agonists decrease release of neurotransmitters from the neuron. Medetomidine is a racemic mixture containing 50% dexmedetomidine and 50% levomedetomidine. Dexmedetomidine is the active enantiomer of the mixture (D-isomer); therefore (on a mg/mg basis) dexmedetomidine is twice the potency of medetomidine but with the same pharmacological activity and equivalent analgesic and sedative effects. The proposed mechanism whereby the alpha-2-agonists decrease transmission is via binding to presynaptic alpha₂-receptors (negative feedback receptors). The result is decreased sympathetic outflow, analgesia, sedation, and anesthesia. Other drugs in this class include xylazine, detomidine, and clonidine. Receptor-binding studies indicate that alpha₂/alpha₁-adrenergic receptor selectivity for medetomidine was more than 1000-fold greater than xylazine.

Indications and Clinical Uses

Because of potency and availability, dexmedetomidine has replaced medetomidine for most indications in small animals. Medetomidine, like other alpha₂-agonists, is used as a sedative, anesthetic adjunct, and analgesic. It has been used to sedate animals for intradermal skin testing without affecting results. Duration of effect is 0.5-1.5 hours at the low dose and up to 3 hours for the high dose. Compared to xylazine, medetomidine has produced better sedation and analgesia than xylazine in dogs. Many anesthesiologists have recommended combinations of medetomidine and ketamine, medetomidine and butorphanol, or medetomidine and hydromorphone in dogs for sedation and short-term procedures. Medetomidine combined with an opiate (butorphanol or hydromorphone) has produced a longer duration of sedation and more desirable degree of sedation than medetomidine used alone.

Precautionary Information

Adverse Reactions and Side Effects

In small animals, vomiting is the most common acute effect. Alpha₂-agonists decrease sympathetic output. Cardiovascular depression may occur. Constant rate infusion (CRI) of 1.5 mcg/kg/hr has caused decreased heart rate and sinus arrhythmia in dogs. Doses as low as 1 mcg/kg IV can reduce cardiac output to less than 40% of resting value. Medetomidine will cause initial bradycardia and hypertension, but bradycardia usually does not require intervention with anticholinergic drugs (e.g., atropine). If adverse reactions are observed, reverse with atipamezole. If atipamezole is not available, yohimbine also can reverse medetomidine.

Contraindications and Precautions

Use cautiously in animals with heart disease. Use may be contraindicated in older animals with preexisting cardiac disease. Xylazine causes problems in pregnant animals, and this also should be considered for other alpha₂-agonists. Use cautiously in animals that are pregnant because it may induce labor. In addition, it may decrease oxygen delivery to the fetus in late gestation.

Drug Interactions

Do not use with other drugs that may cause cardiac depression. Do not mix in a vial or syringe with other anesthetics, except as listed under the dosing section. Reverse with atipamezole at a dose of 25-300 mcg/kg IM. Use with opioid analgesic drugs will greatly enhance the CNS depression, so consider lowering doses if administered with opioids.

Instructions for Use

Medetomidine, dexmedetomidine, and detomidine are more specific for the α_2 -receptor than xylazine. Dexmedetomidine has twice the potency of medetomidine. Therefore, these drugs should not be used interchangeably without consulting the dose recommendations. The α_2 -agonists may be used for sedation, analgesia, and minor surgical procedures. Many veterinarians use doses that are much less than the doses listed on the label. For example, lower doses are sometimes used for short-term sedation and analgesia, particularly when combined with other drugs such as opiates. Reverse with atipamezole at a dose of 25-300 mcg/kg (equal to volume of medetomidine used) IM.

Patient Monitoring and Laboratory Tests

Monitor vital signs during anesthesia. Monitor heart rate, blood pressure, and ECG if possible during anesthesia.

Formulations

Medetomidine is available in a 1.0-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 750 mcg/m² IV or 1000 mcg/m² IM. The IV dose is equivalent to 18-71 mcg/kg IV.
- Lower doses are often used for short-term sedation and analgesia of 5-15 mcg/kg (0.005-0.015 mg/kg) IV, IM, or SQ. These doses may be increased up to 60 mcg/kg when severe pain is involved. 20 mcg/kg has been used in combination with butorphanol (0.2 mg/kg), hydromorphone (0.1 mg/kg), or ketamine for short-term procedures.
- CRI: Loading dose of 1 mcg/kg IV, followed by 0.0015 mg/kg/hr (1.5 mcg/kg/hr). CRI may produce adverse cardiovascular effects and should be monitored closely.

Cats

- 750 mcg/m² IV or 1000 mcg/m² IM. The IV dose is equivalent to 18-71 mcg/kg IV. Doses in the lower range are used for short-term sedation and analgesia (e.g., 10-20 mcg/kg), but higher doses (up to 80 mcg/kg) have been used for more severe pain. Medetomidine may be administered IM or IV.
- Combination with ketamine: 5 mg/kg ketamine + 5 mcg/kg medetomidine, mixed in one syringe and administered IM.

Large Animal Dosage

Lambs

- 30 mcg/kg (0.03 mg/kg) IV.

Horses

- 10 mcg/kg IM as a sedative prior to induction for anesthesia. Some horses may need an additional dose of 4 mcg/kg IV. In horses, guaifenesin (5% solution) and ketamine (2.2 mg/kg) have been used in combination.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Medroxyprogesterone Acetate

meh-droks'ee-proe-jess'teh-rone ass'ih-tate

Trade and other names: Depo-Provera (injection), Provera (tablets), and Cycrin (tablets)

Functional classification: Hormone

Pharmacology and Mechanism of Action

Progestin hormone. Medroxyprogesterone is a derivative of acetoxyprogesterone. Medroxyprogesterone acetate replaces progesterone in the body and will mimic progesterone's hormone effects. In the Depo-Provera formulation a single injection can produce long-acting effects.

Indications and Clinical Uses

Medroxyprogesterone acetate is used to replace progesterone in animals. Most often it is used as progesterone hormone treatment to control the estrus cycle. It also is used for management of some behavioral and dermatologic disorders (such as urine spraying in cats and alopecia). However, its use for behavioral therapy in animals is discouraged because of high relapse rates and incidence of hormone-related adverse effects. In horses it has been used to prevent estrus.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include polyphagia, polydipsia, adrenal suppression (cats), increased risk of diabetes mellitus, pyometra, diarrhea, and increased risk of neoplasia. In cats a single injection of medroxyprogesterone acetate has produced feline mammary fibroepithelial hyperplasia.

Contraindications and Precautions

Do not use in animals at a high risk for diabetes. In humans it increases the risk of thromboembolic problems. Do not use in pregnant animals.

Drug Interactions

No drug interactions are reported. However, clearance of medroxyprogesterone is increased with drugs known to induce hepatic P450 enzymes (see Appendix).

Instructions for Use

Intervals of administration vary with condition. Intervals may range from once/week to once/month.

Clinical studies in animals have studied primarily the reproductive use and effects on behavioral use. Medroxyprogesterone acetate may have fewer side effects than megestrol acetate.

Patient Monitoring and Laboratory Tests

It may increase concentrations of serum cholesterol and some liver enzymes.

Formulations

Medroxyprogesterone is available in 150- and 400-mg/mL suspension injection and 2.5-, 5-, and 10-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 1.1-2.2 mg/kg every 7 days IM.
- Behavior problems: 10-20 mg/kg SQ.
- Prostatic disease (dogs): 3-5 mg/kg IM or SQ.

Large Animal Dosage

Horses

- Prevent estrus: 250-500 mg/horse IM.

Regulatory Information

There are no withdrawal times established because this drug should not be administered to animals that produce food.

Megestrol Acetate

meh-jess'trole ass'ih-tate

Trade and other names: Ovaban and Megace

Functional classification: Hormone

Pharmacology and Mechanism of Action

Progestin hormone. Megestrol acetate mimics the effects of progesterone in animals.

Indications and Clinical Uses

Megestrol acetate is used in animals as a progesterone hormone treatment to control the estrus cycle. It also has been used for management of some behavioral and dermatologic disorders (such as urine spraying in cats and alopecia). However, its use for behavioral therapy in animals is discouraged because of high relapse rates and incidence of hormone-related adverse effects.

In horses, it has been used to prevent estrus, but efficacy for this indication has not been good at doses of 10-20 mg/day/horse.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include polyphagia, polydipsia, adrenal suppression (cats), increased risk of diabetes, pyometra, diarrhea, and increased risk of neoplasia.

Contraindications and Precautions

Do not use in diabetic animals or animals that may be at risk for developing diabetes. Do not use in pregnant animals.

Drug Interactions

No drug interactions are reported. However, clearance of medroxyprogesterone is increased with drugs known to induce hepatic P450 enzymes (see Appendix).

Instructions for Use

Clinical studies in animals have studied primarily the reproductive use and effects on behavioral use. Medroxyprogesterone acetate may have fewer side effects than megestrol acetate.

Patient Monitoring and Laboratory Tests

Because of risk of diabetes mellitus, monitor glucose concentrations during treatment periodically.

Formulations

Megestrol acetate is available in 5-mg tablets (veterinary preparation) and 20- and 40-mg tablets (human preparation).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Proestrus: 2 mg/kg q24h PO for 8 days.
- Anestrus: 0.5 mg/kg q24h PO for 30 days.
- Treatment of behavior problems: 2-4 mg/kg q24h for 8 days (reduce dose for maintenance).

Cats

- Dermatologic therapy or urine spraying: 2.5-5 mg/cat q24h PO for 1 week then reduce to 5 mg once or twice/week cat.
- Suppress estrus: 5 mg/cat/day for 3 days, then 2.5-5 mg once/week for 10 weeks.

Large Animal Dosage

Horses

- Suppress estrus: 0.5 mg/kg q24h PO.

Regulatory Information

There are no withdrawal times established because this drug should not be administered to animals that produce food.

Melarsomine Dihydrochloride

mel-ar'soe-meen

Trade and other names: Immiticide

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Organic arsenical compound. Arsenicals alter glucose uptake and metabolism to eliminate heartworms. Melarsomine has replaced older arsenicals such as thiacetarsamide (Caparsolate).

Indications and Clinical Uses

Melarsomine is used for heartworm adulticide therapy. See Instructions for Use for proper administration. Melarsomine is highly effective for eliminating heartworms in dogs. Efficacy in cats is only 36%. Usually cats are not treated because it is a self-limiting disease and only supportive treatment is administered (corticosteroids, bronchodilators, and antiemetics).

Precautionary Information

Adverse Reactions and Side Effects

Melarsomine may cause pulmonary thromboembolism 7-20 days after therapy, anorexia (13% incidence), injection-site reaction (32% incidence of myositis), or lethargy or depression (15% incidence). It causes elevations of hepatic enzymes. High doses (three times the dose) can cause pulmonary inflammation and death. If high doses are administered, dimercaprol (3 mg/kg IM) may be used as antidote. To prevent adverse reactions of adulticide therapy, many veterinarians administer prednisolone or prednisone at a dose of 0.5 mg/kg q12h for the first week and 0.5 mg/kg, q24h for the second week, followed by 0.5 mg/kg every other day for 1 to 2 weeks. There is also evidence that doxycycline (10 or 20 mg/kg per day, PO) may decrease pulmonary reactions to melarsomine therapy.

Contraindications and Precautions

Use cautiously in animals with high heartworm burden. Specifically, melarsomine is contraindicated in dogs with Class 4 (very severe) heartworm disease.

Drug Interactions

No drug interactions are reported. Administration of prednisolone does not affect efficacy of melarsomine.

Instructions for Use

Dose regimens are based on severity of heartworm disease. Follow product insert carefully for instructions on proper administration. Also evaluate patient to determine class of heartworm disease (Class 1-4) before initiating treatment. Class 1 and 2 are least severe. Class 3 is severe and Class 4 is most severe and should not be treated with adulticide before surgery. In animals with severe burdens, and even including Class 1 and 2 patients, some cardiologists recommend using a three dose protocol. The three dose protocol, which includes a single IM injection of 2.5 mg/kg to decrease the initial worm burden, then administer two additional doses, 24 hours apart, in 2 or 3 months. Alternatively, there may be benefits for administering a preventive dose of a macrocyclic lactone, with doxycycline, for 30 days, followed by the first injection of melarsomine at 60 days, and two more injections of melarsomine at 90 days. Avoid human exposure by washing hands after handling or wearing gloves. There should be strict exercise restriction in dogs during adulticide treatment. More details on the protocol for administration can be found at the American Heartworm Society's website (<http://www.heartwormsociety.org/>).

Patient Monitoring and Laboratory Tests

Monitor heartworm status and microfilaria after treatment. Monitor treated patients carefully for signs of pulmonary thromboembolism.

Formulations

Melarsomine is available in a 25-mg/mL injection.

Stability and Storage

After reconstitution, solution retains potency for 24 hours. Do not freeze solutions after they are prepared.

Small Animal Dosage

Dogs

Administer via deep intramuscular injection.

- Class 1-2: 2.5 mg/kg/day for 2 consecutive days. See Instructions for Use section for more alternative protocols for these patients.
- Class 3: 2.5 mg/kg once, then in 1 month two additional doses 24 hours apart.

Cats

- Not recommended.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

There are no withdrawal times established because this drug should not be administered to animals that produce food.

Meloxicam

mel-oks'ih-kam

Trade and other names: Metacam (veterinary preparation), Mobic (human preparation), Metacam suspension (equine preparation, Europe), and Mobicox (human formulation in Canada)

Functional classification: Anti-inflammatory

M

Pharmacology and Mechanism of Action

Meloxicam is a nonsteroidal anti-inflammatory drug (NSAID). Like other drugs in this class, meloxicam has analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the cyclo-oxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Meloxicam is relatively COX-1 sparing compared to older NSAIDs, but it is not known if the specificity for COX-1 or COX-2 is related to efficacy or safety. Meloxicam has a half-life of 23-24 hours in dogs, 15 hours in cats, and 8.5 (range 5-14.5) in horses. Meloxicam is highly protein bound. Oral absorption is almost complete in dogs when administered with food. Absorption is 85%-98% in horses and is not affected significantly by feeding. Absorption was 100% in ruminant calves, with a half-life of 20-43 hours.

Indications and Clinical Uses

Meloxicam is used to decrease pain, inflammation, and fever. It has been used for the acute and chronic treatment of pain and inflammation in dogs and cats. One of the most common uses is osteoarthritis, but it has also been used for pain associated with surgery. Both acute and long-term safety and efficacy have been established for dogs. In studies performed in dogs, higher doses (up to 0.5 mg/kg) were more effective than lower doses but also were associated with a higher incidence of GI adverse effects. Use in cats is limited to short-term use or long-term use at low doses. In cats, meloxicam has comparable, and even superior, effectiveness compared

to butorphanol for treating pain associated with surgery. Acute response to treating fever in cats also has been demonstrated. In pigs, meloxicam is effective for mastitis–metritis–agalactia syndrome. In horses, meloxicam is effective for treating pain and inflammation associated with surgery. In European countries it is registered for use in horses, pigs, and cattle. In these countries the approved use is adjunctive therapy of acute respiratory disease, diarrhea, and acute mastitis. It has also been effective to decrease discomfort associated with dehorning procedures in cattle.

Precautionary Information

Adverse Reactions and Side Effects

Major adverse effects are gastrointestinal, including vomiting, diarrhea, and ulceration. Because meloxicam appears to be relatively COX-1 sparing, adverse effects are expected to be less than other NSAIDs that are not as selective, but this has not been demonstrated on controlled clinical trials. Renal toxicity, especially in dehydrated animals or animals with preexisting renal disease, has been shown for some NSAIDs. Renal injury has been reported in dogs from doses of 0.3–0.5 mg/kg and higher. GI ulceration has been observed when dogs were administered doses slightly higher than registered doses. In cats at high doses (five times the dose) vomiting and other GI problems were reported. With repeated doses (9 days) of 0.3 mg/kg/day to cats, inflamed GI mucosa and ulceration were observed.

Contraindications and Precautions

Dogs and cats with preexisting GI problems or renal problems may be at a greater risk of adverse effects from NSAIDs. However, at a dose of 0.02 mg/kg per day, long-term use in cats did not cause progression of renal disease in cats with pre-existing renal disease. Safety in pregnant animals is not known, but adverse effects have not been reported. The manufacturer does not recommend a second dose of meloxicam injection to cats. The oral meloxicam solution of meloxicam contains xylitol. Xylitol is an artificial sweetener that can be toxic to dogs and can produce hypoglycemia and liver injury with high doses exceeding 0.1 g/kg. With approved doses of meloxicam oral solution, the toxic level of xylitol is not likely to be exceeded, but one should be cautious about adding other drugs that also contain xylitol.

Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors.

Instructions for Use

Liquid medication may be added to food for dosing. When using veterinary liquid formulation, the dropper bottle is designed to deliver 0.05 mg per drop or one drop per pound body weight (two drops per kg body weight). Observe manufacturer's instructions when using dosing syringe supplied with product.

Patient Monitoring and Laboratory Tests

Monitor GI signs for evidence of diarrhea, GI bleeding, or ulcers. Because of risk of renal injury, monitor renal parameters (water consumption, BUN, creatinine, and urine-specific gravity) periodically during treatment.

Formulations

Meloxicam is available in 0.5 mg/mL (0.02 mg per drop) oral suspension, 1.5 mg/mL (0.05 mg per drop) oral suspension, 0.5% (5 mg/mL) injection, and 7.5- and 15-mg tablets (human preparation).

In Europe, a 15-mg/mL oral suspension is available for horses.

Stability and Storage

Meloxicam has been compounded with water, 1% methylcellulose gel, and simple syrup or a suspending and flavoring vehicle in a ratio of 1:1 at concentrations of 0.25, 0.5, 1.0 mg/mL. These formulations were stable for 28 days at room temperature or under refrigeration.

Small Animal Dosage

Dogs

- 0.2 mg/kg initial loading dose PO, SQ, or IV, and then 0.1 mg/kg q24h thereafter PO, SQ, or IV.

Cats

- 0.05 mg/kg q24h PO, with reduction in dose if chronic treatment is pursued. Long-term treatment may be reduced to 0.05 mg/kg q48h, and as low as q72h, PO.
- Single doses of 0.15 mg/kg SQ, but approved for doses up to 0.3 mg/kg SQ.

Large Animal Dosage

Pigs

- 0.4 mg/kg IM, which may be repeated in 24 hours.

Cattle

- 0.5 mg/kg q24h IV, IM, or SQ.

Horses

- 0.6 mg/kg q24h IV or PO.

Regulatory Information

Recommended withdrawal time for racing horses is 3 days for urine testing. Cattle withdrawal time: 15 days for slaughter, 5 days for milk.

RCI Classification: 3

Melphalan

mel'fah-lan

Trade and other names: Alkeran

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Melphalan is an alkylating agent, similar in action to cyclophosphamide. It alkylates base pairs in DNA and produces a cytotoxic effect.

Indications and Clinical Uses

Melphalan is not used as an anticancer agent as frequently as other alkylating agents. In animals it is used to treat multiple myeloma and certain carcinomas.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are related to its action as an anticancer agent. Melphalan causes myelosuppression.

Contraindications and Precautions

Do not use in animals with bone marrow suppression.

Drug Interactions

No drug interactions are reported. It has been used with other anticancer drug protocols.

Instructions for Use

Consult specific anticancer drug protocols for more dosing information.

Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow toxicity.

Formulations Available

Melphalan is available in 2-mg tablets and 50-mg vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is insoluble in water but is soluble in ethanol. After reconstitution, decomposition occurs rapidly and may precipitate. Use within 1 hour of reconstitution. When prepared in a compounded formulation for oral use, it was unstable with rapid decomposition (80% loss in 24 hours).

Small Animal Dosage

Dogs

- 1.5 mg/m² (or 0.1-0.2 mg/kg) q24h PO for 7-10 days (repeat every 3 weeks).
- Injectable forms have not been used in animals, but in humans 16 mg/m² IV over 15-20 minutes has been used at 2-week intervals for multiple myeloma.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Meperidine Hydrochloride

meh-pare'ih-deen hye-droe-klor'ide

Trade and other names: Demerol, Pethidine (European name)

Functional classification: Analgesic, opioid

Pharmacology and Mechanism of Action

Meperidine is a synthetic opioid agonist with activity primarily at the mu-opiate receptor. It is called pethidine in Europe. It is similar in action to morphine, except with approximately one seventh of the potency. An intramuscular injection of 75 mg or an oral dose of 300 mg of meperidine has similar potency to 10 mg of morphine. Clearance is rapid in small animals after meperidine administration and duration of effect is short.

Indications and Clinical Uses

Meperidine has been used for short-term sedative effects, often used with other sedatives and/or anesthetics. For analgesic use, it is short-acting, usually less than 2 hours and often much shorter. Therefore its use for treating pain has not been popular and has been replaced by other opiate drugs. Meperidine may produce fewer GI motility problems compared to other opioids. The use of meperidine in human medicine has declined because toxic effects have been observed from accumulation of metabolites.

Precautionary Information

Adverse Reactions and Side Effects

Like all opiates, some side effects are predictable and unavoidable. Side effects include sedation, urine retention, constipation, and bradycardia. Respiratory depression occurs with high doses. Tolerance and dependence occurs with chronic administration. Repeated doses in humans may cause toxicity from accumulation of metabolite. One of the metabolites, normeperidine, accumulates with repeated administration because it has a half-life much longer than meperidine. The accumulation of the metabolite causes excitatory effects that may be related to serotonergic properties. Similar reactions have not been reported from clinical use in animals (see Drug Interactions section for other precautions).

Contraindications and Precautions

Meperidine is a Schedule II controlled substance. Cats are more sensitive to excitement than other species, although they have tolerated meperidine relatively well. Avoid repeated doses because accumulation of metabolites may be toxic.

Drug Interactions

Meperidine should not be administered with monoamine oxidase inhibitors (MAOIs), such as selegiline. Meperidine and metabolites may inhibit reuptake of serotonin and cause excess serotonin effect, especially if combined with other drugs that produce similar action, such as selective serotonin reuptake inhibitors (e.g., fluoxetine), tricyclic antidepressants (e.g., clomipramine), or other analgesics such as tramadol.

Instructions for Use

Although comparative clinical studies have not been conducted in animals, meperidine may be effective for short duration but has not been used for long-term pain management.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

Formulations

Meperidine is available in 50- and 100-mg tablets; 10-mg/mL syrup; and 25-, 50-, 75-, and 100-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water. It may be mixed with 0.9% saline or 5% dextrose for 28 days

474 Mepivacaine

without loss of potency or stability. It is stable in syrup formulation. Protect from freezing.

Small Animal Dosage

Dogs

- 5-10 mg/kg IV or IM as often as every 2-3 hours (or as needed).

Cats

- 3-5 mg/kg IV or IM every 2-4 hours (or as needed).

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Schedule II controlled drug.

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 1

Mepivacaine

meh-piv'ah-kane

Trade and other names: Carbocaine-V

Functional classification: Local anesthetic

Pharmacology and Mechanism of Action

Mepivacaine is a local anesthetic of the amide class. It inhibits nerve conduction via sodium channel blockade. It has medium potency and duration of action compared to bupivacaine. Compared to lidocaine, it is longer-acting but has equal potency.

Indications and Clinical Uses

Mepivacaine is used as a local anesthetic used for local infiltration epidural analgesia/anesthesia.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are rare with local infiltration. High doses absorbed systemically can cause nervous system signs (tremors and convulsions). After epidural administration, respiratory paralysis is possible with high doses. Mepivacaine may cause less irritation to tissues than lidocaine.

Contraindications and Precautions

No contraindications have been reported for animals.

Drug Interactions

No drug interactions have been reported.

Instructions for Use

For epidural use, do not exceed 8-mg/kg total dose. Duration of epidural analgesia is 2.5-3 hours.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Mepivacaine is available in a 2% (20 mg/mL) injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

Local infiltration dose varies depending on site. Generally 0.5-3 mL of 2% solution is used.

- Epidural: 0.5 mL of 2% solution q30sec until reflexes are absent.

Large Animal Dosage

Horses

Intra-articular: 150 mg (7.5 mL) injected into horse joint. Other doses are variable doses used for local infiltration, depending on the need.

Regulatory Information

No regulatory information is available. Because of low risk of residues when used for local infiltration, no withdrawal times are suggested.

Horses: Clearance prior to racing is approximately 2 days.

RCI Classification: 2

Mercaptopurine

mer-kap-toe-pyoo'reen

Trade and other names: Purinethol

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Antimetabolite agent that inhibits synthesis of purines in cancer cells. It is cell-cycle specific and acts at the S-phase of cell division.

Indications and Clinical Uses

Mercaptopurine is used for various forms of cancer, including leukemia and lymphoma. A related drug is azathioprine. Administration of azathioprine is metabolized to 6 mercaptopurine, which is further metabolized to cytotoxic products.

Precautionary Information

Adverse Reactions and Side Effects

Many side effects are possible that are common to anticancer therapy (many of which are unavoidable) including bone marrow suppression and anemia.

Contraindications and Precautions

Do not use in animals with known sensitivity to azathioprine. Do not administer to cats.

Drug Interactions

No drug interactions are reported. It has been used with other anticancer drug protocols.

Instructions for Use

Consult the specific anticancer protocol for specific regimen.

Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow toxicity.

Formulations

Mercaptopurine is available in 50-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is prone to oxidation of mixed with alkaline solutions. pH of solutions should be below 8. If mixed with oral vehicles, such as syrups, it was stable for 14 days.

Small Animal Dosage**Dogs**

- 50 mg/m² q24h PO.

Cats

- Contraindicated.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Meropenem

meer-oh-pen'em

Trade and other names: Merrem

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Beta-lactam antibiotic of the carbapenem class (also known as penems) with broad spectrum of activity related to imipenem. Action on the cell wall is similar to other beta-lactams, which is to bind penicillin-binding proteins (PBP) that weaken or interfere with cell wall formation. The carbapenems bind to a specific PBP (PBP-1) that results in more rapid lysis compared to other beta-lactams. This results in greater bactericidal activity and a longer postantibiotic effect. Carbapenems have a broad spectrum of activity and are among the most active of all antibiotics. Spectrum includes gram-negative bacilli, including *Enterobacteriaceae* and *Pseudomonas aeruginosa*. It also is active against most gram-positive bacteria, except methicillin-resistant strains of *Staphylococcus*. It is not active against *Enterococcus*. Meropenem is the most active of all beta-lactams and active against aerobic and anaerobic gram-positive and gram-negative bacteria. Other related carbapenems are doripenem, imipenem, and ertapenem.

Indications and Clinical Uses

Meropenem is indicated primarily for resistant infections caused by bacteria resistant to other drugs. It is especially valuable for treating resistant infections caused by *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*. Meropenem is slightly more active against some bacteria than imipenem.

Precautionary Information

Adverse Reactions and Side Effects

Carbapenems pose similar risks as other beta-lactam antibiotics, but adverse effects are rare. Meropenem does not cause seizures as frequently as imipenem. Subcutaneous injections may cause slight hair loss at the injection site.

Contraindications and Precautions

Some slight yellowish discoloration may occur after reconstitution. Slight discoloration will not affect potency. However, a darker amber or brown discoloration may indicate oxidation and loss of potency.

Drug Interactions

Do not mix in a vial or syringe with other antibiotics.

Instructions for Use

Doses in animals have been based on pharmacokinetic studies rather than efficacy trials. Meropenem is more soluble than imipenem and can be injected via bolus rather than administered in fluid solutions. Meropenem has been injected SQ in dogs with no evidence of tissue reaction.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are ≤ 1 mcg/mL. Sensitivity to imipenem can be used as a marker for meropenem.

Formulations

Meropenem is available in a 500-mg or 1-g vial; both produce 50 mg/mL after reconstitution for injection. Reconstitute with sodium chloride, Ringer's solution, or lactated Ringer's solution.

Stability and Storage

Stable if stored in manufacturer's original vial. In heat and alkaline conditions, the drug may hydrolyze to meropenemic acid. At room temperature IV solutions are stable for 12 hours. However, after reconstitution, stability studies have shown that meropenem is stable for up to 25 days if refrigerated at a concentration of 50 mg/mL. Slight yellow discoloration may occur without loss of potency. Discard if particulates form in vial.

Small Animal Dosage

Dogs and Cats

- 8.5 mg/kg SQ q12h or 24 mg/kg IV q12h.
- UTIs: 8 mg/kg q12h SQ.
- For infections caused by *Pseudomonas aeruginosa* or other organisms that may have higher MIC values (e.g., MIC of 1.0 mcg/mL), administer 12 mg/kg q8h SQ or 25 mg/kg q8h IV.

Large Animal Dosage

No large animal doses have been reported. However, doses similar to the range used in small animals are suggested for foals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Mesalamine

mez-ahl'ah-meen

Trade and other names: 5-aminosalicylic acid, Asacol, Mesasal, Pentasa, and Mesalazine

Functional classification: Antidiarrheal

Pharmacology and Mechanism of Action

Mesalamine is also known as 5-aminosalicylic acid. It is the active component of sulfasalazine, which is commonly administered for treatment of colitis. (See sulfasalazine and olsalazine for additional information.) The action of mesalamine is not precisely known, but it appears to suppress the metabolism of arachidonic acid in the intestine. It inhibits both cyclo-oxygenase and lipoxygenase-mediated mucosal inflammation. Systemic absorption is low; most of the action is believed to be local. There are four formulations of mesalamine used:

1. Asacol. Asacol is a tablet coated with an acrylic-based resin. The resin dissolves at a pH of 7.0 and is designed to release 5-aminosalicylic acid in the colon.
2. Mesasal. Mesasal is a tablet coated with an acrylic-based resin that dissolves at a pH of >6.0. It is designed to release 5-aminosalicylic acid in the terminal ileum and colon. Approximately 35% of the salicylate is absorbed systemically. The dose in people is 1-1.5 g/day.
3. Olsalazine sodium (Dipentum). Olsalazine is a dimer of two molecules of 5-aminosalicylic acid linked by an azo bond that is released by bacterial digestion in the colon. It is used in people who cannot tolerate sulfasalazine. Only 2% of the salicylate from this compound is absorbed systemically. The most common adverse effect in people from this preparation has been watery diarrhea.
4. Pentasa. Pentasa contains microgranules of mesalamine coated with ethyl cellulose, which releases 5-aminosalicylic acid into the small and large intestine gradually, regardless of pH.

Indications and Clinical Uses

Mesalamine is used for treatment of inflammatory bowel disease, including colitis in animals. Most often sulfasalazine is used; however, in some animals, especially those sensitive to sulfonamides, mesalamine may be indicated. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Mesalamine alone has not been associated with side effects in animals. Adverse effects associated with sulfasalazine are caused by the sulfonamide component. (See sulfasalazine for more information.)

Contraindications and Precautions

Drug interactions are possible, but they have not been reported in animals, probably because low systemic drug levels are achieved. Mesalamine if absorbed sufficiently can potentially interfere with thiopurine methyltransferase and, therefore, increase the risk of toxicity from azathioprine.

Drug Interactions

No drug interactions are reported in animals. Omeprazole can potentially increase absorption by increasing intestinal pH.

Instructions for Use

Mesalamine usually is used as a substitute for sulfasalazine in animals that cannot tolerate sulfonamides.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Mesalamine is available in 400-mg tablets and 250-mg capsules. Delayed-release tablets are 400 mg (Asacol) and 1.2 g (film coated Lialda). Controlled release capsules are 250 and 500 mg (ethylcellulose-coated Pentasa).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is slightly soluble in water and ethanol. It should be protected from air and moisture. Darkening may occur after exposure to air. Do not crush coated tablets.

Small Animal Dosage

Veterinary dose has not been established. The usual human dose is 400-500 mg q6-8h PO, and it has been used to extrapolate an animal dose (e.g., 5-10 mg/kg q8h, PO).

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

RCI Classification: 5

Metaflumizone

met-ah' floo-mah-zone

Trade and other names: ProMeris

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Metaflumizone is an insecticide drug used to control fleas and ticks. It blocks the sodium influx that inhibits axonal neuronal function in susceptible parasites. The inhibition of neuron impulses causes paralysis and death of fleas. Little metaflumizone is absorbed systemically. The drug distributes to the skin after application and has residual levels that persist in the hair. It is used in combination with amitraz in dogs and alone in cats. More information on amitraz can be found in that section.

Indications and Clinical Uses

Metaflumizone is used for control of fleas and ticks. Control of fleas persists for 8 weeks, and control of ticks persists for 4 weeks. Monthly application is recommended. The feline formulation does not contain amitraz.

Precautionary Information

Adverse Reactions and Side Effects

Metaflumizone did not produce adverse effects at 3× and 5× the recommended dose when toxicity studies were conducted by the manufacturer. Metaflumizone has been associated with dermatitis in dogs, resembling pemphigus, after application at approved doses. Skin lesions have appeared on the face, ears, and dorsal trunk, but the underlying mechanism has not been identified. When combined with amitraz, other adverse effects are possible. Consult section on amitraz for additional information.

Contraindications and Precautions

Check for other exposure to amitraz before administering this product (e.g., amitraz tick collars).

Drug Interactions

No drug interactions are reported in animals. However, specific cautions apply to amitraz. See the amitraz section for further information.

Instructions for Use

Metaflumizone is used alone or in combination with amitraz for control of parasites. It is recommended for once-monthly application. It is waterproof and can be applied to both indoor and outdoor pets.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Metaflumizone is available in a range of packages for topical administration, ranging from XS, S, M, L, and XL, depending on the dog size. The feline formulation does not contain amitraz.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- Consult packaging for proper dose, ranging from XS, S, M, L, and XL, depending on the dog or cat size.
- Demodex treatment: 20 mg/kg once per 14 days for 90-180 days (duration confirmed by testing for presence of mites).

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

No regulatory information is available. No withdrawal times have been established for large animals. Because of long duration of action in small animals, it is not recommended for food-producing animals.

Metaproterenol Sulfate

met-ha-proe-teer'eh-nole sulf'ate

Trade and other names: Alupent, Metaprel, and Orciprenaline sulphate

Functional classification: Bronchodilator, beta-agonist

Pharmacology and Mechanism of Action

Beta₂-adrenergic agonist. Bronchodilator. Like other beta₂-agonists, it stimulates beta₂-receptors, activates adenylyl cyclase, and relaxes bronchial smooth muscle. It also may inhibit release of inflammatory mediators, especially from mast cells. Pharmacokinetics have not been well-studied in the veterinary species. In people it is well-absorbed from oral administration, but information on oral absorption in animals is incomplete.

Indications and Clinical Uses

Metaproterenol is used in animals to relax bronchial smooth muscle to treat bronchitis, obstructive pulmonary disease, airway obstruction caused by inflammation, and other airway diseases. It is indicated in animals with reversible bronchoconstriction, such as cats with bronchial asthma. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Metaproterenol causes excessive beta-adrenergic stimulation at high doses (tachycardia and tremors). Arrhythmias occur at high doses or in sensitive individuals. Beta-agonists will inhibit uterine contractions in animals in labor.

Contraindications and Precautions

Use cautiously in animals with cardiac disease.

Drug Interactions

Do not administer with monoamine oxidase inhibitors (MAOIs). Use cautiously with other drugs that may cause cardiac arrhythmias in animals. It may be mixed with cromolyn sodium for nebulization if used within 60-90 minutes. It also has been combined with dexamethasone without loss of stability.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Beta₂-agonists also have been used in people to delay labor (inhibit uterine contractions).

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm of animals during treatment.

Formulations

Metaproterenol is available in 10- and 20-mg tablets, 5-mg/mL syrup, and inhalers.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Avoid exposure to air and moisture. Do not freeze. Do not use if formulation turns dark color.

Small Animal Dosage

Dogs and Cats

- 0.325-0.65 mg/kg q4-6h PO.

Large Animal Dosage

No large animal doses have been reported. There is no evidence of oral absorption in large animals.

Regulatory Information

Do not administer to animals that produce food. Other beta-agonists (clenbuterol) are banned for use in food animals.

RCI Classification: 3

Metformin

met-for'min

Trade and other names: Glucophage

Functional classification: Antihyperglycemic

Pharmacology and Mechanism of Action

Metformin is an oral antihyperglycemic agent used to treat noninsulin-dependent diabetes (Type 2 diabetes in people). Metformin is used to decrease hepatic glucose production, decrease intestinal absorption of glucose, and improve insulin sensitivity by increasing peripheral glucose uptake and utilization. It is in the biguanide class of oral drugs for diabetes. Metformin does not have a direct effect on pancreatic beta cells, but it lowers blood glucose by reducing hepatic glucose production and improving peripheral utilization of glucose (e.g., in muscle). It thus lowers insulin requirements without any direct effect to increase insulin secretion. It may increase the insulin receptors on tissues. At therapeutic doses, metformin will not cause hypoglycemia. Half-life in cats is 2.75 hours.

Indications and Clinical Uses

In people, metformin is used to treat Type 2 diabetes. It has been used in people when the sulfonylurea drugs fail. It has been used in cats to treat diabetes. However, in cats treated with 50 mg/cat q12h PO, it showed significant adverse effects and was effective in only one fifth of treated cats. In cats, it has been more common to administer the sulfonylurea class of drugs in animals. Sulfonylurea drugs include glipizide (Glucotrol) and glyburide (DiaBeta, Micronase). Diabetic dogs rarely respond to oral hypoglycemic agents. In horses, the clearance rate is 10 times that of humans and, because of poor bioavailability, it is not recommended.

Precautionary Information

Adverse Reactions and Side Effects

Metformin has caused lethargy, appetite loss, vomiting, and weight loss in cats. Use has not been common enough to document other effects. However, in people, it has caused lactic acidosis in some patients, which was serious. Metformin also has caused megaloblastic anemia by affecting vitamin B₁₂ absorption.

Contraindications and Precautions

Metformin is cleared by the kidneys, so doses will need to be adjusted in patients with renal failure.

Drug Interactions

Use cautiously with drugs that may affect glycemic control such as glucocorticoids.

Instructions for Use

Doses published for cats are based on pharmacokinetic studies that demonstrated oral absorption in cats to be 35%-70%. The half-life was 11.5 hours, which is the basis for the q12h dosage recommendation.

Patient Monitoring and Laboratory Tests

Blood glucose should be monitored carefully. Doses should be adjusted on the basis of glucose monitoring. Some animals may require insulin injections to control hyperglycemia.

Formulations Available

Metformin is available in 500- and 850-mg tablets.

Stability and Storage

Stable if maintained in original formulation.

Small Animal Dosage**Cats**

- 25 or 50 mg/cat q12h PO (5-10 mg/kg q12h). (Efficacy is limited.)

Large Animal Dosage

Because of high clearance and poor bioavailability in horses (4%-7%), its use is not recommended.

Regulatory Information

Do not administer to animals intended for food.

Methadone Hydrochloride

meth'ah-done hye-droe-klor'ide

Trade and other names: Dolophine, Methadose, and generic brands

Functional classification: Analgesic, opioid

Pharmacology and Mechanism of Action

Opioid agonist, analgesic. Action of methadone is to bind to mu-opiate and kappa-opiate receptors on nerves and inhibit release of neurotransmitters involved with transmission of pain stimuli (such as Substance P). Methadone also may antagonize NMDA (n-methyl D-aspartate) receptors, which may contribute to the analgesic effect, decrease adverse CNS effects, and inhibit tolerance. Methadone exists in two forms: levo-methadone and dextro-methadone. Levomethadone has higher affinity for opiate receptors and has been available in a 2.5-mg/mL solution combined with 0.125 mg per mL fempipramide (an anticholinergic agent). Other opiates used in animals include morphine, hydromorphone, codeine, oxymorphone, meperidine, and fentanyl.

Indications and Clinical Uses

Although there are no controlled studies in veterinary medicine to document efficacy and safety of methadone, the use is based on anecdotal experience and some pharmacokinetic studies. Methadone is indicated for short-term analgesia, for sedation, and as an adjunct to anesthesia. It is compatible with most anesthetics and can be used as part of a multimodal approach to analgesia/anesthesia. Administration of methadone may lower dose requirements for other anesthetics and analgesics used. Oral doses to dogs are not absorbed systemically.

Precautionary Information

Adverse Reactions and Side Effects

Like all opiates, side effects from methadone are predictable and unavoidable. However, some side effects such as excitement and dysphoria seen with other opiates have not been as common with methadone in dogs and cats. Side effects from methadone administration may include sedation, vomiting, constipation, urinary retention, and bradycardia. Panting may occur in dogs as a result of changes in thermoregulation. Effects such as excitement and dysphoria have not been observed with administration of methadone as much as some of the other opiates.

Contraindications and Precautions

Methadone is a Schedule II controlled substance. Cats may be more sensitive to excitement than other species, but this has not been examined for methadone.

Drug Interactions

No specific drug interactions have been reported for animals.

Instructions for Use

Oral doses have not been absorbed in dogs. Oral doses have not been evaluated in other species.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

Formulations

Methadone is available in 1- and 2-mg/mL oral solution; 5-, 10-, and 40-mg tablets; and 10-mg/mL injectable solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water and ethanol. It may precipitate from a solution if pH is higher than 6. It has been combined in oral mixtures with juices, syrups, and stable for at least 14 days.

Small Animal Dosage

Dogs

- 0.1-0.5 mg/kg IV, or 0.5-2.2 mg/kg q3-4h SQ or IM.

Cats

- 0.05-0.1 mg/kg IV, or 0.2-0.5 mg/kg q3-4h SQ or IM. Cats have tolerated doses up to 0.6 mg/kg, IM, with a 4-hour duration of activity.

Large Animal Dosage

Horses

Dose not reported.

Regulatory Information

Do not administer to animals intended for food.

Methadone is a Schedule II controlled drug.

RCI Classification: 1

Methazolamide

meth-ah-zole'ah-mide

Trade and other names: Neptazane

Functional classification: Diuretic

Pharmacology and Mechanism of Action

Methazolamide is a carbonic anhydrase inhibitor. Methazolamide, like other carbonic anhydrase inhibitors, produces a diuresis through inhibition of the uptake of bicarbonate in proximal renal tubules via enzyme inhibition. This action results in loss of bicarbonate in the urine and a diuresis. The action of carbonic anhydrase inhibitors results in urine loss of bicarbonate, alkaline urine, and water loss.

Methazolamide, like other carbonic anhydrase inhibitors, also decreases formation of cerebrospinal fluid (CSF) by the choroid plexus and decreases the ocular fluid formation by decreasing bicarbonate secretion by the ocular ciliary body. This effect on aqueous humor formation decreases ocular pressure.

Indications and Clinical Uses

Methazolamide is rarely used as a diuretic any longer. There are more potent and effective diuretic drugs available, such as the loop diuretics (furosemide).

Methazolamide, like other carbonic anhydrase inhibitors, is used primarily to lower intraocular pressure in animals with glaucoma. Its duration is relatively short in dogs, in which more frequent administration may be required to maintain low ocular pressure. Methazolamide is used more often than acetazolamide for this purpose because it is more effective and easily available. However, other regimens are commonly used for the treatment of glaucoma compared to the carbonic anhydrase inhibitors. Methazolamide, like other carbonic anhydrase inhibitors, is sometimes used to produce more alkaline urine for management of some urinary calculi.

Precautionary Information

Adverse Reactions and Side Effects

Methazolamide may produce hypokalemia in some patients. Methazolamide, like other carbonic anhydrase inhibitors, can produce significant bicarbonate loss, and patients should be supplemented with bicarbonate if repeated doses are administered.

Contraindications and Precautions

Do not use in patients with acidemia. Use cautiously in any animal sensitive to sulfonamides. Do not use in patients with hepatic encephalopathy.

Drug Interactions

Use cautiously with other treatments that could cause metabolic acidosis.

Instructions for Use

Methazolamide may be used with other glaucoma agents, such as topical drugs to decrease intraocular pressure, and it may be used to produce alkaline urine to prevent some calculi from forming. However, use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Patient Monitoring and Laboratory Tests

Monitor ocular pressure in treated patients. Monitor urine pH if it is used to produce alkaline urine. Monitor electrolyte and acid–base status if multiple doses are administered.

Formulations Available

Methazolamide is available in 25- and 50-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage**Dogs and Cats**

- 2-3 mg/kg q8-12h PO. There does not seem to be any benefit for increasing the dose to a maximum dose of 4-6 mg/kg, but more frequent administration (every 8 hours) may be beneficial.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Methenamine

meth-en'ah-meen

Trade and other names: Methenamine hippurate: Hiprex and Urex;
Methenamine mandelate: Mandelamine and generic brands

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Methenamine is a urinary antiseptic. Methenamine in the acid environment of the urine is hydrolyzed to formaldehyde and ammonia to produce an antibacterial/antifungal effect. A low urine pH of at least 5.5 or less is needed for optimal effect. If this can be achieved, it is active against a wide range of bacteria, and resistance does not develop. It is less effective against *Proteus* species that produce an alkaline

urine pH. Because there is no systemic absorption, it is not effective for systemic infections. Absorption is rapid and produces a peak effect in urine at 0.5-1.5 hours and has a half-life of 3-6 hours.

Indications and Clinical Uses

Methenamine is used as a urinary antiseptic. There is a lack of well-controlled clinical trials to show its effectiveness. However, it has been used in animals to prevent recurrences of lower UTIs. It is probably less effective for treating ongoing infections. It is critical that the urine pH is low for conversion to formaldehyde.

Precautionary Information

Adverse Reactions and Side Effects

Although formaldehyde formation in bladder may be irritating, in people, high doses were required (greater than 8 g/day). In animals, no adverse effects have been reported.

Contraindications and Precautions

High doses may irritate bladder mucosa. Do not administer with sulfonamides because it may form formaldehyde-sulfonamide complexes.

Drug Interactions

Do not administer with medications that may cause alkaline urine. Because urine acidifiers are added with methenamine, acid urine will decrease the activity of fluoroquinolone and aminoglycoside antibiotics. The tablets should be enteric-coated to protect from hydrolysis in the acid of the stomach and should be administered on an empty stomach.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals is based on experience in people or anecdotal experience in animals. Urine must be acidic for methenamine to convert to formaldehyde (monitor pH periodically). A pH <5.5 is optimal. Supplement with ascorbic acid or ammonium chloride to lower pH.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. Monitor urinalysis or culture of urine to guide therapy of UTI.

Formulations

Methenamine hippurate is available in 0.6-g and 1-g tablets. Methenamine mandelate is no longer available (previous formulations included 1-g tablets, granules for oral solution, and 50- and 100-mg/mL oral suspension).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Methenamine is soluble in water and ethanol. In an acidic environment, it is hydrolyzed to form formaldehyde and ammonia. It has been physically incompatible when mixed with some foods and suspensions.

Small Animal Dosage

Dogs

- Methenamine hippurate: 500 mg/dog q12h PO.
- Methenamine mandelate: 10-20 mg/kg q8-12h PO.

Cats

- Methenamine hippurate: 250 mg/cat q12h PO.
- Methenamine mandelate: 10-20 mg/kg q8-12h PO.

Large Animal Dosage

No large animal doses have been reported. It is unlikely to be effective in large animals because their urine is more alkaline.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Methimazole

meth-im'ah-zole

Trade and other names: Tapazole, Felimazole, Thiamazole, and generic.

Functional classification: Antithyroid agent

Pharmacology and Mechanism of Action

Antithyroid drug. Action is to serve as substrate for thyroid peroxidase (TPO), to inhibit it and decrease incorporation of iodide into tyrosine molecules for the formation of thyroxine (T4) and triiodothyronine (T3). Methimazole inhibits coupling of mono-iodinated and di-iodinated residues to form T4 and T3. Methimazole does not inhibit release of preformed thyroid hormone.

Methimazole does not affect existing thyroid hormones already circulating or stored in the thyroid gland and does not inhibit the peripheral conversion of T4 to T3. It generally takes 2 to 4 weeks for serum T4 to reach the normal range in hyperthyroid cats treated with methimazole. Carbimazole is a similar drug used in Europe that is converted to methimazole in animals. Methimazole also may have immunosuppressive effects. Treatment may decrease antithyrotropin-receptor antibodies. Methimazole has a half-life of 2.3 hours in hyperthyroid cats and 4.7 hours in normal cats.

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Indications and Clinical Uses

Methimazole is used to treat hyperthyroidism in animals, especially cats. There is good evidence for efficacy when administered to cats at recommended doses.

Methimazole is preferred in cats instead of propylthiouracil (PTU) because methimazole has a lower incidence of adverse effects. Evidence supports twice-daily dosing in cats as more effective than once daily. Methimazole has been formulated for use in cats as a transdermal gel for skin absorption (e.g., those combined with pluronic organogel [PLO] gel). These formulations are available through compounding pharmacies. Published data indicate that transdermal methimazole is not as rapidly acting, or as effective, as oral dosing, but it can be effective to reduce T4 concentrations in many cats. An alternative drug that has been used is carbimazole, which is converted to the active drug methimazole. It may produce less frequent GI problems. However, experience with carbimazole is limited in the United States (see carbimazole section for more details).

Precautionary Information

Adverse Reactions and Side Effects

In cats, GI problems are the most common and can include anorexia and vomiting. Most adverse effects caused by methimazole are dose related and can be decreased by lowering the dose. In cats, polyarthritis, alopecia, and scaling and crusting of the head and face have been observed, which may be a manifestation of an allergic reaction. In cats, lupus-like reactions are possible, such as vasculitis and bone marrow changes. In cats, abnormal platelet counts and low blood counts can develop after 1-3 months of treatment. Bleeding abnormalities may be related to thrombocytopenia, but tests conducted in cats did not demonstrate prolongation of bleeding times (prothrombin time and activated partial antithromboplastin time). There were fewer adverse GI effects when methimazole was applied as a transdermal gel compared to administration as an oral tablet. Methimazole treatment may unmask hypothyroidism and renal failure in some cats. Monitor renal function with continued treatment.

Contraindications and Precautions

Do not administer to animals with thrombocytopenia or bleeding problems. Other drugs such as beta blockers are safe to administer with methimazole. Warn pet owners that transdermal methimazole can be absorbed through human skin. If an animal has had an adverse reaction to propylthiouracil (PTU), there may also be cross-sensitivity to methimazole. Methimazole has caused fetal abnormalities and should not be used in pregnant animals.

Drug Interactions

There are no drug interactions reported from the use in animals.

Instructions for Use

Use in cats is based on clinical studies in hyperthyroid cats and information from the feline drug sponsor. Methimazole has, for the most part, replaced propylthiouracil (PTU) for use in cats. Adjust maintenance dose by monitoring thyroid (T4) concentrations in plasma. Because it does not inhibit release of preformed thyroid, it may take 2-4 weeks to achieve maximum effect. When methimazole dosing frequency was evaluated, dosing with 2.5 mg q12h PO was more effective than 5 mg q24h PO. If prepared as a transdermal gel, it is recommended to use a PLO formulation consisting of 0.15 g methimazole, 100 g lecithin soya, 100 g isopropyl palmitate, 0.66 g of sorbic acid powder, and 20% pluronic F127 gel. Final concentration should be 5 mg/0.1 mL of transdermal gel applied to the inner ear. Transdermal gel may be less effective than oral tablets.

Patient Monitoring and Laboratory Tests

Monitor serum T4 levels. Recheck T4 levels after first month of treatment. After methimazole treatment is stabilized, T3 and T4 are suppressed for 24 hours after each dose of methimazole. Therefore, timing of blood sample after oral methimazole in cats does not appear to be a significant factor when assessing response to treatment. TSH concentrations in cats may also be used to test effectiveness of treatment. (Feline TSH has 96% homology with canine TSH.) Monitor CBC and platelet count in cats every week or 14 days for the first 30 days of treatment. Monitor tests of renal function because of concern about increased risk of renal disease in some cats. Methimazole may affect thyroid scintigraphy tests. After treatment, there may be a stimulation from TSH for tissues to have enhanced uptake of $^{99m}\text{TcO}_4$ by the thyroid gland.

Formulations

Methimazole is available in 2.5- and 5-mg coated tablets (veterinary form) and 5- and 10-mg tablets (human form).

Stability and Storage

Methimazole is stable if maintained in its original formulation. However, if prepared in compounded formulations for cats, potency and stability may be less. Potency is assured for 2 weeks with compounded transdermal gel.

Small Animal Dosage

Cats

- 2.5 mg/cat q12h PO for 7-14 days, then 5-10 mg/cat PO q12h and monitor T4 concentrations.
- In some cats, once T4 levels have been normalized, the dose can be decreased to 10-15 mg/cat once a day.
- Transdermal dose: 2.5 mg/cat transdermally twice daily. Alternate ears with each dose and wear gloves when applying.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food.

Methocarbamol

meth-oh-kar'bah-mole

Trade and other names: Robaxin-V

Functional classification: Muscle relaxant

Pharmacology and Mechanism of Action

Skeletal muscle relaxant. Methocarbamol depresses polysynaptic reflexes to cause muscle relaxation.

Indications and Clinical Uses

Methocarbamol has been used for the treatment of skeletal muscle spasms and increased muscle tone. It has also been used to treat pain that is associated with increased muscle spasms or myositis. Higher doses than listed in the dosing section are recommended if it is used for treating tetanus. However, evidence for efficacy in animals is lacking. For some indications (e.g., muscle spasms) methocarbamol has been replaced by other muscle relaxants such as orphenadrine (Norflex). In horses, the half-life is only 60-90 minutes and may need frequent administration for effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Methocarbamol may cause depression and sedation of the CNS. Excess salivation, emesis, weakness, and ataxia have been observed from methocarbamol administration. Adverse effects are usually short in duration.

Contraindications and Precautions

Use cautiously with other drugs that depress the CNS.

Drug Interactions

No drug interactions reported for animals.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Methocarbamol is available in 500- and 750-mg tablets and 100-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage**Dogs and Cats**

- 44 mg/kg q8h PO or IV on the first day, and then 22-44 mg/kg q8h PO. Up to 130 mg/kg for severe conditions.

Large Animal Dosage

- 11-22 mg/kg q8h IV or more frequently if needed. In horses, higher doses of 30 mg/kg IV and 50-100 mg/kg PO have been administered but are more likely to produce mild to moderate depression.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

M

Methohexital Sodium

meth-oe-heks'ih-tahl soe'dee-um

Trade and other names: Brevital

Functional classification: Anesthetic, barbiturate

Pharmacology and Mechanism of Action

Barbiturate anesthetic. Anesthesia is produced by CNS depression without analgesia. Anesthesia is terminated by redistribution in the body. Methohexital is about two to three times more potent than pentothal, but it has a shorter duration.

Indications and Clinical Uses

Methohexital is used as an intravenous anesthetic in animals, given either as a bolus or constant rate infusion (CRI). Frequently other anesthetic adjuncts, such as tranquilizers, are administered prior to methohexital infusion.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are related to the anesthetic effects of the drug. Severe adverse effects are caused by respiratory and cardiovascular depression.

Contraindications and Precautions

Overdoses can be caused by rapid or repeated injections. Avoid extravasation outside of the vein.

Drug Interactions

No drug interactions have been reported for animals.

Instructions for Use

Therapeutic index is low. Use only in patients in which it is possible to monitor cardiovascular and respiratory functions. Methohexital is often administered with other anesthetic adjuncts.

Patient Monitoring and Laboratory Tests

Monitor heart rate and breathing in patients anesthetized with barbiturates.

Formulations

Methohexital is available in 0.5-, 2.5-, and 5-g vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 3-6 mg/kg IV (give slowly to effect). Doses as high as 15 mg/kg IV have been administered to dogs over 30 seconds.
- CRI: 0.25 mg/kg/min for 30 minutes, then 0.125 mg/kg/min.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Schedule III controlled drug

RCI Classification: 2

Methotrexate

meth-oh-treks'ate

Trade and other names: MTX, Mexate, Folex, Rheumatrex, and generic brands

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Action is via antimetabolite action. The structure of methotrexate is similar to folic acid, and methotrexate binds and inhibits the dihydrofolate

reductase enzyme (DHFR). The DHFR enzyme is a reducing enzyme necessary for purine synthesis. The reduced form of folic acid (tetrahydrofolate, FH₄) acts as an important coenzyme for biochemical reactions, particularly DNA, RNA, and protein synthesis.

Indications and Clinical Uses

Methotrexate is used for various carcinomas, leukemia, and lymphomas. In people, methotrexate is also commonly used for autoimmune diseases such as rheumatoid arthritis. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Its major adverse effects in animals are anorexia, nausea, myelosuppression, and vomiting. Anticancer drugs cause predictable (and sometimes unavoidable) side effects that include bone marrow suppression, leukopenia, and immunosuppression. Hepatotoxicity has been reported in people from methotrexate therapy, but this has not been documented in veterinary medicine. In people, higher doses are often used compared to veterinary doses. In people, risk of systemic toxicity is high and rescue therapy with leukovorin (tetrahydrofolic acid) is often used. Leukovorin rescue therapy is used because it is an antagonist of the action of methotrexate on the DHFR enzyme.

Contraindications and Precautions

Do not administer to pregnant animals. It has been used to induce abortion.

Drug Interactions

Concurrent use with nonsteroidal anti-inflammatory drugs (NSAIDs) may cause severe methotrexate toxicity. Do not administer with pyrimethamine, trimethoprim, sulfonamides, or other drugs that may affect folic acid synthesis.

Instructions for Use

Use in animals has been based on experimental studies. Only limited clinical information is available. Consult specific anticancer protocols for precise dosage and regimen.

Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow toxicity.

Formulations

Methotrexate is available in 2.5-mg tablets and 2.5- and 25-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 2.5-5 mg/m² q48h PO (dose depends on specific cancer protocol).
- 0.3-0.5 mg/kg once/week IV.

Cats

- 0.8 mg/kg IV every 2-3 weeks.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent. RCI Classification: 4

Methoxamine

meh-thahk'seh-meen

Trade and other names: Vasoxyll

Functional classification: Vasopressor

Pharmacology and Mechanism of Action

Alpha₁-adrenergic agonist. Methoxamine stimulates alpha₁-receptors on vascular smooth muscle to produce vasoconstriction in vascular beds.

Indications and Clinical Uses

Methoxamine is used primarily in patients in need of critical care or during anesthesia to increase peripheral resistance and blood pressure. There is little experience with this drug in veterinary medicine.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are related to excessive stimulation of alpha₁-receptor (prolonged peripheral vasoconstriction). Reflex bradycardia may occur.

Contraindications and Precautions

Use cautiously in animals with heart disease.

Drug Interactions

Do not use with monoamine oxidase inhibitors (MAOIs), such as selegiline.

Instructions for Use

Methoxamine has a rapid onset and short duration of action.

Patient Monitoring and Laboratory Tests

Monitor heart rate and blood pressure in treated patients.

Formulations

Methoxamine is no longer available on the U.S. market. Some solutions have been compounded. It was previously available as a 20-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 200-250 mcg/kg (0.2-0.25 mg/kg) IM or 40-80 mcg/kg IV; repeat dose as needed.

Large Animal Dosage

Cattle and Horses

- 100-200 mcg/kg (0.1-0.2 mg/kg) IM once or as needed.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Methoxyflurane

meh-thahk'seh-floo'rane

Trade and other names: Metofane

Functional classification: Anesthetic, inhalant

Pharmacology and Mechanism of Action

Inhalant anesthetic. Like other inhalant anesthetics, the mechanism of action is uncertain. They produce generalized, reversible depression of the CNS. The inhalant anesthetics vary in their solubility in blood, their potency, and the rate of induction and recovery. Those with low blood/gas partition coefficients are associated with the most rapid rates of induction and recovery.

Indications and Clinical Uses

Methoxyflurane is not used often as an inhalant anesthetic. In the past 10 years use has declined and been replaced by other agents.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects related to anesthetic effects (e.g., cardiovascular and respiratory depression). Methoxyflurane has been reported to cause hepatic injury in animals.

Contraindications and Precautions

Use cautiously in animals with cardiac disease.

Drug Interactions

Labeling recommendations in some countries state that flunixin should not be administered to animals receiving methoxyflurane anesthesia.

Instructions for Use

Use of inhalant anesthetics requires careful monitoring. Dose is determined by depth of anesthesia.

Patient Monitoring and Laboratory Tests

Monitor heart rate and breathing in patients undergoing anesthesia with inhalant anesthetics. Monitor hepatic enzymes.

Formulations

Methoxyflurane is currently not available through commercial sources. It was previously available as a 4-oz bottle for inhalation.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- Induction: 3%, maintenance: 0.5%-1.5%.

Large Animal Dosage

- Minimum alveolar concentrations (MAC) value is 0.2%-0.3%.

Regulatory Information

No withdrawal times are established for animals intended for food. Clearance is rapid and short withdrawal times are suggested. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Methylene Blue 0.1%

meth'ih-leen bloo

Trade and other names: New Methylene Blue and generic brands

Functional classification: Antidote

Pharmacology and Mechanism of Action

Methylene blue acts as a reducing agent to reduce methemoglobin to hemoglobin. The action of methylene blue is particularly important when it is used to convert methemoglobin to hemoglobin in erythrocytes. It is reduced to leucomethylene blue in the body by combining with reduced nicotinamide adenine dinucleotide phosphate (NADPH) in the presence of NADPH reductase. Leucomethylene blue then transfers an electron to reduce methemoglobin to hemoglobin. Methemoglobin occurs as the result of oxidative damage to hemoglobin, and methylene blue has been used as an antidote for intoxication. Sources of intoxication in animals that cause methemoglobinemia include exposure to nitrate, nitrite, or chlorate in ruminants; acetaminophen and naphthalene (mothballs) in cats (and occasionally dogs); and local anesthetics, such as benzocaine, in cats. For acetaminophen toxicity in cats, acetylcysteine may provide a better response.

Indications and Clinical Uses

Methylene blue is used to treat methemoglobinemia caused by chlorate and nitrate toxicosis. It also has been used to treat cyanide toxicosis.

Precautionary Information

Adverse Reactions and Side Effects

In cats and dogs, administration of methylene blue to treat methemoglobinemia can cause oxidative damage to erythrocytes, including Heinz bodies, limiting the dose that can be used therapeutically. At the doses listed here, it has been safe. Heinz bodies can increase in cats from methylene blue treatment without producing anemia.

Contraindications and Precautions

The dose listed may produce some oxidative damage to erythrocytes (Heinz bodies and other morphologic changes) that is typically subclinical, but a risk of red cell damage and subsequent anemia increases with repeated or higher dosing. Use cautiously in cats.

Drug Interactions

No drug interactions have been reported for animals.

Instructions for Use

For treating acetaminophen intoxication in cats, acetylcysteine produced the best response, but methylene blue also was helpful.

Patient Monitoring and Laboratory Tests

Monitor CBC in patients treated with methylene blue. Monitor mucous membrane color (methemoglobinemia turns the blood and membranes a chocolate color).

Formulations

There are no commercial veterinary methylene blue products for systemic use. The human product (1% solution, 10 mg/mL) may be appropriate for use in some species, but treatment in large animals may require a compounded formulation.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 1.5 mg/kg IV once slowly.

Large Animal Dosage

Cattle, Goats, Sheep

- 4-10 mg per kg, IV, as needed. This dose of methylene blue is typically rapid, within 15 minutes, and the low end of the dosage range may be repeated to titrate to clinical response. Higher doses may be repeated every 6-8 hours if needed. Higher doses are used for severe toxicity (15 to 20 mg/kg).

Regulatory Information

Cattle withdrawal time (meat): 14 days.

Cattle withdrawal time (milk): 4 days.

Methylnaltrexone Bromide

meth'ihl nal-trex-own broe'-mide

Trade and other names: Relistor

Functional classification: Prokinetic agent, intestinal stimulant

Pharmacology and Mechanism of Action

Methylnaltrexone is a modified quarternary form of naltrexone that has opiate-antagonist properties. Because it is modified from naltrexone and charged, it does not cross the blood-brain barrier and it has no centrally acting opiate inhibition, but it will antagonize peripheral mu-receptors in the intestine to restore motility after postsurgical ileus. Opiate mu-receptors in the intestine ordinarily inhibit motility when stimulated because of pain or opiated drug administration. Another drug related to methylnaltrexone and used for similar purposes is alvimopan (Entereg).

Indications and Clinical Uses

Methylnaltrexone is approved for use in people to restore intestinal motility after surgery, after opiate administration, or when caused by a disorder (e.g., severe pain) that has stimulated mu-opiate receptors in the intestine. Use in animals is limited

498 Methylprednisolone

and has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are only reported for people and include abdominal pain and diarrhea. Although it is an opiate antagonist, it has not triggered breakthrough pain.

Contraindications and Precautions

Do not use if there is intestinal obstruction.

Drug Interactions

No drug interactions have been reported for animals.

Instructions for Use

The use in animals is primarily experimental and has been limited in clinical practice.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Methylnaltrexone is available by injection only. It is available in 12-mg vials (0.6 mL), equivalent to 20 mg/mL in each vial.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.15 mg/kg SQ injection, once per 24 or 48 hours.

Large Animal Dosage

Horses

- 0.15 mg/kg SQ injection, once per 24 or 48 hours.

Regulatory Information

No withdrawal information is available for food-producing animals.

Methylprednisolone

meth-il-pred-niss'oh-lone

Trade and other names: Methylprednisolone: Medrol; Methylprednisolone acetate: Depo-Medrol; and Methylprednisolone sodium succinate: Solu-Medrol

Functional classification: Corticosteroid

Pharmacology and Mechanism of Action

Methylprednisolone is a glucocorticoid anti-inflammatory drug. Anti-inflammatory effects are complex, but they operate primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. Compared to prednisolone, methylprednisolone is 1.25 times more potent.

Indications and Clinical Uses

Methylprednisolone acetate is a long-acting depot formulation of methylprednisolone. It is slowly absorbed from the intramuscular injection site producing glucocorticoid effects for 3-4 weeks in some animals. Methylprednisolone acetate is used for intralesional therapy, intra-articular therapy, and inflammatory conditions. Methylprednisolone sodium succinate is a water-soluble formulation intended for acute therapy when high intravenous doses are needed for rapid effect. It is used for treatment of shock and CNS trauma. Methylprednisolone oral tablets are used for treatment of conditions in animals that require short-term to long-term therapy with an intermediate-acting corticosteroid. Conditions treated include dermatitis, immune-mediated diseases, intestinal diseases, and neurological and musculoskeletal diseases. Although high doses have been used to treat spinal cord trauma, this use has questionable benefit in animals. In large animals, methylprednisolone acetate is used for treatment of inflammatory conditions of the musculoskeletal system (intra-articular).

Precautionary Information

Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic-pituitary-adrenal (HPA) axis suppression. However, the manufacturer suggests that methylprednisolone causes less polyuria/polydipsia (PU/PD) than prednisolone. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Dogs that receive high doses of methylprednisolone succinate (e.g., 30 mg/kg) have a high risk of GI bleeding. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and UTIs. In cats, methylprednisolone acetate injections have caused injection-site alopecia. In horses, additional adverse effects may include risk of laminitis (although a direct link to induction of laminitis is controversial). In cats, methylprednisolone acetate administration causes volume expansion as a result of fluid shift secondary to hyperglycemia. This effect appears to increase risk of cats developing congestive heart failure (CHF) following methylprednisolone acetate administration.

Contraindications and Precautions

Use cautiously in patients prone to ulcers and infection or in animals in which wound healing is necessary. Use cautiously in diabetic animals, animals with renal failure, or pregnant animals. Use cautiously in cats because of volume expansion, especially cats at risk of CHF.

Drug Interactions

Like other corticosteroids, if methylprednisolone is administered with nonsteroidal anti-inflammatory drugs (NSAIDs), there is increased risk of GI ulcers.

Instructions for Use

Use of methylprednisolone is similar to other corticosteroids. Dose adjustment should be made to account for difference in potency. Use of methylprednisolone acetate should be evaluated carefully because one injection will cause glucocorticoid effects that persist for several days to weeks. Results of clinical studies in animals have not been reported for use of methylprednisolone sodium succinate.

500 Methylprednisolone

Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an adrenocorticotropic hormone stimulation test to monitor adrenal function. Monitor cats for diabetes and heart disease when treated with methylprednisolone acetate.

Formulations

Methylprednisolone is available in 1-, 2-, 4-, 8-, 18-, and 32-mg tablets.

Methylprednisolone acetate is available in 20- and 40-mg/mL suspension for injection.

Methylprednisolone sodium succinate is available in 1- and 2-g and 125- and 500-mg vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Methylprednisolone is insoluble in water and slightly soluble in ethanol.

Methylprednisolone acetate is slightly soluble in water. Methylprednisolone sodium succinate is highly soluble in water. When methylprednisolone sodium succinate is reconstituted it should be used within 48 hours at room temperature.

Decomposition occurs with longer storage. It may be frozen at -20°C for 4 weeks with no loss of potency.

Small Animal Dosage

Dogs

- Methylprednisolone: 0.22-0.44 mg/kg q12-24h PO.
- Methylprednisolone acetate: 1 mg/kg (or 20-40 mg/dog) IM q1-3wk.
- Methylprednisolone sodium succinate (for emergency use): 30 mg/kg IV and repeat at 15 mg/kg in 2-6 hours IV. Replacement or anti-inflammatory therapy: use 0.25-0.5 mg/kg/day.

Cats

- Methylprednisolone: 0.22-0.44 mg/kg q12-24h PO.
- Methylprednisolone acetate: 10-20 mg/cat IM q1-3wk.
- Methylprednisolone sodium succinate (for emergency use): 30 mg/kg IV and repeat at 15 mg/kg in 2-6 hours IV. Replacement or anti-inflammatory therapy: use 0.25-0.5 mg/kg/day.

Large Animal Dosage

Horses

- 200 mg as a single total dose injected IM.
- Intra-articular dose: 40 to 240 mg total dose, with the average dose of 120 mg injected in the joint space using sterile technique.

Regulatory Information

Withdrawal times are not established. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Methyltestosterone

meth-ill-tess-toss'teh-rone

Trade and other names: Android and generic brands

Functional classification: Hormone, anabolic agent

Pharmacology and Mechanism of Action

Anabolic androgenic agent. Injections of methyltestosterone will mimic effects of testosterone.

Indications and Clinical Uses

Methyltestosterone is used for anabolic actions or testosterone hormone replacement therapy (androgenic deficiency). Testosterone has been used to stimulate erythropoiesis. Other similar agents used include testosterone cypionate and testosterone propionate.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects caused by excessive androgenic action of testosterone. Prostatic hyperplasia is possible in male dogs. Masculinization can occur in female dogs. Hepatopathy is more common with oral methylated testosterone formulations.

Contraindications and Precautions

Do not administer to pregnant animals.

Drug Interactions

No drug interactions have been reported for animals.

Instructions for Use

Use of testosterone androgens has not been evaluated in clinical studies in veterinary medicine. The clinical use is based primarily on experimental evidence or experiences in people.

Patient Monitoring and Laboratory Tests

Monitor hepatic enzymes and clinical signs for evidence of cholestasis and hepatotoxicity during treatment.

Formulations

Methyltestosterone is available in 10- and 25-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

• 5-25 mg/dog q24-48h PO.

Cats

• 2.5-5 mg/cat q24-48h PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not use in animals intended for food.

Methyltestosterone is a Schedule III controlled drug.

RCI Classification: 4

Metoclopramide Hydrochloride

met-oh-kloe-prah'mide hye-droe-klor'ide

Trade and other names: Reglan and Maxolon

Functional classification: Antiemetic

Pharmacology and Mechanism of Action

Prokinetic drug. Antiemetic. Metoclopramide stimulates motility of upper GI tract and is a centrally acting antiemetic. The mechanism of action of metoclopramide is not completely understood. Among the proposed mechanisms is stimulation of 5-HT₄ (serotonin) receptors or an increase in the release of acetylcholine in the GI tract, possibly through a prejunctional mechanism. It also has anti-dopamine (D₂) action. It inhibits gastric relaxation induced by dopamine, thus enhancing the cholinergic responses of gastric smooth muscle to increase motility. It also increases the tone of the esophageal sphincter. Metoclopramide acts centrally to inhibit dopamine in the chemoreceptor trigger zone (CRTZ), which is responsible for antiemetic effects. The half-life in dogs has ranged from less than 1 hour to 2 hours; effects on esophageal sphincter persisted for only 30-60 minutes.

Indications and Clinical Uses

Metoclopramide is used primarily for gastroparesis and treatment of vomiting. It is not effective for dogs with gastric dilation. Because this drug transiently increases prolactin secretion, there has been interest in using this drug for treating agalactia in animals, but efficacy has not been determined. In horses, it has been used to treat intestinal postoperative ileus, but adverse effects have limited the use. In people, metoclopramide has been also used to treat hiccups and lactation deficiency.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are primarily related to blockade of central dopaminergic receptors. Adverse effects similar to what is reported for phenothiazines (e.g., acepromazine) have been reported in addition to behavioral changes. In horses, undesirable side effects have been common and limit the therapeutic use. Adverse effects in horses include behavioral changes, excitement, and abdominal discomfort. Excitement from intravenous infusions can be severe. In calves at doses >0.1 mg/kg, it produced neurologic effects.

Contraindications and Precautions

Do not use in patients with epilepsy or with diseases caused by GI obstruction. Use cautiously in horses because dangerous behavior changes may occur. In people, it has been safe to use in the first trimester of pregnancy.

Drug Interactions

Efficacy is diminished when administered with parasympatholytic (atropine-like) drugs.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Most use is for general antiemetic purposes, but doses as high as 2 mg/kg have been used to

prevent vomiting during cancer chemotherapy. In horses, there is some increase in intestinal motility at recommended doses, but little effect on the large bowel has been seen. In calves metoclopramide had little effect on rumen motility.

Patient Monitoring and Laboratory Tests

Monitor GI motility during treatment.

Formulations Available

Metoclopramide is available in 5- and 10-mg tablets, 1-mg/mL oral solution, and 5-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. It is incompatible with other drugs when mixed in solution. Stability is less than 24 hours if not protected from light.

Small Animal Dosage

Dogs and Cats

- 0.2-0.5 mg/kg q6-8h IV, IM, or PO.
- Constant rate infusion (CRI): Administer a loading dose of 0.4 mg/kg, followed by 0.3 mg/kg/hr. In refractory cases, CRI dose may be increased up to 1.0 mg/kg/hr. For antiemetic treatment with cancer chemotherapy, the dose used is up to 2 mg/kg per 24 hours.

Large Animal Dosage

Horses

- Infusion of metoclopramide (0.125-0.25 mg/kg/hr) added to IV fluids to reduce postoperative ileus in horses.

Calves and Cattle

Not recommended.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Metoprolol Tartrate

meh-toe'proe-lole tar'trate

Trade and other names: Lopressor

Functional classification: Beta blocker

Pharmacology and Mechanism of Action

Beta₁-adrenergic blocker. Metoprolol has similar properties to propranolol, except that metoprolol is specific for beta₁-receptor, with less effect on beta₂-receptors. Metoprolol is a lipophilic beta blocker and relies on the liver for clearance. Lipophilic beta blockers, such as metoprolol, undergo high first-pass clearance, which reduces oral bioavailability and causes high interpatient variability in plasma concentrations and effects. Alternative beta₁ blockers used in animals include atenolol.

Indications and Clinical Uses

Metoprolol is used to control tachyarrhythmias and to control the response from adrenergic stimulation. Beta blockers effectively slow heart rate. Metoprolol is used in animals in which it is important to control ventricular rate, decrease conduction through the AV and SA nodes, and improve diastolic function. In animals it has been used for tachyarrhythmias, hypertrophic cardiomyopathy, atrial fibrillation, and other cardiac diseases. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are primarily caused by excessive cardiovascular depression (decreased inotropic effects). Metoprolol may cause AV block.

Contraindications and Precautions

Use cautiously in animals prone to bronchoconstriction.

Drug Interactions

Lipophilic beta blockers, such as metoprolol, are subject to hepatic metabolism and may be prone to drug interactions that affect hepatic metabolizing enzymes. If administered with digoxin, it may potentiate an AV-nodal conduction block.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during treatment.

Formulations

Metoprolol is available in 50- and 100-mg tablets and 1-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Metoprolol tartrate is soluble in water and ethanol. Protect tablets from moisture and freezing. Suspensions have been prepared in syrups and other flavorings with no loss of stability after 60 days of storage.

Small Animal Dosage

Dogs

- 5-50 mg/dog (0.5-1 mg/kg) q8h PO.

Cats

- 2-15 mg/cat q8h PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Metronidazole, Metronidazole Benzoate

meh-troe-nye'dah-zole

Trade and other names: Flagyl and generic brands

Functional classification: Antibacterial, antiparasitic

Pharmacology and Mechanism of Action

Antibacterial and antiprotozoal drug. It is a second-generation nitroimidazole in which the activity involves generation of free nitroradicals via metabolism within protozoa and bacteria. Metronidazole disrupts DNA in organism via reaction with intracellular metabolite. Its action is specific for anaerobic bacteria and protozoa. Resistance is rare. It is active against some protozoa, including *Trichomonas*, *Giardia*, and intestinal protozoal parasites. It also has in vitro activity against anaerobic bacteria and *Helicobacter*. Metronidazole oral absorption is nearly complete in animals (75%-85% in horses and 60%-100% in dogs). Rectal absorption in horses is 30%. The half-life is 3-4 hours in horses and 4-5 hours in dogs. Metronidazole benzoate is formulated for cats to improve palatability. In this form, the oral absorption (12.4 mg/kg of the base) is 64%, with a half-life of 5 hours.

Indications and Clinical Uses

Metronidazole is indicated to treat diarrhea and other intestinal problems caused by intestinal protozoa such as *Giardia*, *Trichomonas*, and *Entamoeba*. Metronidazole may be used in small animals and horses for treatment of a variety of anaerobic infections. Metronidazole may have some immune-modulating activity in the intestine of animals and has been used to treat inflammatory bowel disease in animals. Metronidazole benzoate has been used in cats because it is more palatable.

Precautionary Information

Adverse Reactions and Side Effects

The most severe adverse effect is caused by toxicity to CNS. High doses have caused lethargy, CNS depression, ataxia, tremors, seizures, vomiting, and weakness. Most CNS toxicity caused from metronidazole in animals occurs at high doses (>60 mg/kg/day). The CNS signs are related to inhibition of action of GABA and are responsive to benzodiazepines (diazepam 0.4 mg/kg q8h for 3 days). Like other nitroimidazoles, it has the potential to produce mutagenic changes in cells, but the clinical significance of this effect is uncertain. Like other nitroimidazoles, it has a bitter taste and can cause vomiting and anorexia. Metronidazole benzoate has been used in some cats safely at 25 mg/kg q12h for 7 days. However, there is a caution about the effect of benzoate salts in cats because it is a benzoic acid derivative. Benzoic acid can be toxic to cats and causes ataxia, blindness, respiratory problems, and other CNS disorders. Despite this concern, it is estimated that 500 mg/kg/day of metronidazole benzoate would be needed to provide a toxic dose of benzoic acid to cats. Nevertheless, any cat showing CNS or other signs of toxicity should have the metronidazole benzoate discontinued immediately.

Contraindications and Precautions

Fetal abnormalities have not been demonstrated in animals with recommended doses, but use cautiously during pregnancy.

Drug Interactions

Like other nitroimidazoles, it can potentiate the effects of warfarin and cyclosporine via inhibition of drug metabolism.

Instructions for Use

Metronidazole is one of the most commonly used drugs for anaerobic infections. Although it is effective for giardiasis, other drugs used for *Giardia* include albendazole, fenbendazole, and quinacrine. CNS toxicity is a concern, but it is dose related. The maximum dose that should be administered is 50-65 mg/kg per day in any species. Metronidazole is unpalatable and can produce a metallic taste. In cats, when the tablet is crushed or broken, the unpalatability is particularly a problem. Metronidazole benzoate has a bland taste and is better tolerated. It is a formulation not commercially available in the US. However, it may be available from compounding pharmacies. Metronidazole benzoate of 25 mg/mL contains 40 mg of benzoate. Because of the weight of metronidazole benzoate versus metronidazole hydrochloride, a factor of 1.6 times is used to convert a metronidazole hydrochloride dose to a metronidazole benzoate dose. Metronidazole benzoate is 62% metronidazole; therefore 20 mg/kg of metronidazole benzoate delivers 12.4 mg/kg of metronidazole.

Metronidazole should not be injected directly; it is too acidic. See Stability and Storage section for mixing instructions.

Patient Monitoring and Laboratory Tests

Monitor for neurological adverse effects.

Formulations

Metronidazole is available in 250- and 500-mg tablets, 375-mg capsules, 50-mg/mL suspension, and 5-mg/mL injection.

Metronidazole benzoate is a formulation not available in the US but has been compounded for veterinary use. Metronidazole benzoate is 62% metronidazole.

Metronidazole benzoate has been formulated in Oral-Plus and Ora-Sweet (drug excipients) to a concentration of 16 mg/mL and was stable at room temperature for 90 days.

Stability and Storage

The base is slightly soluble in water. The benzoate form is practically insoluble; the hydrochloride form is soluble in water. Metronidazole has been crushed and mixed with some flavorings to mask the taste. When mixed with some syrups or water, with exceptions listed here, decomposition occurs within 28 days. Metronidazole benzoate prepared in vehicles such as Ora-Plus or Ora-Sweet was stable for 90 days. Metronidazole base (from tablets) also was mixed with these vehicles and was found to be stable for 90 days. Reconstituted injectable forms are stable for 96 hours but after dilution should be discarded after 24 hours.

Metronidazole hydrochloride when reconstituted is too acidic (pH 0.5-2) for direct injection. Injection of 5 mg/mL should be further diluted with 100 mL (0.9% saline, 5% dextrose, or Ringer's solution) and neutralized with 5 mEq sodium bicarbonate per 500 mg for a pH of 6-7. Reconstituted injectable forms are stable for 96 hours but after dilution should be discarded after 24 hours.

Small Animal Dosage

Dogs

- Anaerobes: 15 mg/kg q12h or 12 mg/kg q8h PO.
- *Giardia*: 12-15 mg/kg q12h for 8 days PO.

Cats

- Anaerobes: 10-25 mg/kg q24h PO.
- *Giardia*: 17 mg/kg (one third tablet per cat) q24h for 8 days.
- Metronidazole benzoate (for treatment of *Giardia*): 25 mg/kg PO 12h for 7 days. Metronidazole benzoate is 62% metronidazole; therefore 20 mg/kg of metronidazole benzoate delivers 12.4 mg/kg metronidazole.

Large Animal Dosage

Horses

- Treatment of anaerobic and protozoal infections: 10 mg/kg q12h PO. Note: Some clinicians have used higher doses (up to 15-20 mg/kg q6h), but at these doses side effects are more likely.

Cattle

- Treatment of trichomoniasis (bulls): 75 mg/kg q12h IV for three doses.

Regulatory Information

Do not administer to animals that produce food. Administration of nitroimidazoles to animals intended for food is prohibited. Treated cattle must not be slaughtered for food.

Mexiletine

meks-il'eh-teen

Trade and other names: Mexitil

Functional classification: Antiarrhythmic

Pharmacology and Mechanism of Action

Antiarrhythmic drug. Mexiletine is a Class IB antiarrhythmic agent. Mechanism of action is to block fast sodium channel and depress Phase 0 of depolarization.

Indications and Clinical Uses

Mexiletine has been used to treat ventricular arrhythmias. However, its use is not common in veterinary medicine. The first choice for acute treatment of ventricular arrhythmias is usually lidocaine.

Precautionary Information

Adverse Reactions and Side Effects

High doses may cause excitement and tremors. Mexiletine can be arrhythmogenic in some animals. In people, related drugs (flecainide and encainide) can be proarrhythmogenic and associated with excessive mortality.

Contraindications and Precautions

Use cautiously in animals with liver disease.

Drug Interactions

No drug interactions have been reported.

508 Mibolerone

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

Monitor ECG during use.

Formulations

Mexiletine is available in 150-, 200-, and 250-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is freely soluble in water and ethanol.

Small Animal Dosage

Dogs

- 5-8 mg/kg q8-12h PO (use cautiously).

Cats

No safe dose has been established.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Mibolerone

mih-bole'er-one

Trade and other names: Cheque-drops

Functional classification: Hormone

Pharmacology and Mechanism of Action

Androgenic steroid. Mibolerone will mimic androgens in the body.

Indications and Clinical Uses

Mibolerone is used to suppress estrus in animals.

Precautionary Information

Adverse Reactions and Side Effects

Many bitches show clitoral enlargement or discharge from treatment.

Contraindications and Precautions

Do not use in Bedlington terriers. Do not administer to pregnant animals. Do not use with perianal adenoma or carcinoma. Do not use in cats. Mibolerone has been abused in people for use as a body-building drug. Therefore, extreme caution should be used when dispensing this medication to animal owners.

Drug Interactions

No drug interactions have been reported.

Instructions for Use

Treatment ordinarily is initiated 30 days prior to onset of estrus. It is not recommended to be used for more than 2 years.

Patient Monitoring and Laboratory Tests

Monitor hepatic enzymes periodically if used chronically.

Formulations

Mibolerone has been discontinued by the manufacturer. However, it may be available from some other sources. Originally it was available in 100-mcg/mL oral solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 2.6-5 mcg/kg/day PO.
- Bitches weighing 0.45-11.3 kg: 30 mcg/day PO.
- Bitches weighing 11.8-22.7 kg: 60 mcg/day PO.
- Bitches weighing 23-45.3 kg: 120 mcg/day PO.
- Bitches weighing more than 45.8 kg: 180 mcg/day PO.

Cats

Safe dose not established.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not administer to animals that produce food.

Midazolam Hydrochloride

mid'az'oe-lam hye-droe-klar'ide

Trade and other names: Versed

Functional classification: Anticonvulsant, Sedative

Pharmacology and Mechanism of Action

Benzodiazepine. Central-acting CNS depressant. Midazolam, like other benzodiazepines, binds to a specific GABA-binding site. It may modify the GABA-binding sites and increase the action of GABA on nerve cells. Sedative effects of midazolam may be attributed to potentiation of GABA pathways that act to regulate release of monoamine neurotransmitters in the CNS. Benzodiazepines may act as muscle relaxants by inhibiting certain spinal pathways or directly depressing motor nerve and muscle function.

Indications and Clinical Uses

Midazolam is used as an anesthetic adjunct. It is used for similar indications as diazepam, but because it is water soluble, midazolam can be administered in an

510 Midazolam Hydrochloride

aqueous vehicle and administered IM compared to other drugs of this class (drugs such as diazepam are not water soluble).

It has been used as an anticonvulsant, muscle relaxant, sedative, and adjunct with anesthetic agents. In foals, it has been used to treat neonatal seizures (see dose protocols).

Precautionary Information

Adverse Reactions and Side Effects

Midazolam administered IV can cause serious cardiorespiratory depression. Some animals may experience paradoxical excitement. Chronic administration may lead to dependence and a withdrawal syndrome if discontinued. If severe adverse reactions occur, consider administering an antagonist (flumazenil, Romazicon).

Contraindications and Precautions

Use cautiously IV, especially with opiates.

Drug Interactions

No drug interactions have been reported. Compared to diazepam it is water-soluble and is more compatible with fluid solutions. It has been administered safely with several anesthetics, sedatives, preanesthetics, and anticonvulsants.

Instructions for Use

Clinical trials have not been reported, although use of midazolam is reported in some anesthetic protocols for animals. Unlike other benzodiazepines, midazolam can be administered IM.

Patient Monitoring and Laboratory Tests

Samples of plasma or serum may be analyzed for concentrations of benzodiazepines. Plasma concentrations in the range of 100-250 ng/mL have been cited as the therapeutic range for people. Other references have cited this range as 150-300 ng/mL. However, there are no readily available tests for monitoring in many veterinary laboratories. Laboratories that analyze human samples may have nonspecific tests for benzodiazepines. With these assays, there may be cross-reactivity among benzodiazepine metabolites.

Formulations

Midazolam is available in 5-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Solubility of midazolam in water is pH-dependent. At lower pH values (pH <4), it becomes more soluble.

Small Animal Dosage

Dogs

- 0.1-0.25 mg/kg IV or IM.
- 0.1-0.3 mg/kg/hr IV infusion.
- Status epilepticus: 0.1-0.2 mg/kg IV bolus.

Cats

- Sedation: 0.05 mg/kg IV.
- Induction of anesthesia: 0.3-0.6 mg/kg IV, combined with 3 mg/kg ketamine. (Additional doses of ketamine at 1-2 mg/kg can be administered as needed.)

Large Animal Dosage

Pigs

- Up to 0.5 mg/kg IM, usually in combination with ketamine.

Horses

- Neonatal seizures in foals: 2-5 mg/kg IV, over 15-20 min or IM, followed by 1-3 mg/hr IV (2-6 mL/hr) constant rate infusion (CRI) to control seizures. Infusion dose is prepared by adding 10 mL (5 mg/mL) to 100 mL saline to make a solution of 0.5 mg/mL.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Schedule IV controlled drug

RCI Classification: 2

Milbemycin Oxime

mil-beh-mye'sin ahk'seem

Trade and other names: Interceptor, Interceptor Flavor Tabs, and SafeHeart
Milbemycin also is an ingredient in Sentinel.

Functional classification: Antiparasitic

M

Pharmacology and Mechanism of Action

Antiparasitic drug. Avermectins (ivermectin-like drugs) and milbemycins (milbemycin and moxidectin) are macrocyclic lactones and share similarities, including mechanism of action. These drugs are neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in parasites. Paralysis and death of the parasite is caused by increased permeability to chloride ions and hyperpolarization of nerve cells. These drugs also potentiate other chloride channels, including ones gated by GABA. Mammals ordinarily are not affected because they lack glutamate-gated chloride channels, and there is a lower affinity for other mammalian chloride channels. Because these drugs ordinarily do not penetrate the blood-brain barrier, GABA-gated channels in the CNS of mammals are not affected. Milbemycin is active against intestinal parasites, mites, bots, heartworm microfilaria, and developing larvae. Milbemycin has no effect on trematode or cestode parasites.

Indications and Clinical Uses

Milbemycin is used as heartworm preventative, miticide, and microfilaricide. It is also used to control infections of hookworm, roundworms, and whipworms. It also has been used in combination with flea control drugs (See Sentinel, which contains milbemycin oxime and lufenuron.) At high doses it has been used to treat *Demodex* infections in dogs.

Precautionary Information

Adverse Reactions and Side Effects

At doses of 5 mg/kg, it was well-tolerated in most dogs (10 times the heartworm dose). At 10 mg/kg (20 times the heartworm dose), it caused depression, ataxia, and salivation in some dogs. Toxicity may occur at high doses

and in breeds in which milbemycin crosses the blood–brain barrier at doses as low as 1.5 mg/kg per day. Sensitive breeds include Collies, Australian shepherds, Old English sheepdogs, longhaired Whippets, and Shetland sheepdogs. Toxicity is neurotoxic and signs include depression, ataxia, difficulty with vision, coma, and death. Sensitivity to milbemycin occurs in certain breeds because of a mutation in the multidrug resistance gene (MDR1, also called the ABCB1 gene) that codes for the membrane pump p-glycoprotein. This mutation affects the efflux pump in the blood–brain barrier. Therefore, milbemycin can accumulate in the brain of susceptible animals. High doses in normal animals may also produce similar toxicosis. However, at doses used for heartworm prevention, this effect is unlikely. At high doses used for treating *Demodex* infections, diarrhea may occur in some dogs.

Contraindications and Precautions

Do not use in dogs that have shown sensitivity to ivermectin or other drugs in this class (see previous breed list). Treatment using three times the daily doses from mating to 1 week before weaning did not produce any adverse effects in the pregnant bitch, the fetus, or puppies. One-time doses of three times the monthly rate before or shortly after whelping caused no adverse effects on the puppies. Milbemycin is excreted in milk. Puppies given milbemycin at 19 times the regular dose showed adverse effects, but signs were transient for only 24–48 hours.

Drug Interactions

Do not use with drugs that may increase penetration across the blood–brain barrier. Such drugs include p-glycoprotein inhibitors such as ketoconazole, cyclosporine, quinidine, and some macrolide antibiotics (see Appendix for list of p-glycoprotein inhibitors).

Instructions for Use

Doses vary depending on parasite treated. Treatment of demodicosis requires a higher dose administered daily than the heartworm preventative dose. Using a protocol of 1 mg/kg/day until clinical cure followed by 3 mg/kg/wk for a parasitological cure requires 4 months for a clinical cure and 8 months for a parasitological cure.

Patient Monitoring and Laboratory Tests

Monitor for heartworm status in dogs before initiating treatment with milbemycin.

Formulations Available

Milbemycin is available in 2.3-, 5.75-, 11.5-, and 23-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Heartworm prevention and control of endoparasites: 0.5 mg/kg q30days PO.
- Demodicosis: 2 mg/kg q24h PO for 60–120 days or 1 mg/kg daily until a clinical cure is observed, followed by 3 mg/kg once per week until a parasitological cure (negative scraping) is observed.
- Sarcoptic mange: 2 mg/kg q7days for 3–5 weeks PO.
- Cheyletiellosis: 2 mg/kg/wk PO.

Cats

- Heartworm and endoparasite control: 2 mg/kg q30days PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Mineral Oil

Trade and other names: Generic brands

Functional classification: Laxative

Pharmacology and Mechanism of Action

Lubricant laxative. Mineral oil increases water content of stool and acts as a lubricant for intestinal contents.

Indications and Clinical Uses

Mineral oil is administered orally (via stomach tube in horses) to increase passage of feces for treatment of impaction and constipation.

Precautionary Information**Adverse Reactions and Side Effects**

Adverse effects have not been reported. Chronic use may decrease absorption of fat-soluble vitamins.

Contraindications and Precautions

Use caution when administering via stomach tube. Accidental administration into the lungs has produced fatal reactions.

Drug Interactions

No drug interactions reported. Chronic use may inhibit absorption of fat-soluble vitamins.

Instructions for Use

Use is empirical. No clinical results reported.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Mineral oil is available in an oral liquid.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage**Dogs**

- 10-50 mL/dog q12h PO.

Cats

- 10-25 mL/cat q12h PO.

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Large Animal Dosage

Horses and Cattle

- 500-1000 mL (1 pint to 1 quart) per horse or cow PO, as needed. Up to 2-4 L per adult horse or cow PO (usually administered via stomach tube).

Sheep and Pigs

- 500-1000 mL PO, as needed.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Minocycline Hydrochloride

min-oh-sye'kleen hye-droe-klor'ide

Trade and other names: Minocin, Solodyn

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Tetracycline antibiotic. Like other tetracyclines, the mechanism of action of minocycline is to bind to 30S ribosomal subunit and inhibit protein synthesis. It is usually bacteriostatic. It has a broad spectrum of activity including gram-positive and gram-negative bacteria, some protozoa, *Rickettsiae*, and *Ehrlichiae*. Resistance among *Staphylococcus* species and gram-negative bacilli is common. Minocycline also may have some anti-inflammatory properties that may benefit joint diseases. Minocycline has a similar pharmacokinetic profile to doxycycline, but it is less protein binding. In horses, oral minocycline at 4 mg/kg every 12 hours produced a peak concentration of 0.6 mcg/mL and had a half-life of approximately 13 hours; after IV administration at 2.2 mg/kg the half-life is 7.7 hours.

Indications and Clinical Uses

Minocycline is used when tetracyclines are indicated for treating bacterial infections in animals. It may be effective for *Rickettsiae* and *Ehrlichiae* infections. The other oral tetracycline most often used in animals is doxycycline.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported for minocycline. It has been used safely in experimental animals without adverse effects. However, as with any oral tetracycline, changes in intestinal microflora could increase risk of diarrhea in some animals.

Contraindications and Precautions

No specific precautions have been reported for animals.

Drug Interactions

No drug interactions are reported for animals. Oral absorption is not affected by calcium products as much as with other tetracyclines.

Instructions for Use

Minocycline has received little attention for clinical veterinary use in North America. Clinical use has not been reported, but properties are similar to

doxycycline. Doxycycline is more commonly used as the tetracycline of choice in small animals.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are ≤ 2 mcg/mL for streptococci and ≤ 4 for other organisms. Tetracycline is used as a marker to test susceptibility for other drugs in this class such as doxycycline, minocycline, and oxytetracycline.

Formulations

Minocycline is available in 50-, 75-, and 100-mg tablets and capsules and 10-mg/mL flavored oral suspension. Vials for injection should be reconstituted in 5 mL and then diluted in 500-1,000 mL for IV infusion. Solution may be stored at room temperature for 24 hours.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with other drugs.

Small Animal Dosage

Dogs and Cats

- 5-12.5 mg/kg q12h PO.

Large Animal Dosage

Horses

- 4 mg/kg q12h, PO, or 2.2 mg/kg q12h, IV.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Mirtazapine

Mir taz' a peen

Trade and other names: Remeron

Functional classification: Antiemetic agent

Pharmacology and Mechanism of Action

Mirtazapine is used as an antiemetic in animals, but in people it also has antidepressant and anxiolytic activity. The antiemetic action is via blockade of serotonin (5HT₃, 5HT₂, and 5HT₁) receptors and antagonism of alpha₂-receptors. Because it is active on three serotonin receptors, it is not as selective as ondansetron and other related drugs that affect 5HT₃ receptors. Presynaptic alpha₂ antagonism increases noradrenergic and serotonergic transmission. Serotonin 5HT₂ and 5HT₃ receptors are blocked postsynaptically. After administration to cats, the half-life was 15 hours after a high dose (3.75 mg per cat) and 10 hours after a low dose (1.9 mg per cat).

Indications and Clinical Uses

Mirtazapine is used as an antiemetic and appetite stimulant, primarily in cats. Although there also has been some use in dogs, it is primarily anecdotal. After

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introduction of other antiemetics for animals (e.g., maropitant) the use of mirtazapine has declined. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been commonly reported because of the infrequent use. However, some adverse effects in cats—such as twitching and other abnormal behavior—have been observed. In people, sedation and weight gain have been reported. Some antihistaminic effects have been reported. Sedation observed in people has not been as common in animals.

Contraindications and Precautions

No known contraindications in animals.

Drug Interactions

No drug interactions have been reported for animals. However, avoid use with selective serotonin reuptake inhibitors (SSRI) and monoamine oxidase inhibitors (MAOIs) such as selegiline.

Instructions for Use

Doses and recommendations are based on anecdotal reports and limited field use.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Mirtazapine is available in 15- and 30-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 3.75-7.5 mg per dog, daily, PO.

Cats

- 1.9 mg per cat, PO. Doses have ranged from 3.75 to 7.5 mg per cat, per day, PO (one fourth to one half of a 15-mg tablet). Intervals have been increased, depending on the use and response, to q48h to q72h.

Large Animal Dosage

No large animal doses are available.

Regulatory Information

No withdrawal time information is available for food-producing animals.

Misoprostol

mee-soe-pross'tole

Trade and other names: Cytotec

Functional classification: Antiulcer agent

Pharmacology and Mechanism of Action

Misoprostol is a synthetic prostaglandin. It is a synthetic analogue of PGE₁ and produces a cytoprotective effect on the GI mucosa. It has been shown in dogs and people to decrease the injury to GI mucosa caused by nonsteroidal anti-inflammatory drugs (NSAIDs), such as aspirin. In studies in dogs, misoprostol was not effective for decreasing adverse effects caused by corticosteroids. Misoprostol also has anti-inflammatory effects and has been used to treat pruritus in dogs.

Indications and Clinical Uses

Misoprostol is used to decrease the risk of GI ulceration when administered concurrently with NSAIDs. Efficacy has been established for this indication in trials with aspirin but not with other NSAIDs in animals. There is no evidence to show that it decreases GI bleeding caused from other drugs (e.g., corticosteroids). Clinical trials also are available to show that misoprostol is effective for treating pruritus in patients with atopic dermatitis, although it is less effective than other drugs.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are caused by effects of prostaglandins. Most common side effect is GI discomfort, vomiting, and diarrhea.

Contraindications and Precautions

Do not administer to pregnant animals; it may cause abortion. Women should handle this medication carefully because it can induce abortion.

Drug Interactions

No drug interactions reported for animals.

Instructions for Use

Doses and recommendations are based on clinical trials in which misoprostol was administered to prevent GI mucosal injury caused by aspirin.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Misoprostol is available in 0.1-mg (100 mcg) and 0.2-mg (200-mcg) tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 2-5 mcg/kg q12h PO.
- Treating atopic dermatitis 5 mcg/kg q8h PO.

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Cats

- Dose has not been established.

Large Animal Dosage

Horses

- 5 mcg/kg q8h PO. However, there may be unacceptable GI adverse effects in large animals.

Regulatory Information

Do not use in animals that produce food.

RCI Classification: 4

Mitotane

mye'toe-tane

Trade and other names: Lysodren and op-DDD

Functional classification: Adrenolytic agent

Pharmacology and Mechanism of Action

Mitotane is a cytotoxic agent. Mitotane binds to adrenal proteins and is then converted to a reactive metabolite, which then destroys cells of the zona fasciculata and zona reticularis of the adrenal cortex. Destruction of the adrenal cells is relatively specific and can be complete or partial, depending on the dose used. If only partial destruction of adrenal cortical cells occurs, repeated administration or maintenance doses are needed to suppress hypercortisolemia.

Mitotane is a highly lipophilic drug. It is poorly absorbed without food, but oral absorption is enhanced when administered with food or oil.

Indications and Clinical Uses

Mitotane is used primarily to treat pituitary-dependent hyperadrenocorticism (PDH) (Cushing's disease). It also has been used to treat adrenal tumors. Treatment is initiated with a loading dose, followed by weekly maintenance doses. Other drugs used to suppress cortisol in dogs include ketoconazole, selegiline, and trilostane. Treatment with mitotane has been compared with trilostane and has shown that each drug, although acting through different mechanisms, produces similar survival times in dogs with PDH.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects, especially during the induction period, include lethargy, weakness, anorexia, ataxia, depression, and vomiting. Discontinue if signs of liver disease are observed. Adverse effects may occur in 25%-30% of dogs. Corticosteroid supplementation (e.g., hydrocortisone or prednisolone) may be administered to minimize side effects (prednisone dose 0.25 mg/kg/day). In some dogs, adverse neurologic signs may be observed, which include ataxia, head pressing, and blindness. CNS effects are the result of enlargement of the pituitary gland in response to suppression of the adrenal cortex and lack of feedback by cortisol. Loss of feedback control stimulates CRH and ACTH secretion.

Contraindications and Precautions

Do not administer to animals unless there is an ability to monitor response with cortisol serum measurements, preferably after adrenocorticotropic hormone (ACTH) stimulation.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Dose and frequency are often based on patient response. Typically, the induction period lasts 5-14 days in dogs. During the induction period monitor water consumption, appetite, and behavior. Adverse effects are common during initial therapy. Administration with food increases oral absorption. The maintenance dose should be adjusted on the basis of periodic cortisol measurements and ACTH stimulation tests. Prednisolone at 0.25 mg/kg is sometimes administered as a replacement in patients with PDH during the induction treatment. Trilostane, an approved drug for dogs, has also been used instead of mitotane in dogs and should be considered when dogs do not respond to or tolerate mitotane. Cats usually have not responded to mitotane treatment.

Patient Monitoring and Laboratory Tests

Monitor water consumption and appetite during the induction phase. Monitor ACTH response test to adjust dose. Monitor electrolytes periodically to screen for hyperkalemia that could result from adrenal destruction (iatrogenic hypoadrenocorticism).

Formulations

Mitotane is available in 500-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Mitotane is not stable in aqueous solutions and may lose potency in some compounded formulations.

Small Animal Dosage**Dogs**

- PDH: 50 mg/kg/day (in divided doses) PO for 5-14 days, then 50-70 mg/kg/week PO.
- Adrenal tumor: 50-75 mg/kg/day for 10 days, then 75-100 mg/kg/week PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Do not use in animals that produce food.

Mitoxantrone Hydrochloride

mye-toe-zan'trone hye-droe-klar'ide

Trade and other names: Novantrone

Functional classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer antibiotic. Mitoxantrone is an anticancer agent that is similar to doxorubicin in action. Like doxorubicin, it acts to intercalate between bases on DNA, disrupting DNA and RNA synthesis in tumor cells. Mitoxantrone may affect tumor cell membranes.

Indications and Clinical Uses

Mitoxantrone is used in anticancer drug protocols in animals for treatment of leukemia, lymphoma, and carcinomas.

Precautionary Information

Adverse Reactions and Side Effects

As with all anticancer agents, certain adverse effects are predictable and unavoidable and related to the drug's action. Mitoxantrone produces myelosuppression, vomiting, anorexia, and GI upset, but it may be less cardiotoxic than doxorubicin.

Contraindications and Precautions

Do not administer to animals with bone marrow suppression.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Proper use of mitoxantrone usually follows a specific anticancer protocol. Doses listed are based on input from reputable oncologists, but consult specific protocol for dosing regimens that may deviate from these recommendations.

Patient Monitoring and Laboratory Tests

Monitor CBC to look for evidence of bone marrow toxicity.

Formulations

Mitoxantrone is available in 2-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 5-5.5 mg/m² IV every 21 days, and up to 6 mg/m² if dogs tolerate it well.

Cats

- 6-6.5 mg/m² IV every 21 days.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Mitratapide

Mi-trat'-a-pyed

Trade and other names: Yarvitan

Functional classification: Weight loss medication

Pharmacology and Mechanism of Action

Mitratapide is used to produce weight loss in dogs. It is related to another medication used for obesity in dogs, dirlotapide (Slentrol). Mitratapide is an inhibitor of the microsomal triglyceride transfer protein (MTP). Inhibition of this enzyme reduces the ability of intestinal enterocytes to process triglycerides. The accumulation of these triglycerides in the intestinal cells sends a signal to the central nervous system to suppress the appetite. In dogs the effect on the intestinal cells reduces the uptake of dietary lipids in association with decreased postprandial serum triglycerides, phospholipids, and cholesterol. The accumulation of triglycerides inside the enterocytes can be observed macroscopically and histopathologically. The weight loss is attributed to the reduced appetite, rather than impaired processing of dietary lipids. It does not produce a direct centrally acting effect. Bioavailability of oral mitratapide is 16%-21%, with a large volume of distribution (VD) of 5 l/kg. It is highly protein bound (99%). It has a plasma half-life of 6.3 hours for mitratapide and longer (9.8, 11.7, 44.7 hours) for various metabolites, some of which are active.

Indications and Clinical Uses

Mitratapide is used in the management of obesity in dogs. During the treatment protocol, there is a relatively moderate loss of weight, (6%-7% of the weight before treatment). It should not be used without instituting the proper protocol, as outlined by the sponsor. It should be used in an overall weight management program, which also includes appropriate dietary changes. Before using to treat overweight or obesity, rule out other diseases such as hypothyroidism or hyperadrenocorticism. At this time, it is approved in Europe, but it has not been approved in the US. It should not be used in cats.

Precautionary Information

Adverse Reactions and Side Effects

Decreased appetite occurs as a mode of action of the drug. Vomiting may also occur as a common effect related to the drug's mechanism of action. Nausea and diarrhea also may occur. None of these signs are necessarily cause to stop the medication, and they may resolve with time. However, if vomiting and nausea persist, evaluation and adjustment of dose may be necessary. Administration with food may decrease vomiting. Changes in liver enzymes also are expected. There may be decreases in serum albumin, globulin, total protein, calcium, and alkaline phosphatase and increases in ALT associated with treatment. Hyperkalemia may also be observed. The severity of these changes is proportional to dose. These changes may normalize after continued treatment. There may be decreased absorption of fat-soluble vitamins A and E. The reduced absorption of these vitamins has not been clinically significant.

Contraindications and Precautions

Do not administer to cats. Do not use in dogs with liver disease. Do not use in dogs during pregnancy and lactation or in young dogs less than 18 months of age. Humans should not take this drug.

Drug Interactions

No drug interactions have been reported. It has been safely administered with NSAIDs and ACE inhibitors.

Instructions for Use

There is a specific protocol (see dosing section) that must be followed for proper use of this drug. If reductions in diet are not maintained and diet is not restricted, animals will regain weight following cessation of treatment. To avoid this rebound weight gain, it is important to continue the feeding for maintenance regimen after the end of treatment with the product. Treatment should be given with food. The appetite suppression is less in dogs that are fed a low-fat diet compared to a diet higher in fat content.

Patient Monitoring and Laboratory Tests

Monitor patient's weight. Monitor blood chemistry profile for increases in liver enzymes and reduced albumin and electrolytes.

Formulations

Mirtapide is available in 5-mg/ml oral solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Once opened it has a shelf life of 3 months. Do not refrigerate.

Small Animal Dosage**Dogs**

- 0.63 mg/kg, once daily (1 mL of the product per 8 kg). This dose is administered for two periods of 21 days with a break of 14 days without treatment between each period. Weighing the animal during treatment is important. Weigh the dog on day 1 and on day 35 (i.e., at the start of each treatment period). During the first 21 days of treatment, the quantity of food should not be changed. Thereafter, adjust the amount of food according to energy requirements for maintenance with a regular pet food or with a low-calorie (diet) pet food. The lower amount can be continued after treatment is discontinued.

Cats

Do not use.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food.

Morphine Sulfate

mor'feen sul'fate

Trade and other names: Generic brands, MS Contin extended-release tablets, Oramorph SR extended-release tablets, and generic brand extended-release tablets

Functional classification: Analgesic, opioid

Pharmacology and Mechanism of Action

Opioid agonist, analgesic. Prototype for other opioid agonists. Action of morphine is to bind to mu-opiate and kappa-opiate receptors on nerves and inhibit release of neurotransmitters involved with transmission of pain stimuli (such as Substance P). Morphine also may inhibit release of some inflammatory mediators. The central nervous system effects and euphoric properties are related to mu-receptor effects in brain. Other opiates and opioids used in animals include hydromorphone, codeine, oxycodone, meperidine, and fentanyl. Oral morphine formulations are poorly bioavailable in dogs and may not be effective.

Indications and Clinical Uses

Morphine is indicated for short-term analgesia, for sedation, and as an adjunct to anesthesia. It is compatible with most anesthetics and can be used as part of a multimodal approach to analgesia/anesthesia. Administration of morphine may lower dose requirements for other anesthetics and analgesics used. Duration of morphine in dogs is short (2-4 hours). Morphine has been used in animals for treatment of pulmonary edema. Presumably, this effect is attributed to vasodilation and reduction of preload in animals. Although oral morphine (regular and sustained release) has been used in dogs, its absorption is poor and inconsistent. The oral dose formulations should not be relied on for treating severe pain in dogs. Morphine oral administration has not been investigated in cats. Injectable forms can be used in cats, but doses are generally lower than in dogs to prevent excitement. In horses, it is rarely used alone or without other sedatives because undesirable behavior and cardiovascular effects may occur at doses that are needed for analgesia. The adverse effects in horses diminish its routine use.

Precautionary Information

Adverse Reactions and Side Effects

Like all opiates, side effects from morphine are predictable and unavoidable. Side effects from morphine administration include sedation, vomiting, constipation, urinary retention, and bradycardia. Panting may occur in dogs as a result of changes in thermoregulation. Histamine release occurs from administration of morphine, but it may be less likely with other opioids. Excitement can occur in some animals, but it is more common in cats and horses. Respiratory depression occurs with high doses. As with other opiates, a slight decrease in heart rate is expected. In most cases this decrease does not have to be treated with anticholinergic drugs (e.g., atropine), but it should be monitored. Tolerance and dependence occur with chronic administration. In horses, there was ileus, constipation, and CNS stimulation (pawing and pacing) following 0.5 mg/kg. In horses, undesirable and even dangerous behavior actions can follow rapid intravenous opioid administration. If used in horses, they should receive a preanesthetic of acepromazine or an alpha₂-agonist.

Contraindications and Precautions

Morphine is a Schedule II controlled substance. Cats and horses are more sensitive to excitement than other species.

Drug Interactions

Like other opiates, it will potentiate other drugs that cause CNS depression.

Instructions for Use

Effects from morphine administration are dose dependent. Low doses (0.1-0.25 mg/kg) produce mild analgesia. Higher doses (up to 1 mg/kg) produce greater analgesic effects and sedation. Usually morphine is administered IM, IV, or SQ. Constant rate infusions (CRI) also have been used, and doses cited have been shown to produce morphine concentrations in a therapeutic range. Oral morphine is available in sustained-release forms, but oral dosing can be highly variable and inconsistent. Epidural administration has been used for surgical procedures. Combination protocols include MMK, which is morphine (0.2 mg/kg) + medetomidine 60 mcg/kg (or dexmedetomidine) + ketamine (5 mg/kg) all mixed in one syringe and administered IM to produce short-term analgesia and anesthesia for approximately 120 minutes.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, if necessary atropine can be administered. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

Formulations

Morphine is available in 1-, 2-, 4-, 5-, 8-, 10-, 15-, 25-, and 50-mg/mL injection (most common is 15 mg/mL); 15- and 30-mg tablets; and extended-release tablets in 15, 30, 60, 100, and 200 mg (MS Contin, Oramorph SR, or generic brands). Morphine pentahydrate (Avinza) is available in 60-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Morphine sulfate is slightly water soluble and soluble in ethanol. It is more stable at pH <4. If mixed with high pH vehicles, oxidation occurs, which may darken the formulation (brownish yellow). Solutions may be repackaged in plastic syringes and kept stable for 70 days. If mixed with sodium chloride (0.9%) for epidural injection, it is stable for 14 weeks. Protect from freezing.

Small Animal Dosage**Dogs**

- Analgesia: 0.5 mg/kg q2h IV or IM. However, a dose range of 0.1-1 mg/kg IV, IM, or SQ q4h has also been used (dose is escalated as needed).
- CRI: Loading dose of 0.2 mg/kg IV, followed by 0.1 mg/kg/hr. This may be increased to a loading dose of 0.3 mg/kg, followed by 0.17 mg/kg/hr for more severe pain. Doses as high as a loading dose of 0.6 mg/kg, followed by 0.34 mg/kg IV have been used in experimental dogs.
- Oral dosing: Regular tablets should not be used. Sustained-release tablets have been used at a dose of 15 or 30 mg per dog, q8-12h PO, but studies have shown these tablets to be inconsistently and poorly absorbed in dogs.
- Epidural: 0.1 mg/kg.

Cats

- Analgesia: 0.1 mg/kg IM or SQ q3-6h (or as needed).
- Epidural 0.1 mg/kg, diluted in saline to 0.3 mL/kg.

Large Animal Dosage

Horses

- For light chemical restraint, use 0.3-0.5 mg/kg IV. For more severe pain, administer 0.5-1 mg/kg IV or IM. Give IV doses slowly. Morphine may cause excitement in horses and it is advised to first sedate with an α_2 -agonist.
- Intra-articular (use preservative free solutions): 0.05 mg/kg; start with initial concentration of 20 mg/mL solution and dilute in saline to 5 mg/mL and administered at a rate of 1 mL per joint per 100 kg of body weight.

Ruminants

- The benefits of using morphine in ruminants are controversial. However, 0.05-0.1 mg/kg IV and up to 0.4 mg/kg IV have been used to treat pain and in perioperative situations.

Regulatory Information

Morphine is a Schedule II controlled drug.

Avoid use in animals intended for food.

RCI Classification: 1

Moxidectin

moks-ih-dek'tin

Trade and other names: ProHeart (canine), Quest (equine), and Cydectin (bovine and ovine)

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic drug in the milbemycin class. Avermectins (ivermectin-like drugs) and milbemycins (milbemycin and moxidectin) are macrocyclic lactones and share similarities, including mechanism of action. Compared to ivermectin, moxidectin is 100 times more lipophilic. These drugs are neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in parasites. Paralysis and death of the parasite are caused by increased permeability to chloride ions and hyperpolarization of nerve cells. These drugs also potentiate other chloride channels, including ones gated by GABA, but GABA-mediated mechanism may not be important for parasites. Mammals ordinarily are not affected because they lack glutamate-gated chloride channels, and there is a lower affinity for other mammalian chloride channels. Because these drugs ordinarily do not penetrate the blood-brain barrier, GABA-gated channels in the CNS of mammals are not affected. Moxidectin is active against intestinal parasites, mites, bots, heartworm microfilaria, and developing larvae. Moxidectin has no effect on trematode or cestode parasites. One of the equine formulations also contains praziquantel to control additional parasites.

Indications and Clinical Uses

Moxidectin is used in dogs to prevent infection of heartworm (*Dirofilaria immitis*). In dogs it can be used to treat hookworm (*Uncinaria stenocephala*) in larval and

adult stages. In horses, moxidectin is used for treatment of a variety of parasites, including large strongyles (*Strongylus vulgaris* [adults and L4/L5 arterial stages], *S. edentatus* [adult and tissue stages], *Triodontophorus brevicauda* [adults], and *T. serratus* [adults]); small strongyles ([adults] *Cyathostomum* species, *Cylicocycilus* species, *Cylicocostephanus* species, *Coronocycilus* species, and *Gyalocephalus capitatus*). It is also used to treat small strongyles, including larvae. It is used to treat ascarids, including *Parascaris equorum* (adults and L4 larval stages), pinworms (*Oxyuris equi* [adults and L4 larval stages]), hairworms (*Trichostrongylus axei* [adults]), large-mouth stomach worms (*Habronema muscae* [adults]), and horse stomach bots (*Gasterophilus intestinalis* [2nd and 3rd instars] and *G. nasalis* [3rd instars]). One dose also suppresses strongyle egg production for 84 days. Some formulations for horses also contain praziquantel for horses. This increases the spectrum to include other intestinal parasites such as tapeworms.

In cattle, moxidectin injectable is used to treat GI roundworms (*Ostertagia ostertagi* [adults and inhibited fourth-stage larvae], *Haemonchus placei* [adults], *Trichostrongylus axei* [adults], *T. colubriformis* [fourth-stage larvae], *Cooperia oncophora* [adults], *C. punctata* [adults and fourth-stage larvae], *C. surnabada* [adults and fourth-stage larvae], *Oesophagostomum radiatum* [adults and fourth-stage larvae], *Trichuris* spp. [adults]), lungworms (*Dictyocaulus viviparus* [adults and fourth-stage larvae]), grubs (*Hypoderma bovis* and *H. lineatum*), mites (*Psoroptes ovis* [*P. communis* var. *bovis*]), and lice (*Linognathus vituli* and *Solenopotes capillatus*). One injection will protect cattle from reinfection with *D. viviparus* and *O. radiatum* for 42 days, *H. placei* for 35 days, and *O. ostertagi* and *T. axei* for 14 days after treatment. In sheep the oral drench is used for the treatment and control of the adult and L4 larval stages of *Haemonchus contortus*, *Teladorsagia circumcincta*, *T. trifurcata*, *Trichostrongylus axei*, *T. colubriformis*, *T. vitrinus*, *Cooperia curtipicei*, *C. oncophora*, *Oesophagostomum columbianum*, *O. venulosum*, *Nematodirus battus*, *N. filicollis*, and *N. spatiger*.

Precautionary Information

Adverse Reactions and Side Effects

Toxicity is the result of potentiation of glutamate-gated chloride channels and GABA channels resulting in hyperpolarization of membranes. Toxicity may occur at high doses and in breeds in which moxidectin crosses the blood–brain barrier. Sensitive breeds may include Collies, Australian shepherds, Old English sheepdogs, longhaired Whippets, and Shetland sheepdogs. Toxicity is neurotoxic and signs include depression, ataxia, difficulty with vision, coma, and death. Sensitivity to moxidectin occurs in certain breeds because of a mutation in the multidrug resistance gene (MDRI, also known as ABCB1 gene) that codes for the membrane pump p-glycoprotein. This mutation affects the efflux pump in the blood–brain barrier. Adverse effects may occur when high doses of moxidectin are used to treat dogs for demodicosis. These effects include lethargy, depressed appetite, vomiting, and lesions at the site of an SQ injection. Toxicity is more likely at high doses in dogs. At five times the label dose rate (15 mcg/kg) once every month, moxidectin was administered safely to Collies that were ivermectin sensitive. However, at a single dose of 90 mcg/kg (30 times the label dose) administered to sensitive Collies, ataxia, lethargy, and salivation occurred in one sixth of dogs. At 30, 60, and 90 mcg/kg to ivermectin-sensitive Collies (10 times, 20 times, and 30 times the label dose) there were no adverse effects observed. Nevertheless, caution is advised when administering moxidectin to

sensitive breeds listed previously. Because of concern about adverse reactions and deaths in dogs from the 6-month injectable formulation (Pro-Heart 6), this product was temporarily discontinued. The safety concerns have been addressed by reformulating the product, which is now available. In horses, moxidectin has been safe at three times the label dose. However, adverse effects (ataxia, depression, and lethargy) have been reported in young horses (younger than 6 months) or debilitated animals after treatment. Other adverse effects reported in horses include sedation, weakness, bradycardia, dyspnea, coma, and seizures.

Neurological toxicity in animals producing seizures can be treated with diazepam, barbiturates, or propofol.

Contraindications and Precautions

Do not use in dogs younger than 2 months of age. The canine long-acting formulation ProHeart 6 was temporarily discontinued but reintroduced after reformulation. Despite the safety margin listed in the Adverse Reactions and Side Effects section, caution is advised when administering moxidectin at high doses to ivermectin-sensitive breeds. Affected breeds may include Collies, Australian shepherds, Old English sheepdogs, longhaired Whippets, and Shetland sheepdogs. Susceptible breeds may also be sensitive to other drugs such as loperamide, cardiovascular drugs, and anticancer drugs. Administration to foals younger than 6 months of age is not recommended. Do not apply the pour-on formulation to small animals. It has been used safely in queens and kittens during pregnancy and lactation.

Drug Interactions

Do not administer with drugs that could potentially increase the penetration of ivermectin across the blood-brain barrier. Such drugs include ketoconazole, itraconazole, cyclosporine, and calcium-channel blockers.

Instructions for Use

Caution is recommended if bovine or equine formulation is considered for use in small animals. Toxic overdoses are likely because these formulations are highly concentrated. It is approved for use in dogs for the prevention of heartworm disease caused by *Dirofilaria immitis* and for treatment of existing larval and adult hookworm infections in dogs.

Patient Monitoring and Laboratory Tests

Animals should be checked for heartworm status prior to initiating treatment.

Formulations

Moxidectin is available in 30-, 68-, and 136-mcg tablets for dogs; 20-mg/mL equine oral gel; 5-mg/mL cattle pour-on; 1-mg/mL oral drench for sheep; 10-mg/mL injectable solution for cattle; and Quest 2% gel for horses (20 mg/mL). Quest Plus gel for horses contains 20 mg/mL (2%) plus 125 mg praziquantel (12.5%). The 6-month injectable (Pro-Heart 6) formulation consists of two separate vials: one contains 10% moxidectin microspheres, and the other contains a vehicle for constitution of the moxidectin microspheres. Each milliliter of constituted, sustained-release suspension contains 3.4 mg of moxidectin.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Heartworm prevention: 3 mcg/kg every 30 days PO.
- Heartworm prevention (long-acting injectable): 0.17 mg/kg (170 mcg/kg) SQ as a single dose.
- Endoparasite control: 25-300 mcg/kg.
- Sarcoptic mange: 200-250 mcg/kg (0.2-0.25 mg/kg) PO or SQ, once per week, for 3-6 weeks.
- Demodicosis: 200 mcg/kg SQ, weekly or every other week for 1-4 doses; alternatively, 400 mcg/kg/day PO. Higher doses are used for refractory *Demodex* cases: 500 mcg/kg (0.5 mg/kg)/day PO for 21-23 weeks or 0.5-1.0 mg/kg SQ, q72h, for 21-22 weeks. Duration of treatment for demodicosis is variable. Treat until two negative *Demodex* skin scrapings are achieved.

Large Animal Dosage

Horses

- GI parasites: 0.4 mg/kg PO. Avoid use in young horses, small ponies, or debilitated animals.

Cattle

- 0.2 mg/kg SQ, once.
- GI parasites, lungworms, mites, grubs, and lice: Topical treatment (pour-on): 0.5 mg/kg (0.23 mg/pound or 45 mL per 1000 pounds). Apply topically along the midline from the withers to the tail head. Avoid exposure to human skin and to other animals.

Sheep

- 1 mL per 5 kg (1 mL per 11 pounds) by mouth of the 1-mg/mL oral solution.

Regulatory Information

Do not use in horses intended for food.

Cattle withdrawal time (meat): 21 days.

Sheep withdrawal time (meat): 7 days.

Goat withdrawal time (meat): 14 days.

No milk withholding time has been established. Do not use in female dairy cattle of breeding age. Do not use in female sheep providing milk for human consumption. Do not use in veal calves.

Moxifloxacin

moks-ih-floks'ah-sin

Trade and other names: Avelox

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Fluoroquinolone antibacterial. Moxifloxacin, like other quinolones, inhibits DNA gyrase and prevents bacterial cell DNA and RNA synthesis. Moxifloxacin is bactericidal with broad antimicrobial activity. It has a chemical structure slightly different from older veterinary fluoroquinolones (8 methoxy substitution). As a result of this modification, this newer generation of drugs, such as moxifloxacin, has

greater activity against gram-positive bacteria and anaerobes than the veterinary fluoroquinolones (enrofloxacin, orbifloxacin, danofloxacin, and marbofloxacin).

Indications and Clinical Uses

Moxifloxacin, although a human drug, has been used in small animals for treatment of infections refractory to other drugs, including skin infections, pneumonia, and soft tissue infections. The spectrum of activity includes gram-positive cocci and anaerobic bacteria that may be resistant to other quinolones. Because other veterinary fluoroquinolones are preferred for initial use (enrofloxacin, orbifloxacin, danofloxacin, and marbofloxacin), moxifloxacin use is not common. Data for use in small animals are sparse and regimens are primarily extrapolated from the human label. In horses it has been administered at 5.8 mg/kg/day for 3 days. Although pharmacokinetics were favorable in horses, it caused diarrhea that may present a risk.

Precautionary Information

Adverse Reactions and Side Effects

High concentrations may cause CNS toxicity, especially in animals with renal failure. Moxifloxacin causes occasional vomiting. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4 to 28 weeks of age. Large, rapidly growing dogs are the most susceptible. In horses, moxifloxacin at high doses caused diarrhea and is not recommended for routine use. Moxifloxacin at high doses has caused a dose-related prolongation of the Q-T interval. The clinical consequences of this observation for animals are not known.

Contraindications and Precautions

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures. Avoid use in horses, rodents, and rabbits because of risk of diarrhea.

Drug Interactions

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, and calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

Instructions for Use

Doses are based on plasma concentrations needed to achieve sufficient plasma concentration above minimum inhibitory concentrations (MIC) value. Efficacy studies have not been performed in dogs or cats.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are ≤ 1.0 mcg/mL. Most sensitive gram-negative bacteria of the *Enterobacteriaceae* have MIC values ≤ 0.1 mcg/mL. If ciprofloxacin is used to treat *Pseudomonas*, it may be several times more active than other fluoroquinolones. Otherwise, one should assume that if the organism is susceptible to ciprofloxacin, it is likely susceptible to others.

Formulations

Moxifloxacin is available in 400-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with products that contain ions (iron, aluminum, magnesium, and calcium).

Small Animal Dosage

Dogs and Cats

- 10 mg/kg q24h PO.

Large Animal Dosage

Horses

- 5.8 mg/kg q24h for 3 days, but it caused diarrhea. Therefore, there may be risks with long-term use.

Regulatory Information

There are no withdrawal times established because this drug should not be administered to animals that produce food.

Mycophenolate Mofetil

mye-koe-fen'oh-late

Trade and other names: CellCept

Functional classification: Immunosuppressant

Pharmacology and Mechanism of Action

Mycophenolate is a prodrug metabolized to mycophenolic acid (MPA). It is used to suppress immunity for transplantation and for treatment of immune-mediated diseases. Mycophenolate, when metabolized to mycophenolic acid, inhibits inosine monophosphate dehydrogenase (IMPDH), which is an important enzyme for the de novo synthesis of purines in immune cells, especially stimulated lymphocytes. T and B lymphocytes are critically dependent on de novo synthesis of purine nucleotides. Therefore it effectively suppresses lymphocyte proliferation and decreases antibody synthesis by B-cells. In people it is used as a replacement for azathioprine and has been primarily used for immune suppression in patients undergoing liver or kidney transplants, but other uses are being explored. It is usually used in combination with glucocorticoids and/or cyclosporine. The half-life in dogs is only 45 minutes, but it is longer (as long as 8 hours) for the metabolite.

Indications and Clinical Uses

Mycophenolate is used to treat immune-mediated diseases in animals.

In dogs, mycophenolate has been used on a limited basis to treat some immune-mediated diseases. According to pharmacokinetic studies with mycophenolate in dogs, the elimination rate was rapid (half-life less than 1 hour), which may require frequent dosing in dogs for successful therapy. For treatment of pemphigus foliaceus, it was given at a dose of 22-39 mg/kg/day divided into three treatments. It was well-tolerated, but only three out of eight dogs completed the study and were improved. Azathioprine is more commonly used as an immunosuppressive agent.

Precautionary Information

Adverse Reactions and Side Effects

In dogs, GI problems (diarrhea and vomiting) have been the most common effects reported. Use in veterinary medicine has been rare, however.

Cointraindications and Precautions

Mycophenolate is a potent immunosuppressive drug. Patients will be more prone to infection when receiving mycophenolate.

Drug Interactions

No drug interactions are reported. It is frequently administered with corticosteroids.

Instructions for Use

Mycophenolate is used in some patients that cannot tolerate other immunosuppressive drugs, such as azathioprine or cyclophosphamide. Mycophenolate has been used in combination with corticosteroids and cyclosporine.

Patient Monitoring and Laboratory Tests

Monitor for signs of infection in patients.

Formulations

Mycophenolate is available in 250- and 500-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is slightly soluble in water. It is more stable at low pH values (<4). It may be prepared in a syrup suspension for flavoring and stable for 121 days.

Small Animal Dosage

Dogs

- 10 mg/kg q8h, or 20 mg/kg q12h, PO.

Large Animal Dosage

No large animal dose has been reported.

Regulatory Information

There are no withdrawal times established because this drug should not be administered to animals that produce food.

Naloxone Hydrochloride

nal-oks'one hye-droe-klor'ide

Trade and other names: Narcan and Trexonil

Functional classification: Opioid antagonist

Pharmacology and Mechanism of Action

Opiate antagonist. Naloxone competes for opiate receptors and displaces opioid drugs from these receptors, thus reversing their effects. Naloxone is capable of antagonizing all opiate receptors.

Indications and Clinical Uses

Naloxone is used to reverse the effects of opiate agonists on receptors. Naloxone should be used to reverse overdoses or toxicity. It will reverse effects of morphine, oxymorphone, butorphanol, hydromorphone, and other opioids. It is less effective for reversing buprenorphine and may be titrated in gradually to achieve the optimum amount of reversal. At very low doses (one fifth of the dose needed to fully reverse opiates) it has been used to treat opioid-induced side effects such as vomiting, nausea, and dysphoria. A formulation for wildlife use (Trexonil) is more concentrated and used to reverse tranquilization in wild animals. Naloxone may have some temporary benefit for behavior modification (e.g., to suppress compulsive disorders) but the effects are short-lived. For example, in horses, it will temporarily decrease crib biting, but the duration of action is short.

Precautionary Information

Adverse Reactions and Side Effects

Tachycardia and hypertension have been reported in people. In animals, reversal of opioid may precipitate a severe reaction that includes high blood pressure, excitement, pain, tachycardia, and cardiac arrhythmias.

Contraindications and Precautions

Administration to an animal that is experiencing pain will precipitate extreme reactions because of blockade of endogenous opioids.

Drug Interactions

Naloxone will reverse the action of other opioid drugs.

Instructions for Use

Administration may have to be individualized based on response in each patient. Naloxone's duration of action is short in animals (60 minutes) and it may have to be readministered. Start at the low end of the dosage rate and increase the dose to effect. Higher doses may be needed to reverse drugs that are mixed agonists/antagonists such as butorphanol or buprenorphine, compared to reversing drugs that are pure agonists. Low doses may be used to reduced opioid-induced dysphoria in animals. For this use, start with 0.04 mg/mL solution and administer increments of 1 mL every 30 seconds until vocalization or signs of dysphoria stop. A dose of 0.01 mg/kg IV has been given for this purpose without losing analgesic effects.

A dose of 1 mL (0.4 mg) will reverse 1.5 mg oxymorphone, 15 mg morphine, 100 mg meperidine, and 0.4 mg fentanyl.

Patient Monitoring and Laboratory Tests

Naloxone is used to reverse opioid analgesic drugs. When opioids are reversed in some animals, serious reactions may occur. In some patients, changes in blood pressure, tachycardia, and discomfort may result.

Formulations Available

Naloxone is available in injectable vials with preservatives in 0.4 or 1 mg/mL, without preservatives in 0.02 mg (20 mcg), 0.4 mg or 1 mg per mL, and as Trexonil in 50 mg/mL.

Stability and Storage

When used IV, it may be diluted in other fluids. For intravenous infusion, it may be added to sodium chloride or 5% dextrose. After dilution it should be used within 24 hours. Do not mix with other drugs or solutions that are alkaline. Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.01-0.04 mg/kg IV, IM, or SQ, as needed to reverse opiate.
- Low dose to partially reverse dysphoric reaction: Administer 1 mL every 30 seconds (0.04 mg/mL solution) as needed.

Large Animal Dosage

Horses

- 0.02-0.04 mg/kg IV (duration of effect is only 20 minutes).

Regulatory Information

No withdrawal times are established. It is anticipated that naloxone is cleared rapidly after administration. Because of low risk of residues, short (24-48 hour) withdrawal times are suggested.

RCI Classification: 3

Naltrexone

nal-treks'one

Trade and other names: Trexan, Vivitrol

Functional classification: Opioid antagonist

Pharmacology and Mechanism of Action

Opiate antagonist. Naltrexone competes for opiate receptors and displaces opioid drugs from these receptors, thus reversing their effects. It is capable of antagonizing all opiate receptors. Its action is similar to naloxone except that it is longer-acting and administered orally. A related drug that does not have central-acting effects is methylnaltrexone (used to treat intestinal ileus). For humans, there is a long-acting injection formulated in microspheres that persists for 1 month after a single injection. The long-acting form has not been used in animals.

Indications and Clinical Uses

Naltrexone is used in people for treatment of opiate dependence and alcoholism. In animals some obsessive-compulsive disorders are believed to be mediated by

534 Naltrexone

endogenous opioids. It has been used successfully for treatment of some obsessive-compulsive behavioral disorders, such as tail chasing in dogs, acral lick granuloma in dogs, and crib biting in horses. The effect for each of these disorders is short-lived.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. In people, it can precipitate opioid withdrawal signs.

Contraindications and Precautions

Do not administer to animals in pain, or it may elicit a severe reaction.

Drug Interactions

Naltrexone will reverse the action of other opioid drugs.

Instructions for Use

For acute treatment of opiate toxicity, use naloxone instead because it can be injected with a more rapid onset of effects. Treatment for obsessive-compulsive disorders (canine compulsive disorder) in animals has been reported with naltrexone. Relapse rates may be high.

Patient Monitoring and Laboratory Tests

Monitor heart rate in treated animals.

Formulations

Naltrexone is available in 50 mg tablets. Vivitrol for humans is an encapsulated microsphere that can be injected to produce a long-lasting effect (one injection per month) to treat substance dependence. One vial contains 380 mg in microspheres in a 4 mL injection for IM use.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Naltrexone is soluble in water. It has been mixed with juices and syrups to mask the bitter taste and was stable for 60-90 days.

Small Animal Dosage

Dogs

- For behavior problems: 2.2 mg/kg q12h PO.

Large Animal Dosage

Horses

- Crib biting: 0.04 mg/kg IV or SQ. (Because injectable formulations are not available, it must be compounded for this indication.) Duration of effect is 1-7 hours.
- For reversal of opiates: 100 mg/animal IV or SQ. (Because injectable formulations are not available, it must be compounded for this indication.)

Regulatory Information

Withdrawal times are not established for animals that produce food. In wild animals that are captured with opiates and administered naltrexone for reversal, a 45-day withdrawal time is suggested. For additional extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Nandrolone Decanoate

nan'droe-lone dek-ah-noe'ate

Trade and other names: Deca-Durabolin

Functional classification: Hormone, anabolic agent

Pharmacology and Mechanism of Action

Anabolic steroid. Nandrolone is a derivative of testosterone used as an anabolic agent. Anabolic agents are designed to maximize anabolic effects while minimizing androgenic action.

Indications and Clinical Uses

Anabolic agents have been used for reversing catabolic conditions, promoting weight gain, increasing muscling in animals, and stimulating erythropoiesis. There are no differences in efficacy among the anabolic steroids reported in animals.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects from anabolic steroids can be attributed to the pharmacologic action of these steroids. Increased masculine effects are common. There has been an increased incidence of some tumors in people. Some of the oral anabolic steroids that are 17 alpha-methylated (oxymetholone, stanozolol, and oxandrolone) are associated with hepatic toxicity.

Contraindications and Precautions

Use cautiously in patients with hepatic disease. Do not use in pregnant animals.

Drug Interactions

No drug interactions have been reported.

Instructions for Use

Results of clinical studies in animals have not been reported. Nandrolone use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes in treated patients.

Formulations

Nandrolone decanoate is available in 50-, 100-, and 200-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 1-1.5 mg/kg/wk IM.

Cats

- 1 mg/kg/wk IM.

Large Animal Dosage

Horses

- 1 mg/kg q4wk IM.

Regulatory Information

Nandrolone is a Schedule III controlled drug.
Do not administer to animals intended for food.
RCI Classification: 4

Naproxen

nah-proks'en

Trade and other names: Naprosyn, Naxen, and Aleve (naproxen sodium)

Functional classification: Nonsteroidal anti-inflammatory drug (NSAID)

Pharmacology and Mechanism of Action

Naproxen and other NSAIDs have produced analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the cyclo-oxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, there are overlapping functions of the mediators derived from these isoforms. Naproxen is a nonselective inhibitor of COX-1 and COX-2.

Indications and Clinical Uses

Naproxen is approved for use in people and is popular for treating osteoarthritis. It has been used for treatment of musculoskeletal problems, such as myositis and osteoarthritis in dogs and horses. There are no veterinary formulations marketed. Its use has diminished because there are registered drugs approved for these indications for horses and dogs.

Precautionary Information

Adverse Reactions and Side Effects

Naproxen is a potent NSAID. Adverse effects attributed to GI toxicity are common to all NSAIDs. Naproxen has produced serious ulceration in dogs because elimination in dogs is many times slower than in people or horses. Renal injury caused by renal ischemia also is possible with repeated doses.

Contraindications and Precautions

Caution is advised when using the OTC formulation designed for people because the tablet size is much larger than the safe dose for dogs. Therefore, warn pet owners about administration to dogs without consulting a veterinarian first. Dosing rates for people are not appropriate for dogs. Do not administer to animals prone to GI ulcers. Do not administer with other ulcerogenic drugs, such as corticosteroids.

Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on pharmacokinetic studies in experimental animals.

Patient Monitoring and Laboratory Tests

Monitor for signs of GI ulceration.

Formulations

Naproxen is available in 220-mg tablets (OTC). (A 220-mg dose of naproxen sodium is equivalent to 200 mg naproxen.) It is also available in 25-mg/mL oral suspension and 250-, 375-, and 500-mg tablets (prescription).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Naproxen is practically insoluble in water at low pH, but it increases at high pH. It is soluble in ethanol.

Small Animal Dosage**Dogs**

- 5 mg/kg initially, then 2 mg/kg q48h PO.

Large Animal Dosage**Horses**

- 10 mg/kg q12h PO.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

N-Butylscopolammonium Bromide (Butylscopolamine Bromide)

en-byoo-til-skoe-pahl'ah-moe-nee-um broe'mide

Trade and other names: Buscopan

Functional classification: Antispasmodic

Pharmacology and Mechanism of Action

Antispasmodic, antimuscarinic, anticholinergic drug. This is a quarternary ammonium compound derived from belladonna alkaloid. Butylscopolamine, like other antimuscarinic drugs, blocks cholinergic receptors and produces a parasympatholytic effect. It affects receptors throughout the body, but it is used more commonly for its GI effects. It effectively inhibits secretions and motility of the GI tract by blocking parasympathetic receptors. It has a short half-life (15-25 minutes) and short duration of action.

Indications and Clinical Uses

Butylscopolamine bromide is indicated for treating pain associated with spasmodic colic, flatulent colic, and intestinal impactions in horses. It is also used

to relax the rectum and reduce intestinal strain to facilitate diagnostic rectal palpation.

Precautionary Information

Adverse Reactions and Side Effects

Adverse reactions from anticholinergic drugs are related to their blocking of acetylcholine receptors and producing a systemic parasympatholytic response. As expected with this class of drugs, animals will have increased heart rate, decreased secretions, dry mucous membranes, decreased GI tract motility, and dilated pupils. In target animal safety studies in which doses of 1, 3 and 5 times the approved dose and up to 10 times the dose were administered to horses, the clinical signs described previously were observed. However, at high doses there were no CBC or biochemical abnormalities or lesions identified at necropsy.

Contraindications and Precautions

N-butylscopolammonium bromide will decrease intestinal motility. Use cautiously in conditions where decreased motility will be a concern.

Drug Interactions

N-butylscopolammonium bromide is an anticholinergic drug and therefore will antagonize any other medications that are intended to produce a cholinergic response (e.g., metoclopramide).

Instructions for Use

Experience is limited to treating spasmodic colic, flatulent colic, and intestinal impactions in horses. There is no experience in other animals.

Patient Monitoring and Laboratory Tests

Monitor equine intestinal motility (gut sounds and fecal output) during treatment. Monitor heart rate in treated animals.

Formulations

N-butylscopolammonium is available in a 20-mg/mL solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

No dose is reported for small animals.

Large Animal Dosage

Horses

- 0.3 mg/kg, slowly IV as a single dose (1.5 mL per 100 kg).

Regulatory Information

Do not administer to animals intended for food.

Neomycin

nee-oh-mye'sin

Trade and other names: Biosol

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Aminoglycoside antibiotic. The action of neomycin is to inhibit bacteria protein synthesis via binding to 30S ribosome. It is bactericidal with a broad spectrum of activity except against streptococci and anaerobic bacteria. Neomycin differs from other aminoglycosides because it is only administered topically or orally. Systemic absorption is minimal from oral absorption.

Indications and Clinical Uses

Neomycin is only available in topical formulations. It is often combined with other antibiotics (triple antibiotics) in ointments for topical treatment of superficial infections. It is also used locally (oral local) for treatment of intestinal infections (colibacillosis). It is given orally and, because it is not absorbed systemically, it produces a local effect.

Precautionary Information

Adverse Reactions and Side Effects

Although oral absorption is so small that systemic adverse effects are unlikely, some oral absorption has been demonstrated in young animals (calves). Alterations in intestinal bacterial flora from therapy may cause diarrhea.

Contraindications and Precautions

Use cautiously in animals with renal disease. If oral absorption occurs because of compromised mucosal integrity, oral absorption may occur. Do not use longer than 14 days. Neomycin has been mixed with water and injected, but this practice is strongly discouraged.

Drug Interactions

Neomycin should not be mixed with other drugs before administration. Other drugs may bind and become inactivated.

Instructions for Use

Efficacy for treatment of diarrhea, especially for nonspecific diarrhea, is questionable.

Patient Monitoring and Laboratory Tests

Monitor for signs of diarrhea. If sufficiently absorbed systemically, it could cause renal injury; therefore monitor BUN and creatinine with chronic use.

Formulations

Neomycin is available in 500-mg bolus, 50-mg/mL (equivalent to 35 mg/mL neomycin base) and 200-mg/mL oral liquid (equivalent to 140 mg/mL of neomycin base), and 325-mg soluble powder (equivalent to 20.3 g per ounce of neomycin base).

Stability and Storage

It may be added to drinking water or milk. Do not add to other liquid supplements. Prepare a fresh solution daily. It is freely soluble in water and slightly soluble in ethanol. Aqueous solutions are stable over a wide pH range with optimum stability at pH 7. Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 10-20 mg/kg q6-12h PO.

Large Animal Dosage

Calves, Sheep, and Goats

- 22 mg/kg/day PO.

Regulatory Information

Slaughter withdrawal times: cattle 1 day; goats and sheep 2 days; swine and goats 3 days. Oral administration may cause residues in animals intended for food; therefore, do not administer to veal calves.

Neostigmine

nee-oh-stig'meen

Trade and other names: Prostigmin, Stiglyn, Neostigmine bromide, and Neostigmine methylsulfate

Functional classification: Anticholinesterase

Pharmacology and Mechanism of Action

Cholinesterase inhibitor. Anticholinesterase drug and antimuscarinic drug. This drug inhibits the enzyme that metabolizes acetylcholine into inactive products. Therefore it prolongs the action of acetylcholine at the synapse. The major difference between physostigmine and neostigmine or pyridostigmine is that physostigmine crosses the blood-brain barrier, and the others do not.

Indications and Clinical Uses

Neostigmine is used as an antidote for anticholinergic intoxication. It is also used as a treatment for myasthenia gravis, treatment (antidote) for neuromuscular blockade, and treatment for ileus. It also has been used as a treatment of urinary retention—such as the retention observed in postoperative patients—by increasing the tone of bladder smooth muscle. In ruminants, it has been used to stimulate rumen and intestinal motility.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are caused by the cholinergic action resulting from inhibition of cholinesterase. These effects can be seen in the GI tract as diarrhea and increased secretions. Other adverse effects can include miosis, bradycardia, muscle twitching or weakness, and constriction of bronchi and ureters. Adverse effects can be treated with anticholinergic drugs such as atropine. Pyridostigmine may be associated with fewer adverse effects than neostigmine.

Contraindications and Precautions

Do not use in urinary obstruction, intestinal obstruction, asthma or bronchoconstriction, pneumonia, and cardiac arrhythmias. Do not use in patients sensitive to bromide. Consider the amount of bromide in dose in any patient also receiving bromide (KBr) for treatment of seizures.

Drug Interactions

Do not use with other cholinergic drugs. Anticholinergic drugs (atropine and glycopyrrolate) will block the effects.

Instructions for Use

Neostigmine is indicated primarily only for treatment of intoxication. For routine systemic use of anticholinesterase drug, pyridostigmine may have fewer side effects. When used, frequency of dose may be increased based on observation of effects.

Patient Monitoring and Laboratory Tests

Monitor GI signs, heart rate, and rhythm.

Formulations

Neostigmine bromide is available in 15-mg tablets and neostigmine methylsulfate is available in 0.25-, 0.5-, and 1-mg/mL injections.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 2 mg/kg per day PO in divided doses.
- Antimyasthenic treatment: 10 mcg/kg IM or SQ, as needed.
- Antidote for neuromuscular blockade: 40 mcg/kg IM or SQ.
- Diagnostic aid for myasthenia: 40 mcg/kg IM or 20 mcg/kg IV.

Large Animal Dosage

When used as a treatment for neuromuscular blocking agents (cholinesterase inhibitor), the frequency of administration is determined by clinical response.

Cattle and Horses

- 22 mcg/kg (0.022 mg/kg) SQ.

Sheep

- 22-33 mcg/kg (0.022-0.033 mg/kg) SQ.

Swine

- 44-66 mcg/kg (0.044-0.066 mg/kg) IM.

Ruminants

- Stimulate rumen motility: 0.02 mg/kg IM or SQ.

Regulatory Information

Withdrawal times are not established for animals that produce food. When used to stimulate rumen motility, no withdrawal time has been used. For additional extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Niacinamide

nye'ah-sin'ah-mide

Trade and other names: Nicotinamide and Vitamin B₃

Functional classification: Anti-inflammatory

Pharmacology and Mechanism of Action

Immunosuppressant. Use primarily to treat skin diseases, such as discoid lupus erythematosus and pemphigus erythematosus in dogs. Mechanism of action is not

542 Niacinamide

entirely known. Niacinamide may have some anti-inflammatory action such as suppression of inflammatory cells. Niacin and niacinamide are used to treat vitamin B₃ deficiency. Do not confuse niacin with niacinamide. Niacin is converted to the active form niacinamide by intestinal bacteria.

Indications and Clinical Uses

Niacinamide has been used to treat immune-mediated skin disease in small animals. For skin disorders, it is usually administered with tetracycline. It also has been used to treat vitamin B₃ deficiency. Use in animals has been primarily derived from a few clinical reports and empirical use.

Precautionary Information

Adverse Reactions and Side Effects

Side effects are not common but have included vomiting, anorexia, lethargy, and diarrhea.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions are reported.

Instructions for Use

For treatment of pemphigus skin disease, it is usually administered with a tetracycline.

Patient Monitoring and Laboratory Tests

Monitor blood CBC periodically during treatment.

Formulations

Niacinamide is available in 50-, 100-, 125-, 250-, and 500-mg tablets (OTC) and 100-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 500 mg niacinamide q8h PO, plus 500 mg tetracycline. This dose is approximate based on a 10-kg dog. Eventually taper dose to q12h, then to q24h. For dogs <10 kg, start with 250 mg of each drug.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

No regulatory information is available. Because of the low risk of residues, no withdrawal times are suggested.

Nifedipine

nye-fed'ih-peen

Trade and other names: Adalat and Procardia

Functional classification: Calcium-channel blocker, vasodilator

Pharmacology and Mechanism of Action

Calcium-channel blocking drug of the dihydropyridine class. Vasodilator. The action of nifedipine is similar to other calcium-channel blocking drugs, such as amlodipine. They block voltage-dependent calcium entry into smooth muscle cells. Drugs of the dihydropyridine class are more specific for vascular smooth muscle than the cardiac tissue. Therefore, they have less effect on cardiac conduction than diltiazem.

Indications and Clinical Uses

Nifedipine is used for smooth muscle relaxation and to induce vasodilation. It is indicated for treatment of systemic hypertension. Use in animals is rare because there is more experience with amlodipine. The use of nifedipine in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in veterinary medicine. The most common side effect is hypotension.

Contraindications and Precautions

Do not administer to a patient with hypotension. Nifedipine may be teratogenic in pregnant laboratory animals and/or embryotoxic. Avoid use in pregnant animals.

Drug Interactions

Do not administer with drugs known to inhibit drug metabolizing enzymes (e.g., ketoconazole). Nifedipine may be subject to interactions from drugs that inhibit the membrane multidrug resistance (MDR1) pump (p-glycoprotein), which may lead to toxicity. See Appendix for drugs that may affect p-glycoprotein.

Instructions for Use

Use of nifedipine is limited in veterinary medicine. Other calcium-channel blockers, such as diltiazem, are used to control heart rhythm. Amlodipine is more commonly used for control of systemic hypertension.

Patient Monitoring and Laboratory Tests

Monitor blood pressure during therapy.

Formulations

Nifedipine is available in 10- and 20-mg capsules and 30-, 60-, and 90-mg extended-release capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is decomposed more rapidly if exposed to light. In extemporaneous solutions, nifedipine is unstable. If mixed with solutions, it should be used immediately.

Small Animal Dosage

Animal dose not established. In people, the dose is 10 mg/per person three times a day and increased in 10-mg increments to effect.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Nitazoxanide

nye-taz-oks'ah-nide

Trade and other names: Navigator (horse preparation) and Alinia (human preparation)

Functional classification: Antiprotozoal

Pharmacology and Mechanism of Action

Antiprotozoal drug. Nitazoxanide (NTZ) is a nitrothiazolyl-salicylamide derivative. Its action against protozoa is unknown, but it may be related to the inhibition of the pyruvate-ferredoxin oxidoreductase (PFOR) enzyme-dependent electron transfer reaction essential to anaerobic and protozoal energy metabolism. Activity has been demonstrated against a variety of protozoa, including *Cryptosporidium parvum*, *Giardia*, *Isoospora*, and *Entamoeba*. It also has activity against intestinal helminths, such as *Ascaris*, *Ancylostoma*, *Trichuris*, and *Taenia*. It also may be active against some anaerobic bacteria, including *Helicobacter*. One of the active metabolites is tizoxanide.

Indications and Clinical Uses

Nitazoxanide (NTZ) is used to treat equine protozoal myeloencephalitis (EPM). It has had only limited use in other veterinary species, but there is a form approved for use in people for treatment of protozoal infections, such as *C. parvum* and *Giardia*. There has been only limited use in dogs and cats for intestinal protozoal infections but no reports to document efficacy and safety.

Precautionary Information

Adverse Reactions and Side Effects

Because it may disrupt normal intestinal flora, administration to some animals has produced diarrhea.

Contraindications and Precautions

No known contraindications.

Drug Interactions

No known drug interactions.

Instructions for Use

NTZ is administered for horses to treat EPM. Use in small animals has been extrapolated from the use in humans.

Patient Monitoring and Laboratory Tests

When treating patients for diarrhea, monitor electrolytes and fecal samples.

Formulations

Nitazoxanide is available in a 0.32-mg/mL oral paste. Human formulation is a powder for oral dosing; 100 mg of powder is mixed with 48 mL of water.

Stability and Storage

Stable if stored in manufacturer's original formulation. The oral solution for people can be mixed and remain stable for 7 days.

Small Animal Dosage

There are no small animal dosing instructions available. However, one dose that has been used is 100 mg per animal q12h PO for 3 days.

Large Animal Dosage

Horses

- 25 mg/kg q24h PO on days 1 through 5, followed by 50 mg/kg q24h PO on days 6 through 28.

Regulatory Information

Do not use in animals intended for food.

Nitenpyram

nye-ten-pye'ram

Trade and other names: Capstar

Functional classification: Antiparasitic

N

Pharmacology and Mechanism of Action

Nitenpyram is an antiparasitic drug used for treatment of fleas. It will rapidly kill adult fleas. It is from the class of synthetic insecticides known as the neonicotinoids. It is related to imidacloprid and has the same mechanism of action, which is to inhibit postsynaptic nicotinic acetylcholine receptors, which produces influx of sodium ions. Nitenpyram is absorbed completely (100%) from oral administration and has a half-life in dogs and cats of 2.8 and 7.7 hours, respectively. After oral absorption it produces a rapid kill of adult fleas that has been observed as quickly as 30 minutes after drug administration, and is 98.6% effective in dogs, and 98.4% effective in cats.

Indications and Clinical Uses

Nitenpyram is used to kill fleas on dogs and cats. It produces a rapid kill with fleas killed within an hour of administration. It is often used with other drugs that act to prevent flea infestations as part of a comprehensive flea-control program.

Precautionary Information

Adverse Reactions and Side Effects

No adverse reactions are reported. It was safe in studies in dogs and cats in which up to 10 times the dose was administered. It was tolerated even in young

animals even at 8 weeks of age. Some transient pruritus may occur shortly after administration, which coincides with the initial killing of fleas.

Contraindications and Precautions

Do not use in dogs or cats <1 kg (2 pounds) in weight. Do not use in cats or dogs younger than 4 weeks of age.

Drug Interactions

No drug interactions have been reported. It is safe to use with lufenuron and milbemycin.

Instructions for Use

Nitenpyram is often used with lufenuron to kill adult fleas and prevent flea eggs from hatching. Administer with or without food.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Nitenpyram is available in 11.4- or 57-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- 1 mg/kg daily PO, as needed to kill fleas.

Large Animal Dosage

No large animal dose is reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Nitrofurantoin

nye-troe-fyoo'ran-toyn

Trade and other names: Macrochantin, Furalan, Furatoin, Furadantin, and generic brands

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Antibacterial drug. Urinary antiseptic. Therapeutic concentrations are reached only in the urine. In the urine it is reduced by bacterial flavoproteins, and the reactive metabolites inhibit bacterial macromolecules (DNA and RNA). Resistance among bacteria is unusual, although *Proteus* and *Pseudomonas aeruginosa* are inherently resistant. Macrocrystalline form is slowly absorbed and less likely to cause gastric upset. Microcrystalline form is rapidly absorbed in intestine.

Indications and Clinical Uses

Nitrofurantoin is administered orally for treatment or prevention of UTIs. It does not attain high enough concentrations for systemic infections or kidney infections. Although it is used in animals for UTI, the use in animals has been primarily derived from empirical use or from experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include nausea, vomiting, and diarrhea. It turns urine color rust-yellow brown. In people, respiratory problems (pneumonitis) and peripheral neuropathy have been reported. These effects have not been reported in animals.

Contraindications and Precautions

Do not administer during pregnancy, especially at term because it may cause hemolytic anemia of newborn. Do not administer to neonates.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Two dosing forms exist. Microcrystalline is rapidly and completely absorbed. Macrocrystalline (Macrochantin) is more slowly absorbed and causes less GI irritation. Urine should be at acidic pH for maximum effect. Administer with food to increase absorption.

Patient Monitoring and Laboratory Tests

Monitor urine cultures and/or urinalysis. A microbiologic susceptibility test may overestimate the true activity against some bacteria.

Formulations

Macrochantin and generic brands are available in 25-, 50-, and 100-mg capsules (macrocrystalline) and Furalan, Furatoin, and generic brands are available in 50- and 100-mg tablets (microcrystalline). Furadantin is available in 5-mg/mL oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is slightly soluble at a concentration less than 1 mg/mL in water and ethanol. It decomposes if exposed to metals other than stainless steel or aluminum.

Small Animal Dosage

Dogs and Cats

- 10 mg/kg/day divided into four daily treatments. Then 1 mg/kg at night PO.
- Macrocrystalline formulation: 2-3 mg/kg q8h PO, followed by 1-2 mg/kg once at nighttime.

Large Animal Dosage

Horses

- 2 mg/kg q8h PO.

Regulatory Information

It is prohibited from use in animals intended for food.

Nitroglycerin

nye-troe-glih'ser-in

Trade and other names: Nitrol, Nitro-bid, and Nitrostat

Functional classification: Vasodilator

Pharmacology and Mechanism of Action

Nitrate. Nitrovasodilator. Like other nitrovasodilators, it relaxes vascular smooth muscle (especially venous) via generation of nitric oxide. Nitric oxide stimulates guanylate cyclase to produce cyclic guanosine monophosphate (GMP) in vascular smooth muscle and relax smooth muscle. Nitric oxide-generating compounds may also help decrease gastric adverse effects associated with nonsteroidal anti-inflammatory drugs (NSAIDs).

Indications and Clinical Uses

Nitroglycerin, like other nitrovasodilators, is used primarily in heart failure or pulmonary edema to reduce preload or decrease pulmonary hypertension. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. In people, they are used to treat angina pectoris. In horses, nitroglycerin has been used to improve blood flow to the feet in the management of laminitis. However, in experiments, this treatment was not effective in horses and did not increase blood flow to the feet.

Precautionary Information

Adverse Reactions and Side Effects

The most significant adverse effect is hypotension. Methemoglobinemia can occur with accumulation of nitrites, but it is a rare problem. Tolerance can develop with repeated use. Because of tolerance it is advised to use the drug intermittently.

Contraindications and Precautions

Do not administer to patients with hypotension. Warn pet owners not to apply ointment without wearing gloves.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Tolerance can develop with repeated, chronic use. Use should be intermittent for optimum effect. Nitroglycerin has high presystemic metabolism, and oral availability is poor. When using ointment, 1 inch of ointment is approximately 15 mg.

Patient Monitoring and Laboratory Tests

Monitor patient's blood pressure during therapy.

Formulations

Nitroglycerin is available in 0.5-, 0.8-, 1-, 5-, and 10-mg/mL injection; 2% ointment; and transdermal systems (0.2 mg/hr patch).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 4-12 mg (up to 15 mg) topically q12h. Or apply one-half inch to 1.0 inch of 2% ointment on skin q8h.

Cats

- 2-4 mg topically q12h (or one-quarter inch of ointment per cat).

Large Animal Dosage

Horses

- Treatment of laminitis: Apply 2% ointment to skin above hoof (efficacy questionable).

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 3

Nitroprusside (Sodium Nitroprusside)

nye-troe-pruss'ide

Trade and other names: Nitropress

Functional classification: Vasodilator

Pharmacology and Mechanism of Action

Nitrate vasodilator. Like other nitrovasodilators, it relaxes vascular smooth muscle (especially venous) via generation of nitric oxide. Nitric oxide stimulates guanylate cyclase to produce cyclic guanosine monophosphate (GMP) in smooth muscle, with a predominant effect of relaxing vascular smooth muscle. Nitroprusside is used only as an intravenous infusion, and patients should be monitored carefully during administration. Nitroprusside has a rapid onset of effect (almost immediately) and a duration that lasts only minutes after discontinuation of intravenous administration.

Indications and Clinical Uses

Nitroprusside is used for acute management of pulmonary edema and other hypertensive conditions. It is administered only by intravenous infusion, and the dose is titrated carefully by monitoring systemic blood pressure. Titrate to maintain the arterial blood pressure to 70 mm Hg. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Severe hypotension is possible during therapy. Reflex tachycardia can occur during treatment. Cyanide is generated via metabolism during nitroprusside treatment, especially at high infusion rates (>5 mcg/kg/min). At high infusion rates (>10 mcg/kg/min) seizures may occur, which are signs of cyanide toxicity. Sodium thiosulfate has been used in people to prevent cyanide toxicity. Methemoglobinemia is possible and, if necessary, treated with methylene blue.

Contraindications and Precautions

Do not administer to patients with hypotension or who are dehydrated.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Nitroprusside is administered via intravenous infusion. Intravenous solution should be delivered in 5% dextrose solution. (For example, add 20-50 mg to 250 mL of 5% dextrose to a concentration of 50 to 200 mcg/mL.) Protect from light with opaque wrapping. Discard solutions if color change is observed. Titrate dose carefully in each patient.

Patient Monitoring and Laboratory Tests

Monitor blood pressure carefully during administration. Do not allow blood pressure to fall below 70 mm Hg during treatment. Monitor heart rate because reflex tachycardia is possible during infusion.

Formulations Available

Nitroprusside is available in a 50-mg vial for injection at 10 and 25 mg/mL.

Stability and Storage

Not compatible in some fluids. For IV use, dilute with 5% dextrose. Protect from light and cover infusion solution during administration. Nitroprusside decomposes quickly in alkaline solutions or with exposure to light.

Small Animal Dosage

Dogs and Cats

- 1-5 mcg/kg/min IV, up to a maximum of 10 mcg/kg/min. Generally, start with 2 mcg/kg/min and increase gradually by 1 mcg/kg/min until desired blood pressure is achieved.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Nizatidine

nih-zah'tih-deen

Trade and other names: Axid

Functional classification: Antiulcer agent

Pharmacology and Mechanism of Action

Histamine H₂-blocking drug. Nizatidine blocks histamine stimulation of gastric parietal cell to decrease gastric acid secretion. It is 4 to 10 times more potent than cimetidine. Nizatidine and ranitidine also have been shown to stimulate gastric

emptying and colonic motility via anticholinesterase activity. It is also used to treat gastric ulcers and gastritis.

Indications and Clinical Uses

Nizatidine, like other H₂-receptor blockers, is used to treat ulcers and gastritis. These drugs inhibit secretion of stomach acid and have also been used to prevent ulcers caused from nonsteroidal anti-inflammatory drugs (NSAIDs), but the efficacy for this use has not been demonstrated. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. In animals, famotidine or ranitidine is used more commonly as an H₂-receptor blocker, or omeprazole is used as a proton pump inhibitor (PPI).

Precautionary Information

Adverse Reactions and Side Effects

Side effects from nizatidine have not been reported for animals.

Contraindications and Precautions

No contraindications have been reported for animals.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Nizatidine use in animals has not been as common as the use of other related drugs such as ranitidine or famotidine.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Nizatidine is available in 150- and 300-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Nizatidine is slightly soluble in water. Nizatidine has been mixed with juices and syrups for oral administration and was stable for 48 hours. Avoid mixing with Maalox liquid.

Small Animal Dosage

Dogs

- 2.5-5 mg/kg q24h PO.

Large Animal Dosage

No large animal doses are reported.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 5

Norfloxacin

nor-floks'ah-sin

Trade and other names: Noroxin

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Fluoroquinolone antibacterial drug. Norfloxacin acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. It is a bactericidal with a broad spectrum of activity. Sensitive bacteria include *Staphylococcus*, *Escherichia coli*, *Proteus*, *Klebsiella*, and *Pasteurella*. *Pseudomonas aeruginosa* is moderately sensitive. However, norfloxacin is not as active as other drugs in the fluoroquinolone group.

Indications and Clinical Uses

Norfloxacin has been replaced by other veterinary fluoroquinolones because they have more favorable pharmacokinetics and improved spectrum of activity. However, it has been used to treat a variety of infections, including respiratory, urinary tract, skin, and soft tissue infections.

Precautionary Information

Adverse Reactions and Side Effects

High concentrations may cause CNS toxicity, especially in animals with renal failure. Norfloxacin may cause some nausea, vomiting, and diarrhea at high doses. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4 to 28 weeks of age. Large, rapidly growing dogs are the most susceptible.

Contraindications and Precautions

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures. Norfloxacin may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), may decrease absorption.

Drug Interactions

No drug interactions are reported for animals. However, like other quinolones, coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, and calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

Instructions for Use

Use in animals (and doses) is based on pharmacokinetic studies in experimental animals, experience in people, or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are less than or equal to 4 mcg/mL.

Formulations

Norfloxacin is available in 400-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage**Dogs and Cats**

- 22 mg/kg q12h PO.

Large Animal Dosage

No large animal doses have been reported.

Regulatory Information

It is prohibited from use in animals intended for food.

Olsalazine Sodium

ole-sal'ah-zeen soe'dee-um

Trade and other names: Dipentum

Functional classification: Antidiarrheal

Pharmacology and Mechanism of Action

Anti-inflammatory drug composed of two molecules of aminosalicic acid joined by an azo bond. Each component is released in the colon by bacterial enzymes. The released drug is also known as mesalamine (see separate entry for Mesalamine). Mesalamine is also the active component of sulfasalazine, which is commonly administered for treatment of colitis. The action of mesalamine is not precisely known, but it appears to suppress the metabolism of arachidonic acid in the intestine. It inhibits both cyclo-oxygenase- and lipoxygenase-mediated mucosal inflammation. Systemic absorption is small; most of the action is believed to be local. Olsalazine has a similar effect as sulfasalazine but without the sulfonamide component. Other formulations of mesalamine include Asacol, Mesasal, and Pentasa. The others are coated tablets designed to release the active component in the intestine.

Indications and Clinical Uses

Olsalazine, like other forms of mesalamine, is used for treatment of inflammatory bowel disease, including colitis in animals. In small animals, most often sulfasalazine is used; however, in some animals olsalazine may be indicated. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects reported in animals.

Contraindications and Precautions

Do not administer to patients sensitive to salicylate compounds.

Drug Interactions

No drug interactions have been reported for animals.

Instructions for Use

Olsalazine is used in patients that cannot tolerate sulfasalazine.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Olsalazine is available in 500-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dose not established, but 5-10 mg/kg q8h have been used. (The usual human dose is 500 mg twice daily.)

Large Animal Dosage

No doses are reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Omeprazole

oh-mep'rah-zole

Trade and other names: Prilosec (formerly Losec; human preparation), GastroGard, and UlcerGard (equine preparations)

Functional classification: Antiulcer agent

Pharmacology and Mechanism of Action

Proton pump inhibitor (PPI). Omeprazole inhibits gastric acid secretion by inhibiting the K^+/H^+ pump (potassium pump). Omeprazole is more potent and longer acting than most available antisecretory drugs. Other proton pump inhibitors include pantoprazole (Protonix), lansoprazole (Prevacid), and rabeprazole (Aciphex). They all act via similar mechanism and are equally effective. PPIs also have some effect for inhibiting *Helicobacter* organisms in the stomach when administered with antibiotics. Omeprazole is decomposed in the acid environment of the stomach. Oral absorption is decreased if administered with food. Formulations are designed to protect from acid to improve oral absorption (e.g., some capsules contain bicarbonate) and should not be modified (i.e., crushing of capsules) or the stability will be compromised.

Indications and Clinical Uses

Omeprazole, like other PPIs, is used for treatment and prevention of GI ulcers. It has been used in dogs, cats, and exotic species, but most efficacy data for animals have been produced in horses, in which it has been shown that omeprazole is effective for treating and preventing gastric ulcers. In foals, 4 mg/kg q24h suppressed acid secretion for 22 hours (by comparison, ranitidine suppressed acid up to 8 hours at a dose of 6.6 mg/kg). In dogs, 1 mg/kg q24h PO is as effective as pantoprazole (1 mg/kg) and famotidine (0.5 mg/kg q12h) for maintaining stomach pH >3-4. Repeated doses may be necessary (2-5 doses) for complete inhibition of acid secretion. Because of the long duration of effect, PPIs may be more effective than other drugs (e.g., histamine H_2 blockers). In studies performed in horses, omeprazole was more effective than ranitidine for treating gastric ulcers. Effects were observed within 14 days, but recurrence was observed after treatment was discontinued. Omeprazole, like other PPIs, may be effective for preventing nonsteroidal anti-inflammatory drug (NSAID)-induced ulcers. Omeprazole has been used in combination with other drugs (antibiotics) for treatment of *Helicobacter* infections in animals.

Precautionary Information

Adverse Reactions and Side Effects

The only reported adverse effect in dogs has been diarrhea in some cases. Otherwise, adverse effects have not been reported in animals. However, in people there is concern about hypergastrinemia with chronic use. Horses have tolerated 20 mg/kg q24h for 91 days and 40 mg/kg q24h PO for 21 days. Dogs and cats also have tolerated the regimens listed in the dosing section. Overgrowth of *Clostridium* bacteria has been a

concern from chronic use because of chronic gastric acid suppression, but the clinical importance of this concern in animals has not been established.

Contraindications and Precautions

One of the human formulations (Zegerid) is a packet to be mixed with water for oral administration. This formulation contains xylitol, which can be toxic to dogs if administered at high doses, or with other medications that contain xylitol. No contraindications have been reported for animals.

Drug Interactions

Although omeprazole has not been associated with drug interactions in animals, PPIs may inhibit some drug-metabolizing enzymes (CYP-450 enzymes). In people metabolism of clopidogrel to the active metabolite has been a concern. Omeprazole may also inhibit metabolism of other drugs. Because of stomach acid suppression, do not administer with drugs that depend on stomach acid for absorption (e.g., ketoconazole and itraconazole).

Instructions for Use

Omeprazole is the most common drug of this class used in animals. Other PPIs include pantoprazole (Protonix), lansoprazole (Prevacid), and abeprazole (Aciphex). No experience with these other products is reported for veterinary medicine. They are all considered equally efficacious. Pantoprazole and rabeprazole have the advantage in that they are available as tablets that can be crushed, and pantoprazole is less expensive than the other drugs in this class. Rectal administration has been studied in horses but has produced low and inconsistent response. Because there are no small animal formulations available, the human forms have been administered to dogs and cats and the equine formulation has been diluted in oil to 40 mg/mL for administration to small animals. Preliminary studies have shown that the equine formulation administered orally to dogs can be efficacious.

Patient Monitoring and Laboratory Tests

Omeprazole and PPIs are generally considered safe. No routine tests for monitoring adverse effects are recommended.

Formulations

Omeprazole is available in 20-mg capsules (human preparation) and in an equine paste, GastroGard. OTC equine paste is UlcerGard. Paste for horses is 370 mg/g of paste. A human oral formulation (Zegerid) is available either as 40 mg or 20 mg capsules with 1100 mg sodium bicarbonate. Zegerid is also available either as 40 mg or 20 mg single-dose packets of powder for oral suspension with 1680 mg sodium bicarbonate.

Stability and Storage

Omeprazole should be maintained in the manufacturer's original formulation (capsules or paste) for optimum stability and effectiveness. It is stable at pH 11 but rapidly decomposes at pH <7.8. There are no small animal formulations available and either the human formulation or equine formulation has been administered to small animals. The equine formulation should be diluted (e.g., in oil) for small animal use because it is very concentrated. It has been diluted to 40 mg/mL by suspending the approved equine oral paste formulation in sesame oil at a ratio of 1:9 and stored at controlled cold temperature (7°C) and protected from light. However, the stability of extemporaneously prepared mixtures has not been evaluated. Intravenous forms of omeprazole have been formulated in sterile water

and administered to experimental horses, but these formulations are not commercially available. Studies conducted on compounded oral equine formulations have shown that these formulations have low potency.

Small Animal Dosage

Dogs

- 20 mg/dog q24h PO or 1-2 mg/kg q24h PO.

Cats

- 1 mg/kg q24h PO.

Large Animal Dosage

Horses

- Gastrogard to treat ulcers: 4 mg/kg once daily for 4 weeks PO.
- Gastrogard to prevent ulcers: 1-2 mg/kg q24h PO. (1 mg/kg was effective for prevention in studies performed in horses.)
- Intravenous use (if a formulation is available): Loading dose of 1 mg/kg, followed by 0.5 mg/kg per day for 14-28 days.

Ruminants

Oral absorption may not be high enough for effective therapy.

Regulatory Information

Not intended for administration to animals that produce food. Oral absorption in ruminants is not established. Withdrawal times are not established for animals that produce food. For extralabel use with withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 5

Ondansetron Hydrochloride

on-dan'sih-tron hye-droe-klor'ide

Trade and other names: Zofran

Functional classification: Antiemetic

Pharmacology and Mechanism of Action

Antiemetic drug from the class of drugs called serotonin antagonists. Like other drugs of this class, ondansetron acts by inhibiting serotonin type 3 (5-HT₃) receptors. It is used primarily as an antiemetic during chemotherapy, for which it has been effective by blocking emetic stimuli that release serotonin. During chemotherapy, or following GI injury, there may be 5-HT released from the GI tract that stimulates vomiting centrally. This stimulus is blocked by this class of drugs. These drugs also have been used to treat vomiting from other forms of gastroenteritis, pancreatitis, and inflammatory bowel disease. Serotonin antagonists used for antiemetic therapy include granisetron, ondansetron, dolasetron, azasetron, and tropisetron.

Indications and Clinical Uses

Ondansetron, like other serotonin antagonists, is used to prevent vomiting. Although it may be effective for treating nausea and vomiting from other sources, the most common use is for preventing vomiting from chemotherapy. There is only limited efficacy information available for ondansetron effectiveness in animals. Oncologists have found it to be effective for managing vomiting from chemotherapy in animals.

Precautionary Information**Adverse Reactions and Side Effects**

Ondansetron adverse effects have not been reported in animals. These drugs have little affinity for other 5-HT receptors. Because some severe adverse effects can occur from concurrent cancer drugs, it may be difficult to distinguish these from ondansetron effects.

Contraindications and Precautions

There are no important contraindications identified in animals.

Drug Interactions

If infused through an IV catheter, it may precipitate if mixed with other drugs (e.g., metoclopramide). Other drug interactions have not been reported for animals.

Instructions for Use

Ondansetron has been used in dogs and cats. Granisetron is a similar drug that has been substituted for a similar purpose.

Patient Monitoring and Laboratory Tests

Monitor GI signs in a vomiting patient.

Formulations

Ondansetron is available in 4- and 8-mg tablets, 4-mg/5-mL flavored syrup, and 2-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Ondansetron is soluble in water. Solutions are stable, but pH should be <6 to prevent precipitation. Oral preparations have been mixed with syrups, juices, and other oral vehicles (e.g., Ora Sweet). It was stable for 42 days as long as pH remained low.

Small Animal Dosage**Dogs and Cats**

- 0.5 to 1 mg/kg 30 min prior to administration of cancer drugs IV or PO.
Vomiting from other causes: 0.1-0.2 mg/kg slow IV injection and repeated q6-12h. If this dose is initially ineffective, it may be increased to 0.5 mg/kg. These doses can also be administered PO.

Large Animal Dosage

No dosing information is available.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Orbifloxacin

or-bih-floks'ah sin

Trade and other names: Orbox

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Fluoroquinolone antimicrobial. Orbifloxacin acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. It is a bactericidal with a broad

spectrum of activity. Spectrum includes staphylococci, gram-negative bacilli, and some *Pseudomonas* species. In dogs the half-life is 5.6 hours; in cats the half-life is 5.5 hours. In both species the oral absorption is nearly 100%. However, oral suspension absorption is not as high as tablets (see Instructions for Use section below). In horses, it has a half-life of 5 hours and oral absorption of 68%.

Indications and Clinical Uses

Orbifloxacin is registered for use in dogs and cats. Like other fluoroquinolones, it is used to treat susceptible bacteria in a variety of species. Treatment of infections has included skin, soft tissue, and UTIs in dogs and cats and soft tissue infections in horses.

Precautionary Information

Adverse Reactions and Side Effects

High concentrations may cause CNS toxicity, especially in animals with renal failure. It may cause some nausea, vomiting, and diarrhea at high doses. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4 to 28 weeks of age. Large, rapidly growing dogs are the most susceptible. Blindness in cats has been reported from administration of some quinolones (nalidixic acid and enrofloxacin), but at doses up to 15 mg/kg (higher than approved label dose) orbifloxacin has not produced this effect.

Contraindications and Precautions

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures.

Drug Interactions

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, and calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

Instructions for Use

At the registered label dose, orbifloxacin is active against most susceptible bacteria. Within the approved dose range, higher doses are needed for organisms with higher minimum inhibitory concentration (MIC) values. In the cat, orbifloxacin oral suspension and orbifloxacin tablets are not bioequivalent. On a mg/kg basis, orbifloxacin oral suspension provides lower and more variable plasma levels of orbifloxacin than the tablets. The dose of orbifloxacin oral suspension in the cat is 7.5 mg/kg of body weight administered once daily, but tablet dose can be lower.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is ≤ 1 mcg/mL. Other fluoroquinolones may be used in some cases to estimate susceptibility to this fluoroquinolone. However, other drugs may have lower MIC values for *Pseudomonas aeruginosa*. Against *P. aeruginosa*, ciprofloxacin has greater in vitro activity.

Formulations

Orbifloxacin is available in 5.7-, 22.7-, and 68-mg tablets. Oral suspension is 30 mg/mL.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Orbifloxacin is slightly water soluble. It has been mixed with various syrups, flavorings, and vehicles and was stable at room temperature for 7 days. Do not mix

560 Ormetoprim + Sulfadimethoxine

with vehicles that contain aluminum, calcium, or iron because this may decrease oral absorption via chelation.

Small Animal Dosage

Dogs and Cats

- Tablets: 2.5-7.5 mg/kg q24h PO.
- Suspension: 7.5 mg/kg (1 mL per kg), q24h, PO.

Large Animal Dosage

Horses

- 5 mg/kg q24h PO.

Regulatory Information

Do not use fluoroquinolones off-label to animals that produce food. Orbifloxacin is prohibited from use in animals intended for food.

Ormetoprim + Sulfadimethoxine

or-met'oe-prim + sul-fa-dye-meth-oks'een

Trade and other names: Primor

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Antibacterial drug. Ormetoprim sulfadimethoxine is a synergistic combination similar to trimethoprim sulfonamide combinations. Ormetoprim inhibits bacterial dihydrofolate reductase, and sulfonamide competes with para-aminobenzoic acid (PABA) for synthesis of nucleic acids. Bactericidal/bacteriostatic. It has a broad antibacterial spectrum that includes common gram-positive and gram-negative bacteria. It also is active against some coccidia.

Indications and Clinical Uses

Ormetoprim + sulfadimethoxine is used in small animals to treat a variety of bacterial infections caused by susceptible organisms, including pneumonia, skin, soft tissue, and UTIs in dogs and cats. In horses, it may be administered orally for infections caused by susceptible gram-positive bacteria (*Actinomyces*, *Streptococcus* spp., and *Staphylococcus* spp.), but higher doses may be needed for gram-negative infections.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides include allergic reactions, Type II and III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other, more toxic metabolites may persist. Ormetoprim has been associated with some CNS effects in dogs, which include behavioral changes, anxiety, muscle tremors, and seizures. In horses when IV doses were administered to experimental horses (IV formulation not commercially available), nervous system reactions such as tremors and muscle fasciculations were observed.

Contraindications and Precautions

Do not administer to animals sensitive to sulfonamides.

Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine.

Instructions for Use

Doses listed are based on manufacturer's recommendations. Controlled trials have demonstrated efficacy for treatment of pyoderma on a once-daily schedule.

Patient Monitoring and Laboratory Tests

Monitor tear production with long-term use. For susceptibility testing, break point ranges have not been determined for ormetoprim + sulfadimethoxine. Use a test for trimethoprim-sulfonamide as a guide for susceptibility to ormetoprim + sulfadimethoxine. CLSI break point for susceptible organisms is $\leq 2/38$ mcg/mL (trimethoprim/sulfonamide).

Formulations

Ormetoprim + sulfadimethoxine is available in 120-, 240-, 600-, and 1200-mg tablets in 5:1 ratio of sulfadimethoxine:ormetoprim.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage**Dogs**

- 55 mg/kg on first day, followed by 27.5 mg/kg q24h PO. Doses can be divided into twice-daily treatments. (All doses are based on the combined milligram amount of both ormetoprim and sulfadimethoxine.)

Cats

Although doses are not reported by the manufacturer, doses similar to those for dogs have been administered.

Large Animal Dosage**Horses**

- Loading dose of 55 mg/kg (of the combined drugs) followed by 27.5 mg/kg (of the combined drugs) q24h PO.

Regulatory Information

Withdrawal times are not established for animals that produce food. Oral absorption has not been established for ruminants. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Oxacillin Sodium

oks-ah-sill'in soe'dee-um

Trade and other names: Pro-staphlin and generic brands

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Oxacillin, like other beta-lactam antibiotics, binds penicillin-binding proteins (PBP) that weaken or interfere with cell wall formation. After binding to PBP, the cell wall weakens or undergoes lysis. Like other beta-lactams, this drug acts in a time-dependent manner (i.e., it is more effective when drug concentrations are maintained above the minimum inhibitory concentrations [MIC] during the dose interval). Oxacillin has a limited spectrum of activity that includes primarily gram-positive bacteria. Resistance is common, especially among enteric gram-negative bacilli. Staphylococci are susceptible because oxacillin is resistant to the bacterial beta-lactamase produced by *Staphylococcus* spp. Limited pharmacokinetic data are available for animals. Because of a short half-life and low oral absorption, there are limitations to its use in animals.

Oxacillin is not valuable therapeutically but is used as a marker to test for *mec-A*-mediated resistance of PBP2a in *Staphylococcus*. Methicillin-resistant *Staphylococcus* (e.g., MRSA or MRSP) are usually identified by using oxacillin break points (see Patient Monitoring and Laboratory Tests section).

Indications and Clinical Uses

Oxacillin has been used in small animals for treating soft tissue infections caused by gram-positive bacteria. The most common use has been for pyoderma in dogs. Use has diminished because of limited pharmacokinetic information to guide oral dosing and the increased availability of other drugs, such as oral cephalosporins and amoxicillin–clavulanate.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects of penicillin-like drugs are most commonly caused by drug allergy. This can range from acute anaphylaxis when administered or other signs of allergic reaction when other routes are used. When administered orally, diarrhea is possible, especially with high doses.

Contraindications and Precautions

Use cautiously in animals allergic to penicillin-like drugs.

Drug Interactions

No drug interactions are reported. Food may inhibit oral absorption.

Instructions for Use

Doses are based on empiricism or extrapolation from human studies. No clinical efficacy studies are available for dogs or cats. Administer, if possible, on empty stomach.

Patient Monitoring and Laboratory Tests

Culture and sensitivity testing: CLSI break points to define *mec-A*-mediated resistance in *Staphylococcus aureus* is a MIC ≥ 4 mcg/mL, and the zone size is ≤ 10 mm. All other *Staphylococcus* spp. with *mec-A*-mediated resistance, including *S. pseudintermedius* (e.g., MRSP), are disk diffusion ≤ 17 mm and MIC ≥ 0.5 mcg/mL. If staphylococci are resistant to oxacillin, they should be interpreted as being resistant to all cephalosporins and penicillins regardless of sensitivity result. Oxacillin resistance is usually interpreted as equivalent to methicillin resistance; therefore oxacillin-resistant staphylococci are also referred to as methicillin-resistant *Staphylococcus aureus* (MRSA) or *Staphylococcus pseudintermedius* (MRSP).

Formulations

Oxacillin is available in 250- and 500-mg capsules and 50-mg/mL oral solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Oxacillin is soluble in water and alcohol. The reconstituted oral solution is stable for 3 days at room temperature and 14 days in the refrigerator.

Small Animal Dosage

Dogs and Cats

- 22-40 mg/kg q8h PO.

Large Animal Dosage

No doses are reported. Oral absorption has not been established for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. Oral absorption has not been established for ruminants. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Oxazepam

oks-ay'zeh-pam

Trade and other names: Serax

Functional classification: Anticonvulsant

Pharmacology and Mechanism of Action

Benzodiazepine. Oxazepam is a central-acting CNS depressant with action similar to diazepam. Its mechanism of action appears to be via potentiation of GABA-receptor-mediated effects in the CNS. Oxazepam is one of the active products of metabolism from diazepam. In contrast to diazepam, oxazepam does not undergo extensive hepatic metabolism in animals, but it is glucuronidated before excretion. In dogs, oxazepam has a half-life of 5-6 hours, but these values were derived from administration of the parent drug diazepam. Oxazepam is eliminated by direct conjugation with glucuronide, without other intermediate metabolites produced, whereas diazepam and other benzodiazepines may produce other intermediate active metabolites.

Indications and Clinical Uses

Oxazepam is used for sedation and to stimulate appetite. The appetite-stimulating effects have been used, particularly in cats that may have diminished appetites caused by other primary diseases. As a benzodiazepine it also may be considered for behavior problems and anxiety disorders in animals, but it has not been used as commonly as other drugs.

Precautionary Information

Adverse Reactions and Side Effects

Sedation is the most common side effect. It may also produce polyphagia. Some animals may experience paradoxical excitement. Chronic administration may lead to dependence and a withdrawal syndrome if discontinued.

Contraindications and Precautions

Oral administration of another benzodiazepine—diazepam—has caused severe idiosyncratic liver injury in cats. It is not known if the same concern applies to oxazepam, which is a metabolite of diazepam, although no cases of liver injury from oxazepam have been reported.

Drug Interactions

Use cautiously with other drugs that may cause sedation.

Instructions for Use

Doses based on empiricism. There have been no clinical trials in veterinary medicine, although it is widely believed to increase the appetite in cats.

Patient Monitoring and Laboratory Tests

Samples of plasma or serum may be analyzed for concentrations of benzodiazepines. Plasma concentrations in the range of 100-250 ng/mL have been cited as the therapeutic range for people. Other references have cited this range as 150-300 ng/mL. However, there are no readily available tests for monitoring in many veterinary laboratories. Laboratories that analyze human samples may have nonspecific tests for benzodiazepines. With these assays, there may be cross-reactivity among benzodiazepine metabolites.

Formulations

Oxazepam is available in 10-, 15-, and 30-mg capsules and 15- and 30-mg tablets.

Stability and Storage

Stable if stored in manufacturer's original formulation. Although oxazepam has been compounded for veterinary use, the potency and stability have not been evaluated for compounded products.

Small Animal Dosage

Cats

- Behavior disorders: 0.2-0.5 mg/kg q12-24h PO or 1-2 mg/cat q12h PO.
- Appetite stimulant: 2.5 mg/cat PO.

Dogs

- Behavior disorders or sedation: 0.2-1 mg/kg q12-24h PO. For some indications it has been administered q6h.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Schedule IV controlled drug

RCI Classification: 2

Oxfendazole

oks-fen'dah-zole

Trade and other names: Benzelmin and Synanthic

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic drug. Oxfendazole belongs to the benzimidazole class of antiparasitic drugs. Like other benzimidazole drugs it produces a degeneration of the parasite microtubule and irreversibly blocks glucose uptake in parasites. Inhibition of glucose uptake causes depletion of energy stores in parasites, eventually resulting in death. However, there is no effect on glucose metabolism in mammals. It is used to treat intestinal parasites in animals.

Indications and Clinical Uses

Oxfendazole is used in horses for treatment of large roundworms (*Parascaris equorum*), mature and immature pinworms (*Oxyuris equi*), large strongyles (*Strongylus edentatus*, *Strongylus vulgaris*, and *Strongylus equinus*), and small strongyles. In cattle, fendazole is used for treatment of lungworms (*Dictyocaulus viviparus*), stomach worms (barberpole worms [*Haemonchus contortus* and *H. placei*, adult]), small stomach worms (*Trichostrongylus axei*, adult), brown stomach worms (*Ostertagia ostertagi*), intestinal worms, nodular worms (*Oesophagostomum radiatum*, adult), hookworms (*Bunostomum phlebotomum*, adult), small intestinal worms (*Cooperia punctata*, *C. oncophora*, and *C. momasteri*), and tapeworms (*Moniezia benedeni*, adult).

Precautionary Information

Adverse Reactions and Side Effects

Adverse reactions are rare.

Contraindications and Precautions

Do not administer to sick or debilitated horses. Do not administer to female dairy cattle of breeding age.

Drug Interactions

No drug interactions are reported.

Instructions for Use

Administer to horses by mixing in a suspension and administering orally (e.g., via stomach tube) or mixing pellets with food. Administer to cattle orally with a dose syringe or intraruminally with a rumen injector. Treatment may be repeated in 6-8 weeks in horses or in 4-6 weeks in cattle.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Oxfendazole is available in a 90.6- or 225-mg/mL suspension (cattle), 185-mg/gram paste (cattle), 0.375 g per gram of paste (equine), 90.6-mg/mL suspension (equine), and 6.49% pellets (equine).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. After mixing for oral administration, discard unused portion after 24 hours. Mix well before using, do not freeze suspension, and avoid excessive heat.

Small Animal Dosage

Dogs and Cats

Dose has not been established.

Large Animal Dosage

Horses

- 10 mg/kg PO.

Cattle

- 4.5 mg/kg PO.

Regulatory Information

Do not use in dairy cattle.

Cattle slaughter withdrawal time: 7 days for suspension; 11 days for paste.

Oxibendazole

oks-ih-ben'dah-zole

Trade and other names: Anthelcide EQ

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic drug. Oxibendazole belongs to the benzimidazole class of antiparasitic drugs. Like other benzimidazole drugs, it produces a degeneration of the parasite microtubule and irreversibly blocks glucose uptake in parasites. Inhibition of glucose uptake causes depletion of energy stores in parasites, eventually resulting in death. However, there is no effect on glucose metabolism in mammals. It is used to treat intestinal parasites in animals.

Indications and Clinical Uses

Oxibendazole is used in horses for treatment of large strongyles (*Strongylus edentatus*, *S. equinus*, and *S. vulgaris*), small strongyles (species of the genera *Cylicostephanus*, *Cylicocyclus*, *Cyathostomum*, *Triodontophorus*, *Cylicodontophorus*, and *Gyalocephalus*), large roundworms (*Parascaris equorum*), pinworms (*Oxyuris equi*) including various larval stages, and threadworms (*Strongyloides westeri*).

Formulations for dogs may contain both diethylcarbamazine citrate and oxibendazole for prevention of *Dirofilaria immitis* (heartworm disease) and *Ancylostoma caninum* (hookworm infection) and for treatment of *Trichuris vulpis* (whipworm infection) and intestinal *Toxocara canis* (ascarid infection).

Precautionary Information

Adverse Reactions and Side Effects

Adverse reactions are rare. Occasional vomiting and nausea may occur in dogs.

Contraindications and Precautions

Do not administer to dogs that may have heartworms.

Drug Interactions

No drug interactions are reported.

Instructions for Use

Administer suspension to horses by mixing with 1-2 L of water (3-4 pints) and administering orally (e.g., via stomach tube). Alternatively mix powder with grain ration or use the paste. Horses should be re-treated in 6-8 weeks if they are re-exposed. For dogs, medication may be mixed with food daily.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Oxibendazole is available in 10% suspension; 22.7% paste; and 60-, 120-, and 180-mg diethylcarbamazine citrate + 45-, 91-, and 136-mg oxibendazole tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Mix well before using, do not freeze suspension, and avoid excessive heat.

Small Animal Dosage**Dogs**

- 5 mg/kg oxibendazole (combined with 6.6 mg/kg diethylcarbamazine) q24h PO.

Cats

No dose established.

Large Animal Dosage**Horses**

- 10 mg/kg PO.
- Threadworms: 15 mg/kg PO once. Re-treat in 6-8 weeks if necessary.

Regulatory Information

No withdrawal times are established.

Withdrawal times are not established for animals that produce animals. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Oxtriphylline

oks-trih'fih-lin

Trade and other names: Choledyl-SA

Functional classification: Bronchodilator

Pharmacology and Mechanism of Action

Choline theophyllinate. Methylxanthine bronchodilator. Free theophylline is released after absorption. Mechanism of action is unknown but may be related to increased

568 Oxtriphylline

cyclic adenosine monophosphate (AMP) levels or antagonism of adenosine. There appears to be anti-inflammatory and bronchodilating action.

Indications and Clinical Uses

Oxtriphylline is used for similar respiratory conditions as is theophylline. It is indicated in patients with reversible bronchoconstriction, such as dogs with airway disease. The use of oxtriphylline has diminished considerably, and it is more convenient and preferable to administer theophylline in most cases. Large animal uses have not been reported.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include nausea, vomiting, and diarrhea. With high doses, tachycardia, excitement, tremors, and seizures are possible. Cardiovascular and CNS adverse effects appear to be less frequent in dogs than people.

Contraindications and Precautions

Some patients may be at a higher risk for adverse effects. Such patients may include animals with cardiac disease, animals prone to arrhythmias, and animals at risk for seizures.

Drug Interactions

Drugs that inhibit cytochrome P450 enzymes may increase drug concentrations and cause toxicity. See Appendix for list of drugs that may be P450 inhibitors.

Instructions for Use

Some formulations (Theocon) contain oxtriphylline and guaifenesin. When administering a slow-release tablet, do not crush it. Theophylline, which may be more readily available, may be substituted for oxtriphylline.

Patient Monitoring and Laboratory Tests

Therapeutic drug monitoring is recommended for chronic therapy. Interpretation of theophylline concentrations should be used to guide therapy. Generally, 10-20 mcg/mL is considered therapeutic.

Formulations

Oxtriphylline is available in 400- and 600-mg tablets. (Oral solutions and syrup are available in Canada but not in the US.)

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 47 mg/kg (equivalent to 30 mg/kg theophylline) q12h PO.

Large Animal Dosage

No doses have been reported for large animals. Oral absorption has not been established for ruminants.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Oxybutynin Chloride

oks-ih-byoo'tih-nin klor'ide

Trade and other names: Ditropan

Functional classification: Anticholinergic

Pharmacology and Mechanism of Action

Anticholinergic agent. Oxybutynin produces an anticholinergic effect via blockade of muscarinic receptors. It will produce a general anticholinergic effect, but the predominant effect is on the urinary bladder. It inhibits smooth muscle spasms via blocking action of acetylcholine. It does not block skeletal muscle, autonomic ganglia, or receptors on blood vessels. A related drug used in people is tolterodine (Detrol).

Indications and Clinical Uses

Oxybutynin chloride has been used primarily to increase bladder capacity and to decrease spasms of the urinary tract. In people it is used to treat urinary incontinence, but the use in animals is not common.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are related to anticholinergic effects (atropine-like effects), but they are less frequent compared to other anticholinergic drugs. Constipation, dry mouth, and dry mucous membranes are possible from routine use. If an overdose occurs, administer physostigmine for treatment.

Contraindications and Precautions

Use cautiously in animals with heart disease or decreased intestinal motility. Use cautiously in animals with glaucoma.

Drug Interactions

Oxybutynin will potentiate other antimuscarinic drugs.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Although it increases urine retention, it may not be effective to treat incontinence in animals with decreased sphincter tone.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Oxybutynin is available in 5-mg tablets and 1-mg/mL oral syrup.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Oxybutynin is soluble in water and ethanol.

Small Animal Dosage

Dogs

- 0.2 mg/kg q12h, PO; for larger dogs use 5 mg/dog q6-8h PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. Oral absorption has not been established for ruminants. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Oxymetholone

oks-ih-meth'oh-lone

Trade and other names: Anadrol

Functional classification: Hormone, anabolic agent

Pharmacology and Mechanism of Action

Anabolic steroid. Oxymetholone is a derivative of testosterone. Anabolic agents are designed to maximize anabolic effects while minimizing androgenic action. Anabolic agents have been used for reversing catabolic conditions, increasing weight gain, increasing muscling in animals, and stimulating erythropoiesis. Other anabolic agents include boldenone, nandrolone, stanozolol, and methyltestosterone.

Indications and Clinical Uses

Anabolic agents have been used for reversing catabolic conditions, increasing weight gain, increasing muscling in animals, and stimulating erythropoiesis. Although other anabolic agents have been used in animals (methyltestosterone and stanozolol), there are no differences in efficacy among the anabolic steroids demonstrated in animals.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects from anabolic steroids can be attributed to the pharmacologic action of these steroids. Increased masculine effects are common. Increased incidence of some tumors have been reported in people. The 17 α -methylated oral anabolic steroids (oxymetholone, stanozolol, and oxandrolone) have been associated with hepatic toxicity.

Contraindications and Precautions

Do not use in pregnant animals.

Drug Interactions

No drug interactions are reported.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

Monitor hepatic enzymes for evidence of cholestasis and hepatotoxicity.

Formulations

Oxymetholone is available in 50-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 1-5 mg/kg/day PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Oxymetholone is a Schedule III controlled drug.

Do not administer to animals intended for food.

RCI Classification: 4

Oxymorphone Hydrochloride

oks-ih-mor'fone hye-droe-klor'ide

Trade and other names: Numorphan

Functional classification: Analgesic, opioid

Pharmacology and Mechanism of Action

Opioid agonist and analgesic. Action is similar to morphine, except that oxymorphone is more lipophilic than morphine and 10 to 15 times more potent than morphine. Action is to bind to mu-opiate and kappa-opiate receptors on nerves and inhibit release of neurotransmitters involved with transmission of pain stimuli (such as Substance P). Central sedative and euphoric effects related to mu-receptor effects in brain. Other opiates used in animals include hydromorphone, codeine, morphine, meperidine, and fentanyl. In dogs the half-life is 0.8 hours (IV) and 1 hour (SQ), with high clearance rates (>50 mL/kg/min). Effective concentrations are not established for animals, but in people they range from 2.5 to 4.5 ng/mL.

Indications and Clinical Uses

Oxymorphone is indicated for short-term analgesia, for sedation, and as an adjunct to anesthesia. It is compatible with most anesthetics and can be used as part of a multimodal approach to analgesia/anesthesia. Although oxymorphone is registered for dogs, other opiates are used more commonly such as hydromorphone and morphine. Administration of oxymorphone may lower dose requirements for other anesthetics and analgesics used. Duration of action in dogs is short (2-4 hours). The oral dose formulations are only 10% absorbed in people but should not be relied on for treating severe pain in dogs.

Precautionary Information

Adverse Reactions and Side Effects

Like all opiates, side effects from oxymorphone are predictable and unavoidable. Side effects from opiate administration include sedation, vomiting, constipation, urinary retention, and bradycardia. Panting may occur in dogs as a result of changes in thermoregulation. Histamine release, known to occur from administration of morphine, may be less likely with oxymorphone. Excitement

can occur in some animals, but it is more common in cats and horses. Respiratory depression occurs with high doses. As with other opiates, a slight decrease in heart rate is expected. In most cases this decrease does not have to be treated with anticholinergic drugs (e.g., atropine), but it should be monitored. Tolerance and dependence occurs with chronic administration. In horses, undesirable and even dangerous behavior actions can follow rapid intravenous opioid administration. Horses should receive a preanesthetic of acepromazine or an α_2 -agonist.

Contraindications and Precautions

Oxymorphone is a Schedule II controlled substance. Cats and horses may be more sensitive to opiates.

Drug Interactions

Like other opiates, it will potentiate other drugs that cause CNS depression.

Instructions for Use

There is some evidence that oxymorphone may have fewer cardiovascular effects compared to morphine. Because oxymorphone is more lipophilic than morphine, it is readily absorbed from epidural injection. Oxymorphone may be used with acepromazine and other sedatives; together they have synergistic effects.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

Formulations

Oxymorphone is available in 1.5- and 1-mg/mL injection. Five- and 10-mg tablets are available but have not been shown to be absorbed in animals.

Stability and Storage

The pH of solution is 2.7-4.5. Oxymorphone is compatible with most fluid solutions. Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- Analgesia: 0.1-0.2 mg/kg IV SQ or IM (as needed); redose with 0.05-0.1 mg/kg q1-2h.
- Preanesthetic: 0.025-0.05 mg/kg IM or SQ.
- Sedation: 0.05-0.2 mg/kg (with or without acepromazine) IM or SQ.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Schedule II controlled drug.

RCI Classification: 1

Oxytetracycline

oks'ih-tet-rah-sye'kleen

Trade and other names: Terramycin, Terramycin Soluble Powder, Terramycin Scours Tablets, Biomycin, Oxy-Tet, and Oxybiotic Oxy 500 and Oxy 1000. Long-acting formulations include Liqumycin-LA 200 and Biomycin 200.

Functional classification: Antibacterial

Pharmacology and Mechanism of Action

Tetracycline antibiotic. Mechanism of action of tetracyclines is to bind to 30S ribosomal subunit and inhibit protein synthesis. Oxytetracycline is usually bacteriostatic. It has a broad spectrum of activity including gram-positive and gram-negative bacteria, some protozoa, *Rickettsiae*, and *Ehrlichiae*. The spectrum also includes *Chlamydia*, spirochetes, *Mycoplasma*, L-form bacteria, and some protozoa (*Plasmodium* and *Entameba*). Resistance is common among gram-negative bacteria of the *Enterobacteriaceae* (e.g., *Escherichia coli*). Oxytetracycline has been available in a variety of formulations to control the release rate from an injection. Vehicles include polyethylene glycol, propylene glycol, povidone, or pyrrolidine. Although oral preparations are available, oral absorption is poor. For example, oral absorption of 44 mg/kg in dogs was variable and too low to produce therapeutic effects. In pigs oral absorption was only 4% (compared to chlortetracycline, which is 13%). Most pharmacokinetic studies have been performed with injectable oxytetracycline. After IM injection in cattle the half-life is approximately 21 hours, with a maximum concentration (C_{MAX}) of 5.6 mcg/mL. In horses, the half-life (IV) was approximately 10-13 hours. In pigs the half-life (IV) was approximately 4-6 hours.

Indications and Clinical Uses

Oxytetracycline is used to treat infections of the respiratory tract (pneumonia), urinary tract, soft tissues, and dermis. It is used for infections caused by a wide spectrum of bacteria, except that resistance is common among gram-negative bacilli of enteric origin and staphylococci. One of the most common uses is in cattle for treatment of bovine respiratory disease (BRD) caused by *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni* (formerly *Haemophilus somnus*). In pigs, tetracyclines have been used to treat atrophic rhinitis, pneumonic pasteurellosis, and *Mycoplasma* infections. In small animals, doxycycline, rather than oxytetracycline, is used as a treatment for *Rickettsiae* and *Ehrlichiae*. In newborn horses, oxytetracycline has been administered at high doses for the purpose of correcting angular limb deformities. The doses have been as high as 50-70 mg/kg IV q48h. There is no known explanation for the effect of oxytetracycline on tendon or ligament laxity in horses.

Precautionary Information

Adverse Reactions and Side Effects

Tetracyclines may cause renal tubular necrosis at high doses, but this is rare with recommended doses. Tetracyclines can affect bone and teeth formation in young animals. Tetracyclines have been implicated in drug fever in cats. Hepatotoxicity may occur at high doses in susceptible individuals. Oxytetracycline administration to horses has been associated with colic and diarrhea.

Contraindications and Precautions

Use cautiously in young animals because teeth discoloration is possible. Avoid injection volumes for IM greater than 10 mL per site in cattle and greater than 5 mL in pigs.

Drug Interactions

Tetracyclines bind to compounds containing calcium, which decreases oral absorption. Do not mix with solutions that contain iron, calcium, aluminum, or magnesium.

Instructions for Use

Oral dose forms are for large animal use. Use of injectable long-acting forms have not been studied in small animals. Use of tetracyclines in small animals has primarily relied on doxycycline. For large animals, there is both a conventional and long-acting formulation. The long-acting formulation contains a viscosity excipient used to prolong the absorption from the injection site. One such excipient is 2-pyrrolidone. When using long-acting formulations, the long-acting properties only apply to intramuscular use, not intravenous administration. When products that are long-acting are compared to conventional injectable products, the long-acting products usually allow for longer dose intervals. However, in pigs, there were no differences in duration of plasma concentrations when equivalent doses were administered.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive cattle respiratory pathogens is ≤ 2 mcg/mL, and ≤ 0.5 mcg/mL for swine respiratory pathogens. For other organisms the break point is ≤ 2 mcg/mL for streptococci and ≤ 4 for other organisms. Tetracycline is used as a marker to test susceptibility for other drugs in this class, such as doxycycline and minocycline.

Formulations

Oxytetracycline is available in 250-mg tablets; 500-mg bolus; 100- and 200-mg/mL injection; and 25-, 166-, and 450-g/lb of powder. Long-acting formulations are available in a 200-mg/mL injection. Oxytetracycline hydrochloride soluble powder is available to be added to drinking water for poultry, cattle, and pigs. Oxytetracycline is available as a medicated feed for cattle, poultry, fish, and pigs.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. If solutions are diluted prior to injection, they should be discarded if not used immediately. Solution may darken slightly without losing potency.

Small Animal Dosage**Dogs and Cats**

- 7.5-10 mg/kg q12h IV or 20 mg/kg q12h PO.

Large Animal Dosage**Horses**

- Treatment of ehrlichiosis: 10 mg/kg q24h IM or IV (slowly).

Foals

- Treatment of flexural limb deformities: 44 mg/kg, up to 70 mg/kg (2-3 g per foal), two doses 24 hours apart.

Calves

- 11 mg/kg/day PO.
- Treatment of pneumonia: 11 mg/kg q12h PO.

Cattle

- Injection for treatment of anaplasmosis, enteritis, pneumonia, and other infections: 11 mg/kg q12h IV.
- Long-acting formulations: 20 mg/kg, IM, as a single dose.

Pigs

- 6.6-11 mg/kg, up to 10-20 mg/kg q24h IM or 20 mg/kg q48h IM.

Regulatory Information

Cattle and pig withdrawal times (meat): 7 days (oral tablets). For oral soluble powder, the withdrawal times vary greatly from one product to another for cattle and pigs. Generally, they are at least 5 days for meat, but consult specific product label for withdrawal times.

Cattle withdrawal times for injection: 18-22 days, depending on the product.

Cattle withdrawal times for long-acting formulations: 28 days.

Cattle withdrawal times (milk): 96 hours at a dose of 20 mg/kg.

Cattle withdrawal times (intrauterine administration): 7 days (milk) and 28 days (meat). Cattle withdrawal times (intramammary administration): 6 days (milk) and 28 days (meat).

Pig withdrawal times: 28 days and up to 42 days, depending on product.

Oxytocin

oks-ih-toe'sin

Trade and other names: Pitocin, Syntocinon (nasal solution), and generic brands

Functional classification: Labor induction

Pharmacology and Mechanism of Action

Oxytocin stimulates uterine muscle contraction via action on specific oxytocin receptors. When administered around the time of luteolysis it stimulates PGF₂-alpha secretion and disrupts luteolysis. When administered prior to luteolysis, it does not induce PGF₂-alpha, and disrupts luteolysis and prolongs CL function.

Indications and Clinical Uses

Oxytocin is used to induce or maintain normal labor and delivery in pregnant animals. In surgery it may be used postoperatively following cesarean section to facilitate involution and resistance to the large inflow of blood. In large animals, oxytocin is used to augment uterine contractions and stimulate lactation. It will contract smooth muscle cells of the mammary gland for milk letdown if the udder is in a proper physiological state. It is also used to expel the placenta after delivery. However, efficacy for retained placenta is questionable, and some experts believe that estrogen should be administered in addition to oxytocin. Oxytocin does not increase milk production, but it will stimulate contraction leading to milk ejection. Oxytocin administered prior to luteolysis (prior to day 10 post ovulation in horses) prolongs CL function and suppresses estrus behavior in mares.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are uncommon if used carefully. However, careful monitoring of labor is necessary during its use.

Contraindications and Precautions

Do not administer to pregnant animals unless for induction of parturition. Do not administer unless cervix is fully relaxed. Do not use if there is abnormal presentation of the fetus.

Drug Interactions

Beta-adrenergic agonists will inhibit induction of labor.

Instructions for Use

Oxytocin is used to induce labor. In people, oxytocin is administered via injection, constant intravenous infusion, or intranasal solution.

Patient Monitoring and Laboratory Tests

Fetal stress and progression of normal labor should be monitored closely.

Formulations

Oxytocin is available in 10- and 20-units/mL injection and 40-units/mL nasal solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 5-20 units per dog IM or SQ (repeat every 30 min for primary inertia). Note: Manufacturer's label lists higher doses of 5-30 units per dog.

Cats

- 2.5-3 units per cat IM or IV. Repeat up to 3 times every 30-60 minutes. (Maximum dose is 3 units/cat).

Large Animal Dosage

The following doses are all on a per animal basis rather than a per kilogram basis.

Cattle

- To stimulate uterine contractions: 30 units IM and repeat in 30 minutes if necessary. (Manufacturer lists 100 units per cow.)
- For retained placenta: 20 units IM given immediately after calving and repeated in 2-4 hours.
- For milk letdown: 10-20 units per cow, IV or IM.

Mares

- To stimulate uterine contractions: 20 units IM. (Manufacturer lists 100 units per mare.)
- For retained placenta: 30-40 units IM at 60-90-minute intervals or add 80-100 units to 500 mL saline solution and give IV.
- To suppress estrus behavior in mares: 60 units per mare, IM, once or twice daily on days 7-14 post ovulation.

Small Ruminants and Sows

- 5-10 Units IM. (Manufacturer lists 30-50 units per animal.)

Regulatory Information

No withdrawal times have been reported. Because of low risk of residues and rapid clearance after administration, a 24-hour withdrawal time is suggested.

Pamidronate Disodium

pam-ih-droe'nate dye-soe'dee-um

Trade and Other Names: Aredia

Functional Classification: Antihypercalcemic

Pharmacology and Mechanism of Action

Bisphosphonate drug. Drugs in this class include pamidronate, etidronate, tiludronate, and pyrophosphate. These drugs are a group of drugs characterized by a germinal bisphosphonate bond. They slow the formation and dissolution of hydroxyapatite crystals. Their clinical use resides in their ability to inhibit bone resorption. These drugs decrease bone turnover by inhibiting osteoclast activity, inducing osteoclast apoptosis, retard bone resorption, and decrease rate of osteoporosis. Inhibition of bone resorption is via inhibition of the mevalonate pathway. Pamidronate, like other bisphosphonates, is not metabolized by the liver. It is primarily eliminated by the kidneys in animals, and preferentially remains in the bone for prolonged periods.

Indications and Clinical Uses

Pamidronate, like other bisphosphonate drugs, is used in people to treat osteoporosis and treatment of hypercalcemia of malignancy. In animals, pamidronate is used to decrease calcium in conditions that cause hypercalcemia, such as cancer and vitamin D toxicosis. It is helpful for managing neoplastic complications and pain associated with pathologic bone resorption. It also may provide pain relief in patients with pathologic bone disease and may reduce glucocorticoid-induced osteoporosis. Experimental work performed in dogs has shown it to be effective for treating cholecalciferol toxicosis, but it did not prevent decreases in renal function. After treating for hypercalcemia in dogs, the duration of effect was 11 days to 9 weeks (median 8.5 weeks). Some bisphosphonates, such as pamidronate, have been used to treat navicular disease in horses, but this work is only preliminary.

Precautionary Information

Adverse Reactions and Side Effects

Fever, joint pain, and myalgias have been observed, but otherwise no serious adverse effects have been identified. However, the use in animals has not been common enough to identify a wider range of adverse effects. One study in dogs reported a slight decrease in food intake. In humans, acute renal necrosis after intravenous administration has been reported. Because pamidronate is eliminated by the kidneys in dogs, a dose-dependent nephropathy is possible and the risk of renal injury is more likely with doses exceeding 3 mg/kg IV. In people, there is some concern that the use of bisphosphonates produces excessive mineralization and hardening of the bone, which may result in a greater risk of fractures. However, this effect has not been reported for animals.

Contraindications and Precautions

Although SQ administration is listed in dose protocols, the IV route is preferred. No contraindications have been identified in animals.

Drug Interactions

Do not mix with solutions containing calcium (e.g., lactated Ringer's solution).

Instructions for Use

For intravenous infusion, dilute in fluid solution (0.9% saline) and administer over 2 hours. (Dilute 30 mg pamidronate in 250 mL fluids.) Infusion can be repeated every 7 days. Although the SQ route is listed for some veterinary applications, it is not recommended and IV infusion is the preferred route.

Patient Monitoring and Laboratory Tests

Monitor serum calcium and phosphorus. Treatment of vitamin D toxicosis with pamidronate may result in decreased renal function. Monitor urea nitrogen, creatinine, urine-specific gravity, and food intake in treated animals.

Formulations

Pamidronate is available in 30-, 60-, and 90-mg vials for injection and 1 mg/mL in single-use vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Vials may be diluted in fluid solutions (e.g., 250 mL 0.9% sodium chloride) and infused over 2 hours or as long as 24 hours. Diluted solutions are stable for 24 hours at room temperature.

Small Animal Dosage

Dogs

- Treatment for hypercalcemia: 1-2 mg/kg, IV, SQ.
- Treating malignant osteolytic disease: 1-2 mg/kg IV (over 15-30 seconds) every 28 days as a 2-hour IV infusion.
- Treatment of cholecalciferol toxicosis: 1.3-2 mg/kg, IV, SQ for two treatments after toxin exposure.

Cats

- Treatment of hypercalcemia: 1-1.5 mg/kg, IV.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Pancrelipase

pan-kreh-lye'pase

Trade and Other Names: Viokase, Pancrezyme, Cotazym, Creon, Pancoate, Pancrease, and Ultrase

Functional Classification: Pancreatic enzyme

Pharmacology and Mechanism of Action

Pancreatic enzyme. Pancrelipase provides lipase, amylase, and protease. Pancrelipase is a mixture of enzymes (lipase, amylase, and protease) obtained from the pancreas

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of pigs. These enzymes enhance digestion of fats, proteins, and starches in the upper duodenum and jejunum. They are more active in alkaline environment. There are coated and uncoated tablets. The uncoated tablets are not as bioavailable because degradation may occur in the acid of the stomach. Each milligram contains 24 units lipase, 100 units amylase, and 100 units of protease activity.

Indications and Clinical Uses

Pancrelipase is used to treat pancreatic exocrine insufficiency. It provides enzymes lacking for digestion. It should be administered before meals. It is inactivated in gastric acid and should be administered with a drug to suppress stomach acid (e.g., H₂-receptor blocker or proton pump inhibitor [PPI]) to improve activity.

Precautionary Information

Adverse Reactions and Side Effects

Oral bleeding has been reported from administration of tablets. The tablets contain potent enzymes and contact with mucosal membranes may cause lesions and mucosal ulcers. Ensure that tablets are not trapped in the esophagus, or esophageal erosions may occur. Warn owners that if they handle tablets, avoid hand-to-mucosa contact (e.g., contact with eyes).

Contraindications and Precautions

Enteric-coated tablets may not be as effective as mixing powder with food.

Drug Interactions

If antacids are used concurrently, magnesium hydroxide and calcium carbonate may reduce effectiveness.

Instructions for Use

Mix pancrelipase with food when administering approximately 20 minutes prior to feeding. After successful results are obtained, the dose may be reduced gradually to identify the minimum effective dose. Pancreatic enzymes are more effective if administered with acid-suppressing drugs (H₂ blockers, PPIs, bicarbonate, or some antacids). If delayed-release capsules are used (granules), do not crush. Different brands have varying activity. If switching from one brand to another, not all products will result in the same therapeutic results.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Pancrelipase is available in a composition of 16,800 units of lipase, 70,000 units of protease, and 70,000 units of amylase per 0.7 g. It is also available in capsules and tablets. Various formulations contain a variety of activity. For example, Viokase powder contains 16,000 units/70,000 units/70,000 units (lipase/protease/amylase) per 0.7 g of powder. Tablets range from 8000/30,000/30,000 units (lipase/protease/amylase) to 11,000/30,000/30,000 units (lipase/protease/amylase) per tablet.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is inactivated in an acid environment.

Small Animal Dosage

Dogs

- Mix 2 tsp of powder with food per 20 kg body weight or 1-3 tsp/0.45 kg of food 20 minutes prior to feeding. Formulations with granules in capsules may be opened and sprinkled on food (approximately 1 capsule with meals for a dog).

Cats

- Mix one half teaspoon per cat with food.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Because of low risk of residues and rapid clearance after administration, no withdrawal time is suggested.

Pancuronium Bromide

pan-kyoo-roe'nee-um bro'mide

Trade and Other Names: Pavulon

Functional Classification: Muscle relaxant

Pharmacology and Mechanism of Action

Neuromuscular blocking agent (nondepolarizing). Pancuronium, like other drugs in this class, competes with acetylcholine at the neuromuscular end plate to produce paralysis. Sensory nerves are intact.

Indications and Clinical Uses

Pancuronium is a paralytic agent used during anesthesia or for mechanical ventilation. It is used primarily during anesthesia or other conditions in which it is necessary to inhibit muscle contractions. It is sometimes used as an alternative to atracurium because it is longer acting.

Precautionary Information

Adverse Reactions and Side Effects

Pancuronium produces respiratory depression and paralysis. Neuromuscular blocking drugs have no effect on analgesia.

Contraindications and Precautions

Do not use in patients unless mechanical ventilation support can be provided.

Drug Interactions

Some drugs may potentiate the action (e.g., aminoglycosides) and should not be used concurrently.

Instructions for Use

Administer only in situations in which careful control of respiration is possible. Doses may need to be individualized for optimum effect. Do not mix with alkalinizing solutions or lactated Ringer's solution.

Patient Monitoring and Laboratory Tests

Monitor patient's respiration rate, heart rate, and rhythm during use. If possible, monitor the oxygenation status during anesthesia.

Formulations

Pancuronium is available in a 1- and 2-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.1 mg/kg IV, or start with 0.01 mg/kg and additional 0.01 mg/kg doses q30min.
- Constant rate infusion (CRI): 0.1 mg/kg IV, followed by 2 mcg/kg/min infusion.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Pantoprazole

pan-toe-pray'zole

Trade and Other Names: Protonix

Functional Classification: Antiulcer agent

Pharmacology and Mechanism of Action

Proton pump inhibitor (PPI). Pantoprazole inhibits gastric acid secretion by inhibiting the K^+/H^+ pump. Pantoprazole, like other PPIs, has potent and long-acting effects. Acid suppression may have a duration >24 hours in animals. Other PPIs that are administered orally (e.g., omeprazole) have been used in animals. Pantoprazole is the first PPI that can be administered IV. After a dose, it inhibits acid secretion for >24 hours.

Indications and Clinical Uses

Pantoprazole is used for treatment and prevention of GI ulcers. Other PPIs include omeprazole, lansoprazole (Prevacid), and rabeprazole (AcipHex). All PPIs act via a similar mechanism and are equally effective. However, there has been more experience with omeprazole in animals than the other drugs of this group. In dogs, pantoprazole (1 mg/kg) maintained stomach pH >3-4 when administered IV. Pantoprazole, being the only one in an IV formulation, is often used when an intravenous drug is preferred for treatment.

Precautionary Information

Adverse Reactions and Side Effects

Side effects have not been reported in animals. However, in people there is concern about hypergastrinemia with chronic use. Overgrowth of *Clostridium* bacteria has been a concern from chronic use because of chronic gastric acid suppression, but the clinical importance of this concern in animals has not been established.

Contraindications and Precautions

No known contraindications.

Drug Interactions

Do not mix intravenous solution with other drugs. Do not administer with drugs that depend on acid stomach for absorption (e.g., ketoconazole, itraconazole, iron supplements). PPIs may inhibit some drug-metabolizing enzymes (CYP 450 enzymes), although in people there was low risk of drug interactions caused by enzyme inhibition.

Instructions for Use

For treating GI ulcers, administer once per day for 7-10 days. For gastrin-secreting tumors use higher dose (1 mg/kg) twice daily. Other PPIs include omeprazole (Prilosec), lansoprazole (Prevacid), and rabeprazole (AcipHex). They all act via a similar mechanism and are equally effective. The primary difference with pantoprazole is that it is available in an intravenous dosage formulation and can be mixed with fluid solutions. For intravenous use, mix a 40-mg vial with 10 mL saline and further dilute with saline, lactated Ringer's solution, or 5% dextrose to 0.4 mg/mL for intravenous infusion. Administer intravenous infusion over at least 15 minutes.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. When treating ulcers, monitor hematocrit or CBC to detect bleeding. Monitor for signs of vomiting and diarrhea.

Formulations

Pantoprazole is available in a 40-mg vial for intravenous use (diluted to 4 mg/mL) and 20- and 40-mg delayed-release tablets. There are also granules for oral suspension (40 mg), which have been mixed with apple juice or applesauce for administration in people.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze reconstituted solutions. Once diluted for intravenous use, it is stable for 12 hours.

Small Animal Dosage

Dogs and Cats

- 0.5-0.6 mg/kg once daily PO.
- Intravenous administration (24 hours): 0.5-1 mg/kg IV infusion over 24 hours. This dose may be delivered in 2 or 15 minutes (see below).
- Intravenous administration (2 or 15 minutes): First flush IV line. Administer pantoprazole via IV line with dextrose 5% injection, sodium chloride 0.9% injection, or Ringer's lactate injection. For 2-minute infusion mix 40 mg of

584 Paregoric

powder with 10 mL of sodium chloride 0.9% injection for a final concentration of 4 mg/mL. Infuse 1 mg/kg dose over 2 minutes. For 15-minute infusion, mix 40-mg vial with 10 mL sodium chloride 0.9% injection. Then further admix this solution with 100 mL of dextrose 5% injection, sodium chloride 0.9% injection, or Ringer's lactate injection to a total volume of 110 mL, producing a solution with a final concentration of approximately 0.4 mg/mL. Administer final dose (1 mg/kg) over 15 minutes.

Large Animal Dosage

No dose is reported for large animals. Doses have been extrapolated from human use (0.5 mg/kg q24h IV), and infusion protocols listed previously for small animals have been used.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 5

Paregoric

pare-eh-gore'ik

Trade and Other Names: Corrective mixture

Functional Classification: Antidiarrheal

Pharmacology and Mechanism of Action

Paregoric (opium tincture) is an outdated product used to treat diarrhea. Paregoric contains 2 mg of morphine in every 5 mL of paregoric. The action is via stimulation of intestinal mu-opiate receptors to cause a decrease in intestinal peristalsis.

Indications and Clinical Uses

Paregoric will decrease signs of diarrhea via opiate effects, but its use is somewhat outdated.

Precautionary Information

Adverse Reactions and Side Effects

Like all opiates, side effects are predictable and unavoidable. Side effects may include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses. Tolerance and dependence occurs with chronic administration.

Contraindications and Precautions

Contains opium and may be abused by humans. Use cautiously in horses and ruminants because intestinal motility may be decreased.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Use of paregoric has been replaced by more specific products such as loperamide or diphenoxylate.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

For every 5 mL of paregoric, there is 2 mg of morphine.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.05-0.06 mg/kg q12h PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Paromomycin Sulfate

pare-oe-moe-mye'sin sul'fate

Trade and Other Names: Humatin

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Antibiotic drug of the aminoglycoside class. The mechanism of action of paromomycin is similar to other aminoglycosides: It inhibits the ribosomal 30S subunit with subsequent inhibition of bacterial protein synthesis. Spectrum of activity is similar to other aminoglycosides. However, because paromomycin is administered orally and generally not absorbed systemically, its activity is limited to intestinal pathogens.

Indications and Clinical Uses

The use of paromomycin is limited to intestinal infections. It is not absorbed systemically and should not be used for extraintestinal infections. Paromomycin has been used to treat intestinal infections, such as cryptosporidiosis. The use is based on limited accounts in animals and extrapolation from humans. Efficacy in animals has not been tested in controlled studies.

Precautionary Information

Adverse Reactions and Side Effects

Paromomycin has been associated with renal failure and blindness when used in cats. Although systemic absorption is not expected to be high, cats treated with high doses for intestinal organisms developed problems.

Contraindications and Precautions

Extreme caution is recommended when administering this drug to animals that may have a compromised bowel resulting from intestinal disease because increased systemic absorption may occur.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

In cats, doses of 125-165 mg/kg every 12 hours have been administered for 5-7 days, PO. However, there are reports in the veterinary literature that these doses have produced toxicity in cats, including renal injury. It is suggested to use lower doses to avoid toxicity and monitor the patient's renal parameters carefully. When there is a compromised integrity of the intestinal mucosa as may occur with diarrhea, use of paromomycin is discouraged.

Patient Monitoring and Laboratory Tests

Monitor patient's renal function, such as urine-specific gravity, serum creatinine, and BUN, during treatment.

Formulations

Paromomycin is available in 250-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage**Cats**

- Doses of 125-165 mg/kg q12h PO for 7 days have been recommended. However, caution is recommended when using doses this high. Lower doses should be considered (see dog dose) in animals that may be at risk of toxicity.

Dogs

- The dose in dogs has been extrapolated from human medicine, which is 10 mg/kg, q8h, PO, for 5-10 days.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. Although not absorbed systemically to a large extent, it is expected that concentrations may persist in the kidneys, producing long, extended withdrawal times for slaughter.

Paroxetine

par-oks'eh-teen

Trade and Other Names: Paxil

Functional Classification: Behavior modification

Pharmacology and Mechanism of Action

Antidepressant drug. Paroxetine, like other drugs in this class, is classified as a selective serotonin reuptake inhibitor (SSRI). It resembles fluoxetine (Reconcile, Prozac) in action. Its mechanism of action appears to be via selective inhibition of serotonin reuptake and downregulation of 5-HT₁ receptors. SSRI drugs are more selective for inhibiting serotonin reuptake than the tricyclic antidepressant drugs (TCAs).

Indications and Clinical Uses

Paroxetine, like other SSRI drugs, is used to treat behavioral disorders such as compulsive disorders (canine compulsive disorder), anxiety, and dominance aggression. In cats it has been effective for decreasing urine spraying.

Precautionary Information

Adverse Reactions and Side Effects

Some effects similar to fluoxetine, but in some animals paroxetine is better tolerated. Adverse effects observed in dogs and cats include constipation and decreased appetite.

Contraindications and Precautions

Use cautiously in patients with heart disease. Do not use in pregnant animals. There is a risk of fetal malformations if used early in pregnancy.

Drug Interactions

Do not use with monoamine oxidase inhibitors (MAOIs), such as selegiline. Do not use with other behavior-modifying drugs, such as other SSRIs or TCAs.

Instructions for Use

Dosing recommendations are empirical. Paroxetine has been used for conditions similar to what has been treated with fluoxetine (Prozac, Reconcile). In cats, the small tablet size has made it easier to administer convenient doses, compared to chewable tablets or other drugs available in capsules. Paroxetine has caused constipation in some animals, and veterinarians may administer a feline laxative for the first week of therapy to avoid problems.

Patient Monitoring and Laboratory Tests

Use in animals has been relatively safe, and one should only monitor behavior changes.

Formulations

Paroxetine is available in 10-, 20-, 30-, and 40-mg tablets and 2-mg/mL oral suspension.

Stability and Storage

Stable if stored in manufacturer's original formulation. Although paroxetine has been compounded for veterinary use, the potency and stability has not been evaluated for compounded products.

Small Animal Dosage

Dogs

- 0.5 mg/kg/day PO. For some compulsive disorders, increase the dose to 1 mg/kg q24h, PO.

Cats

- One eighth to one fourth of a 10-mg tablet per cat, daily PO (approximately 0.5 mg/kg q24h).

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 2

Penicillamine

pen-ih-sill'ah-meen

Trade and Other Names: Cuprimine and Depen

Functional Classification: Antidote

Pharmacology and Mechanism of Action

Penicillamine is also called 3 mercaptovaline. It is a chelating agent for lead copper, iron, and mercury. When used to treat copper toxicity, it helps to solubilize copper in the cells to allow for more rapid urinary excretion. Treated animals should have increased copper urinary excretion. Other drugs that have been used as chelating agents include tetrathiomolybdate, trientine, and zinc. Penicillamine also has anti-inflammatory properties. It inhibits collagen cross-linking by making it more susceptible to enzyme degradation. This antifibrotic property may contribute to its positive effect for treating animals with hepatitis.

Indications and Clinical Uses

Penicillamine has been used in people to treat rheumatoid arthritis. In animals it is used primarily for treatment of copper toxicity and hepatitis associated with accumulation of copper. Treatment duration for animals with copper-storage hepatic disease may require 2-4 months. It also has been used to treat cystine calculi. Although it may inhibit collagen and reduce fibrosis in patients with hepatic disease, this effect has been disappointing in clinical patients. There is no clear demonstration that it is efficacious for this indication.

Precautionary Information

Adverse Reactions and Side Effects

The most common effect is anorexia and vomiting. In people, allergic reactions, cutaneous reactions, agranulocytosis, and anemia have been reported. It has also produced proteinuria and hematuria and in cats has caused neutropenia. In dogs treated for liver disease, corticosteroid-like hepatopathy has been observed. Therefore it may produce steroid-like effects in the liver.

Contraindications and Precautions

Do not use in pregnant animals. There appears to be little cross-reaction between penicillin and penicillamine in allergic animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Administer on an empty stomach (2 hours before meals).

Patient Monitoring and Laboratory Tests

Monitor liver biochemistry tests during treatment. Monitor metal concentrations if used to treat intoxication.

Formulations

Penicillamine is available in 125- and 250-mg capsules and 250-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Penicillamine is soluble in water. Preparations of penicillamine in a suspension for oral use have been combined with syrups and flavorings and were stable for 5 weeks.

Small Animal Dosage

Dogs and Cats

- 10-15 mg/kg q12h PO.
- Doberman pinschers: use 2500 mg q12h PO.

Large Animal Dosage

Horses and Cattle

- 10-15 mg/kg q12h PO.

Regulatory Information

Cattle withdrawal time: 21 days meat; 3 days milk.

Penicillin G

Trade and Other Names: Penicillin G potassium or sodium, Penicillin G benzathine (Benza-Pen), Penicillin G, Procaine, and generic Penicillin V (Pen-Vee)

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Penicillin G is also called benzyl penicillin. Its action is similar to other penicillins. It binds penicillin-binding proteins (PBP) to weaken or cause lysis of the cell wall. Penicillin G is bactericidal with a time-dependent action. An increased bactericidal effect is observed when drug concentrations are maintained above minimum inhibitory concentration (MIC) values. The spectrum of penicillin G is limited to gram-positive bacteria, anaerobic bacteria, and a few highly susceptible gram-negative bacteria (e.g., *Pasteurella* spp.). Practically all bacteria of the *Enterobacteriaceae* and beta-lactamase-producing *Staphylococcus* spp. are resistant. Penicillin sodium or penicillin potassium when injected IV has a half-life of 1 hour or less in most animals. However, the same dose of procaine penicillin given IM may produce more prolonged concentrations and a half-life of 20-24 hours because of slow absorption from the injection site.

Formulations of penicillin G are designed to control the absorption from site of injection. Formulations include:

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- Sodium or potassium penicillin G (crystallin penicillin), which is water soluble and can be administered IV or IM. It may also be mixed with fluids for IV administration.
- Penicillin G benzathine, which is insoluble and available as a suspension. It is slowly absorbed from an injection site to produce low but prolonged (several days of) penicillin concentrations. All benzathine penicillin G forms are combined with procaine penicillin G in commercial formulation (1:1 ratio).
- Penicillin G procaine is a poorly soluble suspension for intramuscular or subcutaneous administration. It is absorbed slowly, producing concentrations for 12-24 hours after injections.
- Penicillin V, oral penicillin, is not highly absorbed and is narrow spectrum in comparison with other penicillin derivatives.

Indications and Clinical Uses

Penicillin G is administered by injection either IV (potassium or sodium penicillin) or IM (procaine or procaine/benzathine penicillin G). Penicillin G is indicated for treatment of gram-positive cocci that cause respiratory infections, abscesses, and urinary tract infections. Many staphylococci are resistant because of beta-lactamase synthesis. Streptococci are usually susceptible. Other susceptible organisms include gram-positive bacilli and anaerobic bacteria. Most gram-negative bacilli, especially those of enteric origin, are resistant. Some gram-negative respiratory pathogens such as *Pasteurella multocida* and *Mannheimia haemolytica* are susceptible.

Penicillin concentrations in the urine are at least 100-fold higher than plasma concentrations in treated animals; therefore, some urinary pathogens may be more susceptible.

Precautionary Information

Adverse Reactions and Side Effects

Penicillin G is usually well tolerated. Allergic reactions are possible. Diarrhea is common with oral doses. Pain and tissue reactions may occur with IM or SQ injections. Formulations of procaine penicillin G contain varying amounts of free procaine (depending on the formulation). Free procaine in the formulation may elicit a CNS reaction after injection in some horses. Large doses of sodium penicillin IV can decrease potassium concentrations.

Contraindications and Precautions

Use cautiously in animals allergic to penicillin-like drugs. Avoid injection volumes greater than 30 mL per site. Administration of the long-acting benzathine form of penicillin G will increase the risk of residues in food-producing animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

The approved dose listed on the injectable product labels are outdated and do not reflect the current clinical use of penicillin. Penicillin G benzathine is not recommended for most infections because concentrations are too low to provide therapeutic drug concentrations. A possible exception is for treatment of streptococcal infections. Avoid SQ injection with procaine penicillin G because of tissue injury and food animal residue problems. Penicillin V should be administered on an empty stomach for maximum absorption.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are ≤ 8 mcg/mL for enterococci and ≤ 0.12 mcg/mL for staphylococci and streptococci.

Formulations

Penicillin G potassium is available in 5-20 million unit vials. Penicillin G benzathine is available in 150,000 units/mL and is usually combined with 150,000 units/mL of procaine penicillin G suspension. Benzathine penicillin products are not recommended. Procaine penicillin G is available in 300,000 units/mL suspension. Penicillin is one of the few antibiotics that is still measured in terms of units rather than weight in milligrams or micrograms. One unit of penicillin represents the specific activity in 0.6 mcg of sodium penicillin. Thus, 1 mg of penicillin sodium represents 1667 units of penicillin. In some references, an approximate conversion of 1000 units per mg is used.

Penicillin V is available in 250- and 500-mg tablets (250 mg is equal to 400,000 units).

Stability and Storage

Sodium and potassium forms of penicillin G retain their potency for 72 hours at room temperature, but refrigeration is recommended. It is stable for 7 days if refrigerated and retained 90% potency for 14 days. Penicillin potassium or penicillin sodium are freely soluble in water. One gram of penicillin will dissolve in 250 mL of water (4 mg/mL). Degradation and inactivation of penicillin solutions are accelerated at high pH (pH >8), strong acids, or oxidizing agents.

Small Animal Dosage

- Penicillin G potassium or sodium: 20,000-40,000 units/kg q6-8h IV or IM.
- Procaine Penicillin G: 20,000-40,000 units/kg q12-24h IM.
- Penicillin V: 10 mg/kg q8h PO.

Large Animal Dosage

Cattle and Sheep

- Procaine penicillin G: 24,000-66,000 units/kg q24h IM. Subcutaneous use is discouraged.
- Sodium or potassium penicillin G: 20,000 units/kg IM or IV, q6h.

Pigs

- Procaine penicillin G: 15,000-25,000 units/kg q24h IM.

Horses

- Penicillin sodium or penicillin potassium: 20,000-24,000 units/kg q6-8h IV. (Doses up to 44,000 units/kg q6h have been used for refractory cases.)
- Procaine penicillin G: 20,000-24,000 units/kg q24h IM.
- Potassium penicillin G: 20,000-24,000 units/kg q12h IM.

Regulatory Information

Horses: Injections of procaine penicillin may cause a positive test for procaine prior to racing.

Horses may test positive with a procaine urine test for as long as 30 days after an injection.

Withdrawal times for benzathine penicillin at label dose of 6000-7000 units/kg in cattle: 30 days meat (14 days Canada).

Withdrawal times for procaine penicillin at label dose of 6000-7000 units/kg in cattle: 10 days meat, 4 days milk; sheep 9 days; swine 7 days.

Withdrawal times for procaine penicillin G at a dose of 15,000 units/kg in pigs: 8 days.

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Withdrawal times for procaine penicillin G at a dose of 21,000 units/kg in cattle: 10 days meat, 96 hours milk.

Procaine penicillin G at a dose of 60,000 units/kg: 21 days cattle, 15 days pigs.

RCI Classification: Penicillin is not classified; procaine 3

Pentastarch

Trade and Other Names: Pentaspan

Functional Classification: Fluid replacement

Pharmacology and Mechanism of Action

Pentastarch is a synthetic colloid volume expander that is used to maintain vascular volume in animals with circulatory shock. It is prepared from hydroxyethyl starch and is derived from amylopectin. There are two hydroxyethyl starch preparations: hetastarch and pentastarch. Hetastarch (6%) has an average molecular weight of 450,000 and colloid osmotic pressure of 32.7. Pentastarch (10%) has an average molecular weight of 280,000 and colloid osmotic pressure of 40. Because hetastarch is a larger molecular weight compound than pentastarch, it tends to remain in the vasculature and prevent loss of intravascular volume and tissue edema. After administration, pentastarch will be retained in the vasculature and prevent loss of intravascular volume and tissue edema. Other colloids used are dextrans (Dextran 40 and Dextran 70). Hetastarch and the dextrans are discussed in other sections.

Indications and Clinical Uses

Pentastarch is used primarily to treat acute hypovolemia and shock. It is administered IV in acute situations. Pentastarch has a duration of effective volume expansion of 12-48 hours. Pentastarch is used in similar situations as hetastarch, but it is used less frequently.

Precautionary Information

Adverse Reactions and Side Effects

There has only been limited use in veterinary medicine; therefore adverse effects have not been reported. However, it may cause allergic reactions and hyperosmotic renal dysfunction. Coagulopathies are possible but are rare and less likely than with hetastarch.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

Pentastarch is compatible with most fluid solutions.

Instructions for Use

Pentastarch is used in critical care situations and is infused via constant rate infusion (CRI). Pentastarch may be more effective and produce fewer side effects than Dextran. Because of lower molecular weight, it can be infused more quickly than hetastarch.

Patient Monitoring and Laboratory Tests

Monitor patient's hydration status and blood pressure during administration.

Formulations

Pentastarch is available in a 10% injectable solution.

Stability and Storage

Pentastarch is stable in original packaging. Compatible with most fluid administration sets.

Small Animal Dosage

Dogs

- CRI: 10-25 mL/kg/day IV.

Cats

- CRI: 5-10 mL/kg/day IV.

Large Animal Dosage

Horses

- 8-15 mL/kg or delivered as CRI 0.5-1 mL/kg/hr, IV.
No doses have been reported for other large animals.

Regulatory Information

No regulatory requirements.

Pentazocine

pen-taz'oh-seen

Trade and Other Names: Talwin-V

Functional Classification: Analgesic, opioid

Pharmacology and Mechanism of Action

Synthetic opiate analgesic. The action of pentazocine results from its effect as a mu-opiate receptor partial agonist and a kappa-receptor agonist. Most of the sedative and analgesic effects are believed to be caused by the kappa-receptor effects. Pentazocine may partially reverse some mu-receptor agonist effects. Its effects are believed to be similar to buprenorphine or butorphanol, but efficacy is less.

Indications and Clinical Uses

Pentazocine has been used for sedation and analgesia, primarily in horses. However because of the availability of other opioids with better efficacy, the use of pentazocine has declined.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are similar to other opioid analgesic drugs and include constipation, ileus, vomiting, and bradycardia. Sedation is common at analgesic doses. Respiratory depression can occur with high doses. Dysphoric effects are possible in some sensitive individuals and in some species (e.g., horses).

Contraindications and Precautions

Pentazocine is a Schedule IV controlled substance.

Drug Interactions

Pentazocine may potentiate other sedative drugs such as alpha₂-agonists. Pentazocine may interfere with mu-opiate effects of other drugs, such as morphine or fentanyl.

594 Pentobarbital Sodium

Instructions for Use

Pentazocine is a mixed agonist/antagonist. It is relatively modest to weak in efficacy for pain control, and other opioids should be considered for better pain management.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

Formulations

Pentazocine is available in a 30-mg/mL injection (availability has been limited).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 1.65-3.3 mg/kg q4h IM, or as needed.

Cats

- 2.2-3.3 mg/kg q4h IM, IV, or SQ, or as needed.

Large Animal Dosage

Horses

- 200-400 mg per horse, IV.

Regulatory Information

Pentazocine is a Schedule IV controlled drug. Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873 -2723).

RCI Classification: 3

Pentobarbital Sodium

pen-toe-bar'bih-tahl soe'dee-um

Trade and Other Names: Nembutal and generic brands

Functional Classification: Anesthetic, barbiturate

Pharmacology and Mechanism of Action

Short-acting barbiturate anesthetic. The action of pentobarbital is via nonselective depression of CNS. Duration of action may be 3-4 hours.

Indications and Clinical Uses

Pentobarbital is usually used as intravenous anesthetic. It also is used to control severe seizures in animals for treatment during status epilepticus. In some instances, pentobarbital is included in mixtures used to induce euthanasia in animals.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are related to anesthetic action. Cardiac depression and respiratory depression are common.

Contraindications and Precautions

Rapid intravenous doses can be lethal. Monitor respiration rate carefully after injection because respiratory depression may occur.

Drug Interactions

Pentobarbital will potentiate sedative and cardiorespiratory-depressing effects of other anesthetics. Pentobarbital is subject to effects from other drugs that may either induce or inhibit cytochrome P450 metabolizing enzymes (see Appendix).

Instructions for Use

Pentobarbital has a narrow therapeutic index. When administering IV, inject first half of dose initially, then the remainder of calculated dose gradually until anesthetic effect is achieved.

Most euthanasia solutions contain pentobarbital as their active ingredient. Often other ingredients to facilitate euthanasia are included such as muscle relaxants and drugs with lethal cardiac effects (e.g., edetate disodium 0.05%). The concentration of pentobarbital in most euthanasia solutions is 390 mg/mL with a lethal dose of 1 mL per 10 pounds, which is equivalent to 1 mL per 4.5 kg or 87 mg/kg IV.

Patient Monitoring and Laboratory Tests

Monitor vital signs, especially heart rate and rhythm and respiration during anesthesia.

Formulations

Pentobarbital is available in a 50- and 65-mg/mL solution for injection (contains propylene glycol).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. pH of solution is 9-10.5 and may affect stability of other coadministered drugs. It will precipitate if combined with most hydrochloride-based drugs or drugs with low pH. If pentobarbital is used to euthanize animals, it will remain stable even under rendering conditions used for disposal of the carcass.

Small Animal Dosage

Dogs and Cats

- General anesthesia: 25-30 mg/kg IV, to effect.
- Constant rate infusion (CRI): 2-15 mg/kg IV to effect, followed by 0.2-1 mg/kg/hr.
- Status epilepticus: 2-6 mg/kg IV (15-20 minutes may be needed to take full effect).
- Euthanasia: See Instructions for Use section.

Large Animal Dosage

Cattle

- Standing sedation: 1-2 mg/kg IV.

Cattle, Sheep, and Goats

- General anesthesia: 20-30 mg/kg IV given to effect.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Schedule II controlled drug

RCI Classification: 2

Pentoxifylline

pen-toks'ih-fill-in

Trade and Other Names: Trental, Oxpentifylline, and generic brands

Functional Classification: Anti-inflammatory agent

Pharmacology and Mechanism of Action

Methylxanthine. Pentoxifylline is used primarily as a rheological agent in people (increases blood flow through narrow vessels). An improved rheological effect has also been demonstrated with equine red blood cells but not neutrophils. As a phosphodiesterase inhibitor (PDE 4 inhibitor) it produces anti-inflammatory effects. It may have anti-inflammatory action via inhibition of cytokine synthesis. Pentoxifylline suppresses synthesis of inflammatory cytokines, such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNF) alpha and may inhibit lymphocyte activation.

In horses the half-life is only 23 minutes and oral absorption has been 45% but variable and inconsistent. Pentoxifylline undergoes extensive hepatic metabolism in dogs, and systemic availability after oral administration is 50% but can be highly variable and inconsistent. In other studies the oral absorption is only 20%-30% with a short elimination half-life (less than 1 hour). Seven metabolites are produced in animals, with some being biologically active.

Indications and Clinical Uses

Most of pentoxifylline's use in animals (including doses) is based on anecdotal experience. Pentoxifylline is used in dogs for some dermatoses, vasculitis, contact allergy, atopy, familial canine dermatomyositis, increased survival of skin flaps, increased healing of radiation injury, and erythema multiforme. In horses, pentoxifylline is used for a variety of conditions in which suppression of inflammatory cytokines or increased blood perfusion is desired. Such conditions have included intestinal ischemia, colic, sepsis, laminitis, and navicular disease. However, the efficacy for treating these diseases has not been shown. It may have improved efficacy for sepsis if combined with a nonsteroidal anti-inflammatory drug (NSAID; e.g., flunixin).

Precautionary Information

Adverse Reactions and Side Effects

Pentoxifylline may cause effects similar to other methylxanthines, such as nausea, vomiting, and diarrhea. Nausea, vomiting, dizziness, and headache have been reported in people. Vomiting is reported in dogs. Broken tablets taste unpleasant when administered to cats. If crushed tablets are used, plasma concentration will increase more rapidly than with intact tablets, leading to headaches, nausea, and possible vomiting. In horses, IV doses have caused muscle fasciculations, increased heart rate, and sweating.

Contraindications and Precautions

None reported. Broken tablets taste unpleasant when administered to cats.

Drug Interactions

No drug interactions are reported. However, as a methylxanthine, adverse reactions are possible from coadministration with a cytochrome P450 inhibitor (see Appendix).

Instructions for Use

Although pharmacokinetic studies in dogs and horses have been reported, results of clinical studies in animals have been limited. Based on pharmacokinetic studies that show a short half-life in dogs, higher doses than those listed in the dosing section have been advocated. For example, the most effective dose may be as high as 30 mg/kg q8-12h in dogs. Indications for dermatology have used a regimen of every 12 hours, but a frequency of every 8 hours may be considered to get an optimum response in some patients.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Pentoxifylline is available in 400-mg tablets. IV solution is 50 mg/mL.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Aqueous solubility is only 77 mg/mL. Oral suspensions may be stable for up to 90 days, but they will settle, requiring resuspension (shaking) before oral administration.

Small Animal Dosage**Dogs**

- Dermatologic use: 10 mg/kg q12h PO, and up to 15 mg/kg q8h PO.
- Familial canine dermatomyositis: 25 mg/kg q12h PO.
- Other uses: 10-15 mg/kg q8 PO or 400 mg/dog for most animals.

Cats

- 1/4 of a 400-mg tablet (100 mg) q8-12h PO.

Large Animal Dosage**Horses**

- 8.5 mg/kg q8h IV, or 10 mg/kg, q8h, PO (oral absorption is unpredictable).
- Respiratory disease (airway obstruction): 36 mg/kg q12h PO.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Pergolide, Pergolide Mesylate

per'goe-lide

Trade and Other Names: Permax

Functional Classification: Dopamine agonist

Pharmacology and Mechanism of Action

Dopaminergic agonist. Pergolide is a potent dopamine agonist that stimulates postsynaptic dopamine receptors (D_1 and D_2 receptors). It is used to stimulate dopamine receptors in conditions in which dopamine is deficient, regardless of the state of the presynaptic dopamine stores. Other drugs that may share similar effects are selegiline, apomorphine, and lisuride (previously called lysuride). In horses the half-life is 5.9 hours and is rapidly absorbed from oral administration.

Indications and Clinical Uses

In people, pergolide has been used for neurodegenerative disease in which dopamine is deficient, such as Parkinson's disease, in which pergolide is used with levodopa or carbidopa. However, pergolide has been commercially unavailable for humans and its use has diminished because of reports of cardiac valve damage associated with pergolide. In animals it also has been used for dopamine-deficient states. It is believed that horses and some dogs develop hyperadrenocorticism (Cushing's disease)—pituitary-dependent hyperadrenocorticism (PDH)—because of a loss of dopamine antagonism of adrenocorticotropic hormone (ACTH) release. In horses it is used successfully to treat pituitary pars intermedia dysfunction (PPID or equine Cushing's syndrome) and has controlled the disease in horses for longer than 2 years. Most horses with Cushing's disease have hyperplasia or adenoma of the pars intermedia of the pituitary. This adenoma is deficient in dopamine and produces excess ACTH. Administration of dopamine agonists acts to suppress ACTH release from the pituitary and subsequently restore cortisol levels to normal states. The benefits of pergolide administration have not been established for dogs. Because of adverse effects produced, pergolide is not used for treating PDH in dogs.

Precautionary Information

Adverse Reactions and Side Effects

Pergolide was withdrawn from the human market because of evidence that drugs that activate the $2b$ -serotonin receptor ($5-HT_{2b}$) are associated with a distinct form of fibrotic valvulopathy. These effects have not been observed in animals. Pergolide inhibits secretion of prolactin and will increase growth hormone. It may inhibit lactation. CNS effects may include ataxia and dyskinesia. In horses, adverse effects include anorexia, diarrhea, and colic. Worsening of laminitis from pergolide (it is theoretically a vasoconstrictive drug) has not been proved. In dogs, at doses of 100 mcg/kg it produced significant reactions that included vomiting, tremors, anorexia, restlessness, and diarrhea.

Contraindications and Precautions

Unlike bromocriptine, pergolide can be used in pregnant animals.

Drug Interactions

No drug interactions have been reported in animals. It may interact with droperidol and phenothiazines (e.g., acepromazine), and it will exacerbate the effects of selegiline. Do not administer with monoamine oxidase inhibitors (MAOIs).

Instructions for Use

Use in horses is often accomplished by compounding the preparation for horses and administering daily. Start with the low dose listed for 4-6 weeks and gradually increase the dose until desired results are obtained. It may be possible to obtain better efficacy when pergolide is used concurrently with cyproheptadine. When treating horses, consider supplementing their diet with magnesium and chromium.

Patient Monitoring and Laboratory Tests

Monitor ACTH levels in animals to document pituitary function. In horses, endogenous ACTH concentrations that exceed 27-50 pcg/mL are considered abnormal. Dexamethasone suppression tests can also be performed to monitor treatment in horses. Consult Dexamethasone monograph for procedure to perform this test.

Formulations

Pergolide tablets were previously available in 50 mcg (0.05 mg), 250 mcg (0.25 mg), and 1 mg (all strengths as the base). However, after the discontinuation of the oral formulations for people, the only veterinary source has been a compounded formulation. The compounded oral formulation of pergolide mesylate 1 mg/mL is produced as follows:

20 mg pergolide mesylate powder is mixed with 10 mL vehicle for oral suspension (Ora-Plus) and 10 mL vehicle for oral solution (Ora-Sweet). These may be mixed within a 35-mL syringe. Two syringes may be connected and multiple depressions on each syringe can be used until a uniformly suspended mixture of 1 mg/mL is achieved. This formulation should be used within 14 days. Beyond 14 days, degradation occurs that is accelerated by light and warm temperatures. A color change in the formulation is an indication that degradation has occurred.

Stability and Storage

Store in a tightly sealed container, protected from light, and refrigerated or at room temperature. The stability of compounded formulations is described in the Formulations section.

Small Animal Dosage

- Small animal doses have not been established but have been extrapolated from human use, which is to start with 1 mcg/kg (0.001 mg/kg) daily PO and increase the dose gradually by 2 mcg/kg at a time until desired effects are observed.

Large Animal Dosage

Horses

- Low dose: 0.002 mg/kg (2 mcg/kg) q24h PO (1 mg/day for 500 kg horse).
- High dose: 0.006-0.01 mg/kg (6-10 mcg/kg) q24h PO (3-5 mg/day for 500 kg horse).

Start with low dose and increase to high dose gradually if needed.

Regulatory Information

Do not administer to animals intended for food.

Phenobarbital, Phenobarbital Sodium

fee-noe-bar'bih-tahl

Trade and Other Names: Luminal, Phenobarbitone, and generic brands

Functional Classification: Anticonvulsant

Pharmacology and Mechanism of Action

Long-acting barbiturate. Phenobarbital has actions similar to other barbiturates on the CNS. However, phenobarbital will produce anticonvulsant effects without significant other barbiturate effects. As an anticonvulsant it stabilizes neurons by increased chloride conductance via GABA-mediated channels. The pharmacokinetics have been studied in several animal species. Oral absorption is high in most animals. The half-life after administration ranges from 37-75 hours in dogs but longer in some studies. In horses, the half-life is approximately 20 hours, and in cats the half-life ranges from 35 to 56 hours. In all species the half-life may be shorter after multiple administration because of autoinduction of hepatic metabolism.

Indications and Clinical Uses

Phenobarbital is widely used as a drug of choice for treating seizure disorders, such as idiopathic epilepsy, in dogs, cats, horses, and exotic animals. Phenobarbital also has been used as a sedative. Phenobarbital has been effective for the treatment of sialadenosis in dogs caused by submandibular salivary gland enlargement.

Precautionary Information

Adverse Reactions and Side Effects

Most adverse effects are dose related. Phenobarbital causes polyphagia, sedation, ataxia, and lethargy. Some tolerance develops to side effects after initial therapy. Liver enzyme elevations, particularly alkaline phosphatase, are common but may not always be associated with liver pathology. However, hepatotoxicity also has been reported in some dogs and is more likely with high doses. Neutropenia, anemia, and thrombocytopenia have been associated with phenobarbital therapy in dogs. These reactions are likely to be idiosyncratic and recovery may occur if phenobarbital is discontinued. Combinations of phenobarbital and potassium bromide have increased the risk of pancreatitis in dogs. In dogs, superficial necrolytic dermatitis has been associated with phenobarbital administration without concurrent liver pathology. Affected dogs may have high serum concentrations of phenobarbital.

Contraindications and Precautions

Administer with caution to animals with liver disease. Phenobarbital may induce its own metabolism, which shortens the half-life. Therefore, chronic administration may lower plasma concentrations, resulting in increases in the dose requirement. Pregnant animals may have an increase in seizure frequency, and an increase in dose may be necessary.

Drug Interactions

Phenobarbital is one of the most potent drugs for inducing hepatic microsomal metabolizing enzymes. Therefore, many drugs administered concurrently will have lower (and perhaps subtherapeutic) concentrations because of more rapid clearance. Drugs affected may include theophylline, digoxin, corticosteroids, anesthetics, and many others (see Appendix for a list of drugs that affect cytochrome P450 enzymes). Phenobarbital will shorten the half-life of levetiracetam (Keppra) in dogs, which may require higher doses or more frequent administration of levetiracetam. Administration of phenobarbital may lower total T4 thyroid concentrations, but thyroid-stimulating hormone (TSH) and T3 concentrations are unaffected. Solutions are alkaline (pH 9-11); therefore avoid mixing with acidic solutions or drugs that will become unstable at alkaline pH.

Instructions for Use

Adjust dose based on blood levels of phenobarbital. If bromide is used concurrently (sodium or potassium bromide) lower doses of phenobarbital may be used.

Patient Monitoring and Laboratory Tests

Phenobarbital doses should be carefully adjusted via monitoring serum/plasma concentrations. Collect a sample at any time during the dose interval because the timing of the sample is not critical. Avoid the use of plasma separation devices if the tube is to be stored (these devices will cause a false lowering of concentrations). The therapeutic range in dogs is considered 15-40 mcg/mL (65-180 mmol/L). If dogs are also receiving bromide, phenobarbital concentrations in the range of 10-36 mcg/mL have been considered therapeutic. To convert from mmol/L to mcg/mL use a multiplication factor of 0.232. To convert from mcg/mL to mmol/L multiply by 4.3. In cats the optimum range for therapeutic effect is 23-28 mcg/mL (99-120 mmol/L). In horses the optimum range for therapeutic effect is 15-20 mcg/mL (65-86 mmol/L). Monitor liver enzymes periodically in animals receiving phenobarbital because of risk of hepatopathy. However, some liver enzyme elevations may occur—especially with alkaline phosphatase—without liver pathology. Other liver tests may be needed to rule out hepatotoxicity. Liver enzymes usually return to baseline levels 1-5 weeks after discontinuing treatment. Phenobarbital can increase serum triglycerides because of delayed clearance of chylomicrons from the blood and decreased LPL activity. Monitor CBC periodically in animals treated with phenobarbital because of risk of neutropenia, anemia, and thrombocytopenia. Phenobarbital administration will lower other drug concentrations. Phenobarbital did not interfere with the ACTH stimulation test or low-dose dexamethasone suppression test in dogs. It will lower thyroid T4 and free T4 but not T3 and TSH concentrations in dogs.

Formulations

Phenobarbital is available in 15-, 30-, 60-, and 100-mg tablets; 30-, 60-, 65-, and 130-mg/mL injection; and 4-mg/mL oral elixir solution. Because of the bitter taste and alcohol content from the elixir (alcohol based) oral liquid formulation it has been compounded in other vehicles for patients. To prepare this formulation, crush ten 60 mg tablets (600 mg total) and mix with 10 mL Ora Plus and Ora Sweet in a 1:1 ratio for a final concentration of 10 mg/mL. This formulation was stable for 115 days when stored in amber plastic bottles at room temperature.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Phenobarbital is slightly soluble in water (100 mg/mL), but phenobarbital sodium

602 Phenoxybenzamine Hydrochloride

is more soluble (1 g/mL). Solutions prepared in water have an alkaline pH (9-11). Precipitation may occur at lower pH values (avoid mixing with acidic syrups or flavorings). It is subject to hydrolysis in aqueous solutions. However, if prepared in propylene glycol it is stable for 56 weeks. Stability of compounded formulation is described in the Formulations section.

Small Animal Dosage

Dogs

- 2-8 mg/kg q12h PO.
- Status epilepticus: Administer in increments of 10-20 mg/kg IV (to effect).

Cats

- 2-4 mg/kg q12h PO.
- Status epilepticus: Administer in increments of 10-20 mg/kg IV (to effect).

Large Animal Dosage

Horses

- 12 mg/kg q24h PO. Note that in some horses, after initial therapy, higher doses of 12 mg/kg q12h may be needed.
- 5-20 mg/kg IV over 30 minutes (may be diluted in sodium chloride).

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Schedule IV controlled drug

RCI Classification: 2

Phenoxybenzamine Hydrochloride

fen-oks-ih-ben'zah-meen hye-droe-klor'ide

Trade and Other Names: Dibenzyline

Functional Classification: Vasodilator

Pharmacology and Mechanism of Action

Alpha₁-adrenergic antagonist. Phenoxybenzamine binds to and antagonizes alpha₁ receptor on smooth muscle causing relaxation. It is a nonselective alpha-receptor (alpha-1 and alpha-2) antagonist. It affects both alpha-1a and alpha-1b receptors. It is a potent and long-acting vasodilator.

Indications and Clinical Uses

Phenoxybenzamine is used primarily to treat peripheral vasoconstriction. In some animals, it has been used to relax urethral smooth muscle. Urethral smooth muscle is innervated by alpha-1 adrenergic receptors. This property has been used to treat urethral spasm in cats after urethral blockage. Experimentally, phenoxybenzamine has been used to relax vascular smooth muscle in horses for treating laminitis. However, this has not been a common clinical use.

Precautionary Information

Adverse Reactions and Side Effects

Phenoxybenzamine causes prolonged hypotension in animals. Signs of an excessive hypotension may include rapid heart rate, weakness, and syncope. In horses, phenoxybenzamine has caused diarrhea.

Contraindications and Precautions

Use carefully in animals with cardiovascular compromise. Do not use in dehydrated animals. Use carefully in animals with low cardiac output.

Drug Interactions

Phenoxybenzamine is a potent alpha-adrenergic agonist. It will compete with other drugs that act on the alpha-receptor. It will cause vasodilation and should be used cautiously with drugs that may cause vasodilation or depress the heart.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or limited experimental experience in animals.

Patient Monitoring and Laboratory Tests

Phenoxybenzamine can lower blood pressure significantly. Monitor patient's blood pressure and heart rate if possible during treatment.

Formulations

Phenoxybenzamine is available in 10-mg capsules. Smaller-sized tablets for cats have been prepared by compounding pharmacies.

Stability and Storage

Phenoxybenzamine is only slightly soluble in water but soluble in propylene glycol and ethanol. It is not stable in aqueous solutions and undergoes rapid degradation; therefore, it may not be stable in some compounded formulations. Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 0.25 mg/kg q8-12h or 0.5 mg/kg q24h PO.
- For presurgical treatment of pheochromocytoma, 0.6 mg/kg q12h (range is 1-2 mg/kg/day), given 2 weeks prior to surgery to stabilize blood pressure.

Cats

- 2.5 mg/cat q8-12h or 0.5 mg/kg q12h PO. (Doses as high as 0.5 mg/kg IV have been used to relax urethral smooth muscle.)

Large Animal Dosage

Horses

- 1 mg/kg q24h IV or 0.7 mg/kg q6h PO.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Phentolamine Mesylate

fen-tole'ah-meen mess'ih-late

Trade and Other Names: Regitine and Rogitine (in Canada)

Functional Classification: Vasodilator

Pharmacology and Mechanism of Action

Nonselective alpha-adrenergic blocker. Vasodilator. Phentolamine blocks both alpha₁- and alpha₂-receptors on smooth muscle.

Indications and Clinical Uses

Phentolamine is a potent vasodilator and is used primarily to treat acute hypertension.

Precautionary Information

Adverse Reactions and Side Effects

Phentolamine may cause excess hypotension with high doses or in animals that are dehydrated and may cause tachycardia.

Contraindications and Precautions

Use carefully in animals with cardiovascular compromise. Do not use in dehydrated animals. Use carefully in animals with low cardiac output.

Drug Interactions

Phentolamine is an alpha-adrenergic agonist. It will compete with other drugs that act on the alpha-receptor. It will cause vasodilation and should be used cautiously with drugs that may cause vasodilation or depress the heart.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Titrate dose for each patient to produce desired vasodilation.

Patient Monitoring and Laboratory Tests

Phentolamine can lower blood pressure significantly. Monitor patient's blood pressure and heart rate if possible during treatment.

Formulations

Phentolamine is available in 5-mg vials for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.02-0.1 mg/kg IV.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Phenylbutazone

fen-ill-byoo'tah-zone

Trade and Other Names: Butazolidin, PBZ, and generic brands

Functional Classification: Nonsteroidal anti-inflammatory drug (NSAID)

Pharmacology and Mechanism of Action

Phenylbutazone and other NSAIDs produce analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the cyclo-oxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Phenylbutazone, using in vitro assays, is a nonselective inhibitor of COX-1 and COX-2. Phenylbutazone has a half-life of 36-65 days in cattle, 5 hours in horses, and 4-6 hours in dogs.

Indications and Clinical Uses

The major use of phenylbutazone is in horses for musculoskeletal pain and inflammation, arthritis, soft tissue injury, and racing injuries. It is approved in both dogs and horses. The duration of action in horses after a single administration is approximately 24 hours. Phenylbutazone is approved for use in dogs (and cats in Europe); however, the use in small animals is not common because of the availability of other drugs.

Precautionary Information

Adverse Reactions and Side Effects

In horses, GI ulcers have been documented. Ulcers are more likely as the dose increases and in animals undergoing extensive training. Phenylbutazone is generally well tolerated in dogs, but there are no data for cats. In these animals, adverse effects possible are GI toxicity such as gastritis and gastric ulcers. Phenylbutazone is also associated with renal injury. In horses that are dehydrated or have renal compromise, phenylbutazone can cause ischemia and renal papillary necrosis. Phenylbutazone is rarely used in people because it has caused bone marrow depression. This effect also has been observed in dogs. In experimental horses, phenylbutazone (4.4 mg/kg q12h for 14 days) decreased proteoglycan synthesis in articular cartilage.

Contraindications and Precautions

Do not administer injectable formulation IM. Do not administer to animals prone to GI ulcers or with compromised renal function. Do not administer with other ulcerogenic drugs, such as corticosteroids.

Drug Interactions

The use with other NSAIDs or with corticosteroids should be done cautiously because of the risk of GI injury. Corticosteroids have been shown to exacerbate the GI adverse effects. Phenylbutazone has been used in some horses in

combination with flunixin meglumine (NSAID “stacking”), but this combination may increase risk of hypoalbuminemia and decreased total serum protein. Phenylbutazone will interfere with the action of furosemide in horses. Some NSAIDs also may interfere with the action of angiotensin-converting enzyme (ACE) inhibitors.

Instructions for Use

Doses are based primarily on manufacturer’s recommendations and clinical experience. Although a range of 4.4-8.8 mg/kg per day has been administered to horses, studies have not shown an advantage for the higher dose, and the higher dose of 8.8 mg/kg per day is more likely to cause GI injury, hypoalbuminemia, and neutropenia. Combining other NSAIDs with phenylbutazone, such as flunixin (referred to as “stacking”), may improve response when treating lameness and other musculoskeletal problems when compared to phenylbutazone alone. However, this practice must be weighed against an increased risk of GI injury.

Patient Monitoring and Laboratory Tests

Monitor CBC for signs of bone marrow toxicity with chronic use.

Formulations

Phenylbutazone is available in 100-mg, 200-mg, 400-mg and 1-g tablets (bolus); oral paste for horses; and 200 mg/mL (20%) solution for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Phenylbutazone is not water soluble. It should not be compounded in aqueous vehicles.

Small Animal Dosage

Dogs

- 15-22 mg/kg q8-12h (44 mg/kg/day; 800 mg/dog maximum) PO or IV.

Cats

- 6-8 mg/kg q12h IV or PO.

Large Animal Dosage

Horses

- 4.4-8.8 mg/kg/day (generally 2 g to 4 g per horse) PO. It is not recommended to use the highest dose for more than 48-96 hours.
- Injection: 2.2-4.4 mg/kg/day for 48-96 hours. Give injections IV only as intramuscular injections will cause tissue irritation.

Cattle

- 17-25 mg/kg loading dose, then 2.5-5 mg/kg q24h or 10-14 mg/kg q48h PO or IV. (See regulatory restrictions in cattle.)

Pigs

- 4 mg/kg q24h IV.

Regulatory Information

Phenylbutazone is prohibited from use in female dairy cattle younger than 20 months of age. Other withdrawal times have not been established for animals intended for food. However, recommended withdrawal times are 15 days in swine,

40-50 days for slaughter in cattle (oral or IV), and extended to 55 days in cattle if administered IM.

RCI Classification: Not classified

Phenylephrine Hydrochloride

fen-ill-ef'rin hye-droe-klor'ide

Trade and Other Names: Neo-synephrine

Functional Classification: Vasopressor

Pharmacology and Mechanism of Action

Alpha₁-adrenergic receptor agonist. Phenylephrine will stimulate alpha₁-receptors and cause smooth muscle contraction, primarily in vascular smooth muscle to cause vasoconstriction. It may be applied topically (e.g., mucous membranes) to constrict superficial blood vessels.

Indications and Clinical Uses

Phenylephrine is used primarily in critical care patients or during anesthesia to increase peripheral resistance and increase blood pressure. Phenylephrine is also used commonly as topical vasoconstrictor (as in nasal decongestants or for ophthalmic use).

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects related to excessive stimulation of alpha₁-receptor (prolonged peripheral vasoconstriction). Reflex bradycardia may occur. Prolonged topical use may cause tissue inflammation.

Contraindications and Precautions

Do not use in animals with compromised cardiovascular status. It will cause vasoconstriction and can increase blood pressure.

Drug Interactions

Phenylephrine will potentiate other alpha₁-agonists. Use cautiously with alpha-2 agonists such as detomidine, dexmedetomidine, or xylazine.

Instructions for Use

Phenylephrine has a rapid onset and short duration of action.

Patient Monitoring and Laboratory Tests

When administered IV, monitor blood pressure and heart rate.

Formulations

Phenylephrine is available in 10-mg/mL injection, 1% nasal solution, and 2.5 and 10% ophthalmic solutions.

Stability and Storage

Phenylephrine is soluble in water and may be mixed in intravenous solutions. It is also soluble in ethanol. It is subject to oxidation and will turn a darker color in

608 Phenylpropanolamine Hydrochloride

some solutions, especially alkaline solutions. Discard formulations that turn a dark color. Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 10 mcg/kg (0.01 mg/kg) q15min IV, as needed or 0.1 mg/kg q15min IM or SQ.
- Constant rate infusion (CRI): 10 mcg/kg (0.01 mg/kg) IV, followed by 3 mcg/kg/min IV.

Large Animal Dosage

No large animal dose is available.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Phenylpropanolamine Hydrochloride

fen-ill-proe-pah-nole'ah-meen hye-droe-klor'ide

Trade and Other Names: PPA, Proin-ppa, UriCon, and Propalin (veterinary preparations)

Functional Classification: Adrenergic agonist

Pharmacology and Mechanism of Action

Adrenergic agonist. Sympathomimetic. Phenylpropanolamine nonselectively acts as an agonist for the alpha-adrenergic and beta-adrenergic receptor. These receptors are found throughout the body, such as on sphincters, blood vessels, smooth muscle, and heart. The most profound effects observed with phenylpropanolamine are on vascular smooth muscle (vasoconstriction) and urethral smooth muscle (increased tone of urethra). The half-life in dogs is 4-7 hours. However, the duration of effect may be at least 8-12 hours and as long as 24 hours in some animals. A longer interval of administration may prevent some down-regulation of alpha receptors.

Indications and Clinical Uses

Phenylpropanolamine (PPA) has been used as a decongestant, as a mild bronchodilator, and to increase tone of the urinary sphincter. Pseudoephedrine and ephedrine are related drugs that produce similar alpha-receptor and beta-receptor effects. The most common use in animals is for treating urinary incontinence. The mechanism for this action appears to be via stimulating receptors on the sphincter. It has also been used to treat priapism (persistent erection) in dogs. Abuse potential and adverse effects have limited the routine use as a decongestant and appetite suppressant in human medicine. Most of the human preparations have been removed from the market and the only forms readily available are those marketed for veterinary medicine.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are attributed to excess stimulation of adrenergic (alpha and beta) receptors. Side effects include tachycardia, cardiac effects, CNS excitement, restlessness, and appetite suppression. There are reports of adverse effects caused by PPA in people. In particular, it has caused problems with blood pressure and increased risk of strokes. Such a concern should also apply to animals, but there have been no specific reports of these problems in animals.

Contraindications and Precautions

Use cautiously in any animal with cardiovascular disease. PPA has been abused by people and used as a recreational drug.

Drug Interactions

PPA and other sympathomimetic drugs can cause increased vasoconstriction and changes in heart rate. Use cautiously with other vasoactive drugs and alpha-2 agonists such as dexmedetomidine and xylazine. Use cautiously with other drugs that may lower seizure threshold. Use of inhalant anesthetics with PPA may increase cardiovascular risk. Do not use with tricyclic antidepressants (TCAs) or monoamine oxidase inhibitors (MAOIs; e.g., selegiline or amitraz).

Instructions for Use

Although frequency of administration has been every 8-12 hours in most cases, there is evidence that an interval of every 24 hours in dogs at a dose of 1.5 mg/kg is just as effective. In some animals, pseudoephedrine has been substituted for PPA with good success.

Patient Monitoring and Laboratory Tests

Monitor heart rate and blood pressure in animals receiving treatment. Animals with urinary incontinence should be checked periodically for presence of UTIs.

Formulations

Phenylpropanolamine is available in 25, 50, and 75 flavored tablets; 25-mg vanilla-flavored liquid, and 50-mg scored tablets (veterinary preparations). Human formulations of 15-, 25-, 30-, and 50-mg tablets are no longer available, but compounded veterinary formulations have become available.

Stability and Storage

Because human preparations have been taken off the market, the only formulations currently available are nonapproved compounded preparations and other unapproved forms. The stability and potency of these preparations have not been evaluated by the FDA.

Small Animal Dosage

Dogs

- 1 mg/kg q8h PO. Increase dose to 1.5-2 mg/kg q8h PO, if necessary.
In some animals it may be possible to decrease frequency to q12h, and q24h, PO.

Cats

- No dose has been determined. A dose of 1 mg/kg q12h PO has been used (extrapolated from the canine use), and the dose has been adjusted as needed.

610 Phenytoin, Phenytoin Sodium

Large Animal Dosage

No large animal dose is available.

Regulatory Information

There are no formulations currently marketed in the US for human use because of abuse potential and adverse cardiovascular events. Veterinary formulations currently are not regulated.

RCI Classification: 3

Phenytoin, Phenytoin Sodium

fen-ih-toe-in

Trade and Other Names: Dilantin

Functional Classification: Anticonvulsant, antiarrhythmic

Pharmacology and Mechanism of Action

Anticonvulsant. Depresses nerve conduction via blockade of sodium channels. Phenytoin is also classified as a Class I cardiac antiarrhythmic. In cardiac tissue, phenytoin increases the threshold for triggering ventricular arrhythmias. It also decreases conduction velocity and does not shorten the refractory period as much as lidocaine.

Indications and Clinical Uses

Phenytoin is commonly used as an anticonvulsant in people, but it is not effective in dogs and not used in cats. In dogs, elimination is so rapid that dosing is impractical. Phenytoin is used in horses for treating ventricular arrhythmias, controlling myotonia, rhabdomyolysis, hyperkalemic periodic paresis, and stringhalt.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include sedation, gingival hyperplasia, skin reactions, and CNS toxicity. In horses, at high doses recumbency and excitement have been observed. Sedation in horses may be an initial sign of high plasma concentrations. Monitoring plasma concentrations in horses can prevent adverse effects.

Contraindications and Precautions

Do not administer to pregnant animals.

Drug Interactions

Phenytoin will interact with drugs undergoing hepatic metabolism. Phenytoin is a potent cytochrome P450 enzyme inducer. When used with cytochrome P450 inhibitors, increased levels of phenytoin may occur.

Instructions for Use

Because of short half-life and poor efficacy in dogs and questionable safety in cats, other anticonvulsants are used as the first choice before phenytoin.

Patient Monitoring and Laboratory Tests

Therapeutic drug monitoring can be performed; however, therapeutic concentrations have not been established for dogs and cats. In horses, effective plasma

concentrations are 5-20 mcg/mL (average 8.8 mcg/mL). Therapy should be aimed at producing concentrations above 5 mcg/mL in horses.

Formulations

Phenytoin is available in 25-mg/mL oral suspension; 30- and 100-mg capsules (sodium salt); 50 mg/mL injection (sodium salt) and 50 mg chewable tablets.

Stability and Storage

Store protected from light at room temperature. Phenytoin sodium will absorb carbon dioxide and must be kept in a tight container. Phenytoin is practically insoluble in water, but phenytoin sodium has a solubility of 15 mg/mL. It is soluble in ethanol and propylene glycol. pH of phenytoin is 10-12, and it may not be compatible with acidic solutions. It may precipitate from solution if mixed with solutions at a lower pH. Protect from freezing.

Small Animal Dosage

Dogs

- Anticonvulsant: 20-35 mg/kg q8h.
- Antiarrhythmic: 30 mg/kg q8h PO or 10 mg/kg IV over 5 min.

Cats

Do not use.

Large Animal Dosage

Horses

- Initial bolus of 20 mg/kg q12h PO, for four doses, followed by 10-15 mg/kg q12h PO. A single IV dose in horses of 7.5-8.8 mg/kg can be used followed by oral maintenance doses.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Physostigmine

fye-zoe-stig'meen

Trade and Other Names: Antilirium

Functional Classification: Anticholinesterase

Pharmacology and Mechanism of Action

Cholinesterase inhibitor. Anticholinesterase drug. This drug inhibits the enzyme that breaks down acetylcholine. Therefore it prolongs the action of acetylcholine at the synapse. The major difference between physostigmine and neostigmine or pyridostigmine is that physostigmine crosses the blood-brain barrier, and the others do not.

Indications and Clinical Uses

Physostigmine is used as an antidote for anticholinergic intoxication and as a treatment (antidote) for neuromuscular blockade. It has also been used as a

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treatment of ileus and urinary retention (such as postoperative urine retention) by increasing the tone of the bladder smooth muscle.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects caused by the cholinergic action result from inhibition of cholinesterase. These effects can be seen in the GI tract as diarrhea and increased secretions. Other adverse effects can include miosis, bradycardia, muscle twitching or weakness, and constriction of bronchi and ureters. Adverse effects can be treated with anticholinergic drugs such as atropine.

Contraindications and Precautions

Do not administer with choline esters such as bethanechol.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Physostigmine is indicated primarily only for treatment of intoxication. If longer-term or routine systemic use of an anticholinesterase drug is needed, neostigmine and pyridostigmine are used because they have fewer adverse effects. When used, frequency of dose may be increased based on observation of effects.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm and GI signs.

Formulations

Physostigmine is available in a 1-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.02 mg/kg q12h IV.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Phytonadione

fye-toe-nah-dye'one

Trade and Other Names: AquaMEPHYTON, Mephyton. Veta-K1, Vitamin K1, Phylloquinone, and Phytomenadione

Functional Classification: Vitamin

Pharmacology and Mechanism of Action

Vitamin K supplement. Phytonadione and phytonadione are synthetic lipid-soluble forms of vitamin K₁. (Phytonadione is the British spelling of Phytonadione.) Menadiol is vitamin K₄, which is a water-soluble derivative converted in the body to vitamin K₃ (menadione).

Vitamin K₁ is a fat-soluble vitamin used to treat coagulopathies caused by anticoagulant toxicosis (warfarin or other rodenticides). These anticoagulants deplete vitamin K in the body, which is essential for synthesis of clotting factors. Administration of vitamin K, in its various formulations, can be used to reverse the effect of anticoagulant toxicity.

Indications and Clinical Uses

Phytonadione is used to treat coagulopathies caused by anticoagulant toxicosis (warfarin or other rodenticides). In large animals, it is used to treat sweet clover poisoning.

Precautionary Information

Adverse Reactions and Side Effects

In people, a rare hypersensitivity-like reaction has been observed after rapid intravenous injection. Signs resemble anaphylactic shock. These signs also have been observed in animals. To avoid anaphylactic reactions, do not administer IV.

Contraindications and Precautions

Accurate diagnosis to rule out other causes of bleeding is suggested. Other forms of vitamin K may not be as rapidly acting as vitamin K₁; therefore consider using a specific preparation. To avoid anaphylactic reactions, do not administer IV.

Drug Interactions

No drug interactions are reported.

Instructions for Use

Consult poison control center for specific protocol if specific rodenticide is identified. Use vitamin K₁ for acute therapy of toxicity because it is more highly bioavailable. Administer with food to enhance oral absorption. If an injection is used, it can be diluted in 5% dextrose or 0.9% saline but not other solutions. The preferred injectable route is SQ, but IM can also be used. Although vitamin K₁ veterinary labels have listed the intravenous route for administration, these labels have not been approved by the FDA. Therefore, avoid intravenous administration of vitamin K₁.

Patient Monitoring and Laboratory Tests

Monitoring bleeding times in patients is essential for accurate dosing of vitamin K₁ preparations. When treating long-acting rodenticide poisoning, periodic monitoring of the bleeding times is suggested.

Formulations

Phytonadione is available in 5-mg tablets (Mephyton) and 25-mg capsules (Veta-K1).

Phytonadione (AquaMEPHYTON) is available in a 2- or 10-mg/mL injection.

Stability and Storage

Store in a tightly sealed container at room temperature. It is light sensitive and should be protected from light. Phytonadione is practically insoluble in water.

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However, it is soluble in oils and slightly soluble in ethanol. Do not mix with aqueous solutions. If mixed as a suspension for oral use, administer soon after preparation. Do not freeze.

Small Animal Dosage

Dogs and Cats

- Treatment of short-acting rodenticides: 1 mg/kg/day for 10-14 days IV, SQ, or PO.
- Treatment of long-acting rodenticides: 2.5-5 mg/kg/day for 3-4 weeks IM, SQ, or PO.

Birds

- 2.5-5 mg/kg q24h.

Large Animal Dosage

Cattle, Calves, Horses, Sheep, and Goats

- 0.5-2.5 mg/kg SQ or IM.

Regulatory Information

Withdrawal times are not established for animals that produce food. It is anticipated that milk and meat withdrawal times will be short. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Pimobendan

pim-oh-ben'dan

Trade and Other Names: Vetmedin

Functional Classification: Cardiac inotropic agent

Pharmacology and Mechanism of Action

Pimobendan is both a positive inotrope and a vasodilator. The vasodilator effects occur via inhibition of phosphodiesterase III. Phosphodiesterase III is the enzyme that degrades cyclic adenosine monophosphate (cAMP); therefore, its action is to increase intracellular concentrations of cAMP. There may be some inhibition of phosphodiesterase V in the pulmonary circulation. The inotropic effects of pimobendan are attributed to its action as a calcium sensitizer rather than the phosphodiesterase inhibition. By acting as a calcium sensitizer, it increases the interaction of troponin C with contractile proteins and acts as a inotropic agent. The benefits in heart failure are caused by both positive inotropic effects and vasodilating properties. There may be other beneficial effects that include anti-inflammatory activity, increased sensitivity of baroreceptors, increased lusitropy, and decreased platelet aggregation. The cardiovascular effects occur after 1 hour and persist for 8-12 hours after administration. Pimobendan is absorbed best in an acidic environment. Fluctuating pH conditions in stomach and administration with food may produce inconsistent oral absorption.

Indications and Clinical Uses

Pimobendan is indicated for use in dogs for treatment of CHF. It has been used in dogs with either valvular insufficiency or cardiomyopathy. It is considered by many cardiologists as an essential initial treatment for dilated cardiomyopathy in dogs.

When used in dogs, it has improved signs of heart failure and increased survival. When used in dogs, it may be administered with diuretics and angiotensin-converting enzyme (ACE) inhibitors. In trials in North America, pimobendan showed significant improvement compared to placebo in dogs treated with an ACE inhibitor and a diuretic. It has been used with furosemide, ACE inhibitors, and spironolactone. It has been associated with improvement in clinical signs in cats with heart failure as part of a therapeutic regimen that may include other drugs (e.g., furosemide). When administered at 1.25 mg/cat q12h, it has been well tolerated.

Precautionary Information

Adverse Reactions and Side Effects

Pimobendan is potentially arrhythmogenic, but this effect (e.g., atrial fibrillation or ventricular arrhythmias) has been rare and seen primarily in animals with severe underlying cardiac disease. At doses of 0.25-0.5 mg/kg in dogs, pimobendan did not activate the renin-angiotensin-aldosterone system (RAAS), but if furosemide is added to treatment, some activation of the RAAS may occur.

Contraindications and Precautions

Use cautiously in animals prone to cardiac arrhythmias. Compounded formulations will not achieve the same absorption profile in dogs as the proprietary form. There is a critical pH at which the oral absorption is enhanced, and some compounded formulations may lack excipients to attain this effect.

Drug Interactions

Use cautiously with other phosphodiesterase inhibitors such as theophylline, pentoxifylline, and sildenafil (Viagra) and related drugs. Sildenafil is a phosphodiesterase V inhibitor; theophylline is a phosphodiesterase IV inhibitor. Pimobendan is insoluble unless in an acidic environment and it is difficult to mix pimobendan into a solution.

Instructions for Use

Follow label instruction for use. Evaluate stage of heart failure in animals before use. Consider the addition of other drugs such as angiotensin-converting enzyme inhibitors (ACE inhibitors), spironolactone, furosemide, and digoxin in animals as the severity of the heart disease increases. If furosemide is used concurrently with pimobendan, consider the addition of an ACE inhibitor (e.g., enalapril, benazepril) or aldosterone antagonist (e.g., spironolactone) to inhibit RAAS activation.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and rhythm during use.

Formulations

Pimobendan is available in chewable tablets of 1.25, 2.5 and 5 mg. In Europe, pimobendan is available in 2.5- and 5-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Acidic pH conditions are important for the stability of the formulation and to ensure dissolution.

Small Animal Dosage

Dogs

- 0.25-0.3 mg/kg q12h, PO.

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Cats

- 1.25 mg/cat q12h PO (0.1-0.3 mg/kg).

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Piperacillin Sodium

pih'per-ah-sill'in soe'dee-um

Trade and Other Names: Pipracil and Zosyn

Functional Classification: Antibacterial, beta-lactam

Pharmacology and Mechanism of Action

Beta-lactam antibiotic of the acylureidopenicillin class. Like other beta-lactams, piperacillin binds penicillin-binding proteins (PBP) that weaken or interfere with cell wall formation. After binding to PBP, the cell wall weakens or undergoes lysis. Like other beta-lactams, this drug acts in a time-dependent manner (i.e., it is more effective when drug concentrations are maintained above the minimum inhibitory concentration [MIC] values during the dose interval). Compared to other beta-lactam antibiotics, piperacillin has good activity against *Pseudomonas aeruginosa*. It also has good activity against streptococci, but is not active against methicillin-resistant Staphylococcus. Piperacillin has a short half-life in animals and must be given by injection (usually IV), which limits its usefulness. Some formulations of piperacillin also contain tazobactam (Zosyn), which is a beta-lactamase inhibitor and increases the spectrum to include beta-lactamase strains of gram-negative and gram-positive bacteria.

Indications and Clinical Uses

Piperacillin has similar activity as ampicillin, but it is extended to include many organisms that otherwise are resistant to ampicillin, such as *Pseudomonas aeruginosa* and other gram-negative bacilli. The in vitro activity against some gram-negative bacteria is enhanced when administered with an aminoglycoside (e.g., gentamicin or amikacin).

Precautionary Information

Adverse Reactions and Side Effects

Allergy to penicillin is the most common adverse effect. High doses may inhibit platelet function.

Contraindications and Precautions

Do not use in patients allergic to penicillin drugs. High doses contribute to the sodium load in a patient.

Drug Interactions

Do not mix in vials or syringes with other drugs.

Instructions for Use

Piperacillin is combined with tazobactam (beta-lactamase inhibitor) in Zosyn, which increases the spectrum to include beta-lactamase-producing strains of *Staphylococcus* and gram-negative bacteria. Ticarcillin has a similar spectrum of activity and may be used as a substitute for piperacillin.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are ≤ 64 mcg/mL for *Pseudomonas aeruginosa* and ≤ 16 mcg/mL for all other gram-negative organisms.

Formulations

Piperacillin is available in 2-, 3-, 4-, and 40-g vials for injection.

Stability and Storage

Reconstituted solution should be used within 24 hours or 7 days if refrigerated.

Small Animal Dosage

Dogs and Cats

- 40 mg/kg q6h IV or IM.

Large Animal Dosage

No doses have been reported for large animals. (Ticarcillin is usually used for the same indications in horses.)

Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of rapid elimination, it is anticipated that withdrawal times will be similar to that of other beta-lactams such as ampicillin.

For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Piperazine

pih-peer'e-zeen

Trade and Other Names: Pipa-Tabs and generic brands

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic compound. Piperazine produces neuromuscular blockade in parasite through selective antagonism of GABA receptors, resulting in opening of chloride channels, hyperpolarization of parasite membrane, and paralysis of worms. Efficacy is limited primarily to roundworms. In horses it is active against small strongyles and roundworms.

Indications and Clinical Uses

Piperazine is a common antiparasitic drug and is widely available, even OTC. It is used primarily for treatment of roundworm (ascarid) infections in animals.

Precautionary Information

Adverse Reactions and Side Effects

Piperazine is remarkably safe in all species but can cause ataxia, muscle tremors, and changes in behavior.

Contraindications and Precautions

No contraindications in animals. It may be used in all ages.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Piperazine is a widely used antiparasitic drug with a wide margin of safety. It may be used in combination with other antiparasitic drugs.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Piperazine is available in an 860-mg powder; 140-mg capsules; 50- and 250-mg tablets; and 128-, 160-, 170-, 340-, 510-, and 800-mg/mL oral solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 44-66 mg/kg administered once PO.

Large Animal Dosage

Horses and Pigs

- 110 mg/kg PO in the drinking water as the sole water source.
- Oral solution (horses): 30 mL (1 ounce) of 17% piperazine solution administered PO for each 45 kg of body weight.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Piroxicam

peer-oks'ih-kam

Trade and Other Names: Feldene and generic brands

Functional Classification: Nonsteroidal anti-inflammatory drug (NSAID)

Pharmacology and Mechanism of Action

Piroxicam is an NSAID of the oxicam class. Clinical effects are similar to other NSAIDs (see meloxicam). These drugs appear to have analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the cyclo-oxygenase enzyme (COX). The COX enzyme

exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Piroxicam, using in vitro assays, is somewhat more selective for COX-2 than COX-1. In animals, it is not certain that the specificity for COX-1 or COX-2 is related to efficacy or safety. Piroxicam also may have some antitumor or tumor-preventative effects and is used in some anticancer protocols. Piroxicam has a longer half-life than other NSAIDs in dogs, with a half-life of 35-40 hours and near 100% oral absorption. The half-life is shorter in other species, with a half-life in cats of 13 hours and average oral absorption of 89% and a half-life in horses of 3-4 hours.

Indications and Clinical Uses

Piroxicam is primarily used to treat pain and inflammation associated with arthritis and other musculoskeletal conditions. It is not used as much for these conditions as other approved NSAIDs for animals. Another use in dogs and cats has been as an adjunct for treating cancer. This use is based on reports of its activity for treating or suppressing some tumors, including transitional cell carcinoma of the bladder, squamous cell carcinoma, and mammary adenocarcinoma. Piroxicam has been used in combination with cisplatin to treat oral malignant melanoma and oral squamous cell carcinoma in dogs (0.3 mg/kg).

Precautionary Information

Adverse Reactions and Side Effects

Elimination of piroxicam is slow. At 0.3 mg/kg q24h, PO, adverse reactions have been observed in dogs, and an administration interval of every 48 hours should be considered. Adverse effects are primarily GI toxicity (e.g., gastric ulcers). Renal toxicity also is a risk, especially in animals prone to dehydration or that have compromised renal function. Toxic epidermal necrolysis has been reported in some dogs. Piroxicam has been administered to dogs and cats as a treatment for cancer with few adverse effects, but GI erosions and ulcers are possible.

Contraindications and Precautions

Use cautiously in dogs because the long half-life may increase risk of GI ulcers if administered once daily. The human formulation is too large a dose for most dogs and should be reformulated to avoid overdose. Warn pet owners about overdoses that could produce GI ulceration. Do not administer to animals prone to GI ulcers. Do not administer to pregnant animals. Use cautiously in any animal with renal disease or if administered with other drugs that may injure the kidney, such as cisplatin.

Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the gastrointestinal adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors.

Instructions for Use

Most experience with dosing has been accumulated from studies in which dogs were treated with piroxicam for transitional cell carcinoma of the bladder. Some of these dogs tolerated piroxicam better, with respect to GI toxicity, if the drug was administered with misoprostol. Piroxicam has also been used in dogs for treatment of squamous cell carcinoma.

Patient Monitoring and Laboratory Tests

Piroxicam has the potential of inducing GI ulceration. Monitor for signs of vomiting, bleeding, and lethargy. If bleeding is suspected, monitor patient's hematocrit or CBC. Monitor renal function in treated animals.

Formulations

Piroxicam is available in 10-mg capsules.

Stability and Storage

Exposure to light results in photodegradation. Piroxicam is only slightly soluble in water. It is soluble in basic solutions and some organic solvents. Compounded formulations made for small animals may be stable for only 48 hours. Although an IV formulation is not available commercially, a 2-mg/mL solution has been prepared from mixing the pure powder with 0.1 N NaOH and found to be stable if stored in a glass vial, refrigerated, and protected from light.

Small Animal Dosage

Dogs

- 0.3 mg/kg q48h PO.
- Cancer treatment: Dogs also have tolerated 0.3 mg/kg q24h PO.

Cats

- 0.3 mg/kg q24h PO, or alternatively 1 mg per cat, q24h, PO.

Large Animal Dosage

There is insufficient evidence to recommend doses for large animals. Single doses of 0.2 mg/kg PO have been administered to horses without any adverse effects.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Plicamycin

plye-kah-mye'sin

Trade and Other Names: Mithracin and Mithramycin

Functional Classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. The action of plicamycin is to complex with DNA in the presence of divalent cations and inhibit DNA and RNA synthesis. It lowers serum calcium and may have direct action on osteoclasts to decrease serum calcium.

Indications and Clinical Uses

Plicamycin is used in cancer protocols for carcinomas and treatment of hypercalcemia. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. In people, hypocalcemia and GI toxicity have been reported. Plicamycin may cause bleeding problems.

Contraindications and Precautions

Do not use with drugs that may increase the risk of bleeding (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], heparin, or anticoagulants).

Drug Interactions

No drug interactions have been reported.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

Monitor serum calcium concentrations.

Formulations

Plicamycin is available in a 2.5-mg vial for injection and 0.5-mg/mL when diluted.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- Antihypercalcemic: 25 mcg/kg/day IV (slow infusion) over 4 hours.
- Antineoplastic (dogs): 25-30 mcg/kg/day IV (slow infusion) for 8-10 days.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Polyethylene Glycol Electrolyte Solution

pahl-ee-eth"ill-eeen glye'kole

Trade and Other Names: GoLytely, PE.G., Colyte, and Co-Lav

Functional Classification: Laxative

Pharmacology and Mechanism of Action

Saline cathartic. Polyethylene glycol electrolyte solution is a nonabsorbable compound that increases water secretion into bowel via osmotic effect. These

622 Polyethylene Glycol Electrolyte Solution

isosmotic liquids pass through the bowel without absorption. Oral administration produces a profound cathartic effect.

Indications and Clinical Uses

Polyethylene glycol electrolyte solution is a cathartic that is used primarily for evacuating the bowel and cleansing of the intestine prior to endoscopy and surgical procedures. It is administered PO and will induce a rapid osmotic cathartic effect. It is effective for bowel cleansing, but it requires high volumes to be effective. In some human patients, smaller volumes can be used if it is combined with another laxative, such as bisacodyl.

Precautionary Information

Adverse Reactions and Side Effects

Water and electrolyte loss with high doses or prolonged use are common. Large volumes required may cause nausea.

Contraindications and Precautions

Do not administer to animals that are dehydrated because it may cause fluid and electrolyte loss. It is not indicated for chronic use.

Drug Interactions

No specific drug interactions.

Instructions for Use

Used for bowel evacuation prior to surgical or diagnostic procedures. Large volumes are required. In human patients, administration of only half the volume can be used if taken with bisacodyl (one to four tablets) 2 hours prior to procedure. This combination is called HalfLyte^{ly}.

Patient Monitoring and Laboratory Tests

Monitor electrolytes if it is administered repeatedly.

Formulations

Polyethylene glycol electrolyte is an oral solution. Preparations contain polyethylene glycol (PEG) 3350, sodium chloride, potassium chloride, sodium bicarbonate, and sodium sulfate.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 25 mL/kg, repeat in 2-4 hours PO.

Large Animal Dosage

Horses and Cattle

- Via stomach tube: 500 mL to 4 L once PO.

Regulatory Information

No withdrawal times necessary.

Polymyxin B Sulfate

poly mix-in bee

Trade and Other Names: Generic

Functional Classification: Antibacterial agent

Pharmacology and Mechanism of Action

Antibiotic, antibacterial agent. Polymyxin B is from a group of polypeptide antibiotics. Polymyxins are basic surface-active cationic detergents that interact with the phospholipid within the cell membrane. They are capable of penetrating the cell membrane of bacteria and disrupting the structure. This action subsequently induces permeability changes within the cell that result in cell death, giving polymyxins bactericidal properties. Polymyxins contain seven amino acids in a cyclic configuration and have a molecular weight of more than 1000. Other polymyxins have been named A, B, C, D, E, and M, but only B and E in their sulfate salt forms are used clinically. Polymyxin B sulfate is a mixture of polymyxin B1 and polymyxin B2. Polymyxin E is more commonly known as colistin, which is also used systemically for some infections. Polymyxin B has a pKa ranging from 8 to 9 derived from the organism *Bacillus polymyxa*. It is available in many topical formulations, often in formulations considered as “triple-antibiotics.” The injectable formulation of polymyxin B sulfate is a sulfate salt of two forms: Polymyxins B1 and B2. It is available in formulations of not less than 6000 polymyxin B units per milligram (as the anhydrous base). Polymyxins are not absorbed from the GI tract when administered orally but are rapidly absorbed when given parenterally and have 70%-90% plasma protein binding.

Indications and Clinical Uses

Polymyxin B for injection is in powder form suitable for preparation of sterile solutions for intramuscular, intravenous drip, intrathecal, or ophthalmic use. Polymyxin B is most often administered as a topical ointment for managing infections. It is one of the components of “triple antibiotic” ointments used for topical use. Systemically, polymyxin has been used to treat infections that are resistant to other drugs. Bacteria such as *Pseudomonas aeruginosa* and *Acinetobacter* may develop resistance to other drugs that can be treated only with drugs such as colistin and polymyxin. In people, polymyxin B is used to treat UTI, meningitis, and septicemia. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness in animals for treating bacterial infections. In veterinary medicine—particularly horses—polymyxin has been used because of its property to bind bacterial endotoxin in the blood and prevent signs of bacterial septicemia. Infusions ranging from 1000 to 10,000 units per kg (a common dose is 6000 units/kg, equivalent to 1 mg/kg) administered every 8 hours have been shown to be safe and effective for treating endotoxemia in horses. The action is attributed to the cationic portion of polymyxin B binding to the anionic lipid A portion of this endotoxin. This effectively renders the endotoxin inactive, thereby preventing most of the adverse effects that gram-negative endotoxin has on the mammalian body.

Precautionary Information

Adverse Reactions and Side Effects

IM injections will cause pain. Because of its ability to bind to phospholipid membranes and cause injury, the most severe adverse reaction is caused by renal injury. At the dose used for treating bacterial endotoxemia in horses, renal injury

has not been observed. However, at higher doses (18,000-36,000 units/kg) or for longer treatment protocols, renal injury risk increases. Allergic reactions are also possible.

Contraindications and Precautions

Use cautiously, if at all, in patients with renal disease. Animals receiving polymyxin B should receive adequate fluid support to maintain hydration and renal perfusion.

Drug Interactions

Use cautiously with other potentially nephrotoxic agents such as aminoglycosides. Do not administer with curariform muscle relaxant and other neurotoxic drugs because of risk of respiratory depression. Polymyxin antibacterial activity is decreased in the presence of pus, in tissues containing acidic phospholipids, and in the presence of anionic detergents.

Instructions for Use

Use in veterinary medicine has been primarily confined to topical use, and the use in horses to treat endotoxemia. Doses and regimens have been derived from experimental studies. Route of administration have been topical IM, IV infusion, intrathecal, or ophthalmic.

Patient Monitoring and Laboratory Tests

Monitor patient hydration and electrolyte status. Monitor renal parameters (e.g., creatinine and BUN) for evidence of renal disease.

Formulations

Polymyxin B is available in vials containing 500,000 polymyxin B units. In some dosage protocols, the dose is listed in milligrams instead of units. One milligram of polymyxin B base is equivalent to 10,000 units of polymyxin B, and each microgram of pure polymyxin B base is equivalent to 10 units of polymyxin B.

Stability and Storage

Store at room temperature 20°C to 25°C (68°F to 77°F), protected from light. Polymyxin B is soluble in water at 0.5% solution with a pH of 5-7.5. Aqueous solutions of polymyxin B sulfate have been stored up to 12 months without significant loss of potency if refrigerated. Do not mix with strong acid or alkaline solutions. It is not compatible with calcium or magnesium salts.

Small Animal Dosage

Dogs and Cats

- Antibacterial: 15,000-25,000 units/kg q12h IV. To prepare solution, mix 500,000 polymyxin B units with 300-500 mL 5% dextrose for continuous rate infusion.
- Antibacterial: 30,000 units/kg/day, IM. To prepare solution, mix 500,000 polymyxin B units in 2 mL sterile water for injection or sodium chloride injection or 1% procaine hydrochloride.
- Intrathecal (to treat meningitis): Mix 500,000 polymyxin B units in 10 mL sodium chloride (50,000 units per mL). Administer 20,000 units once daily, intrathecally, then continue 25,000 units once every other day.

Large Animal Dosage

Horses (endotoxemia): 1000 to 10,000 units per kg (usually 6000 units/kg, equivalent to 1 mg/kg) administered every 8 hours. The infusion may be mixed in a

1-L saline solution and administered over 15 minutes every 8 hours for 5 treatments.

Regulatory Information

Cattle: Withdrawal time after intramammary administration is 7 days for milk and 2 days for meat. Other withdrawal times have not been reported for food animals. For other extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Polysulfated Glycosaminoglycan

pahl-ee-sul'fate-ed glye-koe-sah-mee-noe-glye-kan

Trade and Other Names: Adequan Canine, Adequan IA, and Adequan IM

Functional Classification: Antiarthritic agent

Pharmacology and Mechanism of Action

Polysulfated glycosaminoglycan (PSGAG) provides large-molecular-weight compounds similar to normal constituents of healthy joints. It is chondroprotective and inhibits enzymes that may degrade articular cartilage, such as metalloproteinase. It may help to upregulate glycosaminoglycan and collagen synthesis and decrease inflammatory mediators (e.g., PGE₂).

Indications and Clinical Uses

PSGAG is injected in dogs and horses to treat or prevent degenerative joint disease. Intra-articular injections have been effective, but intramuscular doses may be too low to be effective in some animals.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are rare. Allergic reactions are possible. PSGAG has heparin-like effects and may elicit bleeding problems in some animals, but this has not been observed clinically.

Potassium Gluconate

Contraindications and Precautions

Intra-articular injections should be done using aseptic technique. Use cautiously in animals receiving heparin therapy.

Drug Interactions

No drug interactions are reported in animals.

P

Instructions for Use

Doses are derived from empirical evidence, experimental studies, and clinical studies. Although effective for acute arthritis, it may not be as effective for chronic arthropathy. In horses, it is sometimes combined with amikacin (125 mg) for intra-articular use to prevent infection.

Patient Monitoring and Laboratory Tests

Observe injected joints for signs of infection after treatment.

Formulations

Polysulfated glycosaminoglycan is available in a 100-mg/mL injection in a 5-mL vial, 100 mg/mL for intramuscular administration, and 250 mg/mL for intra-articular use in horses.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 4.4 mg/kg IM, twice weekly for up to 4 weeks.

Large Animal Dosage

Horses

- 500 mg every 4 days IM for 28 days or 250 mg per joint once weekly for 5 weeks intra-articular.

Regulatory Information

No withdrawal times necessary.

Ponazuril

poe-naz'yoo-ril

Trade and Other Names: Marquis

Functional Classification: Antiprotozoal

Pharmacology and Mechanism of Action

Antiprotozoal drug. Coccidiostat. Ponazuril (also known as toltrazuril sulfone) is a metabolite of the poultry antiprotozoal drug toltrazuril. Ponazuril is a triazine-based drug that acts to inhibit enzyme systems in protozoa and/or decreasing pyrimidine synthesis. It is specific for Apicomplexan organisms because the action attacks the apicoplast organelle in protozoa. It is specific in action as an antiprotozoal agent without affecting other organisms. It has high oral absorption in horses and a half-life of 4.5 days.

Indications and Clinical Uses

Toltrazuril, the parent drug, has been used for protozoa such as *Isospora*, *Coccidia* spp., *Toxoplasma gondii*, and *Eimeria* spp. Ponazuril has a long half-life in horses (>4 days), and concentrations in cerebrospinal fluid (CSF) are 3.5%-4% of serum concentrations but high enough to inhibit protozoa. Ponazuril is specifically approved for use as a treatment of equine protozoal myeloencephalitis (EPM), caused by *Sarcocystis neurona*. In clinical studies in horses with EPM, 62% of 101 horses were treated successfully with doses of 5 or 10 mg/kg for 28 days.

Precautionary Information

Adverse Reactions and Side Effects

Ponazuril is highly specific and relatively safe at approved doses. Administration of 50 mg/kg to horses (10 times the recommended dose) produced minor adverse effects. There were minimal changes in the serum analysis. Soft feces may occur at high doses.

Contraindications and Precautions

Avoid use in pregnant or breeding mares until more information becomes available on safety.

Drug Interactions

No drug interactions have been reported.

Instructions for Use

Use in horses is based on clinical studies, field trials conducted by the drug sponsor, and pharmacokinetic studies in horses. In a trial with either 5 or 10 mg/kg per day in horses, 62% were improved by 28 days. Although successful treatment was reported after 28 days, longer treatment duration may be needed in some animals to resolve the infection and prevent relapse. Use of ponazuril clinically in other animals has not been reported.

Patient Monitoring and Laboratory Tests

In horses treated for EPM, monitor neurological status during treatment. The IgG and albumin quotient has been measured in CSF of treated horses to monitor treatment, but this may not indicate clinical cure.

Formulations

Ponazuril is available in 15% (150 mg/mL) oral paste for horses.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

No small animal dose has been reported.

Large Animal Dosage**Horses**

- Treatment of EPM: 5 mg/kg q24h PO for 28 days.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Posaconazole

Poe-sa-Kon'-a-zole

Trade and Other Names: Noxafil

Functional Classification: Antifungal

Pharmacology and Mechanism of Action

Antifungal drug. Posaconazole is a relatively new antifungal of the azole group, similar to itraconazole in structure and activity. Action against fungi is similar to other azoles, which is to inhibit ergosterol synthesis in the fungal cell membrane and produce fungistatic activity. It is active against the same fungal organisms as itraconazole, but in vitro activity is twice as great. The most important difference in activity is that posaconazole has better activity against *Mucor* and *Zygomycetes*

compared to other azoles. In dogs, there is a food effect on absorption with oral systemic availability of 11% and 27% in fasted and fed dogs, respectively. It is highly protein bound with binding greater than 97% in dogs.

Indications and Clinical Uses

The use of posaconazole has been limited to a few case reports and anecdotal experience. In cats it has been used to treat fungal infections refractory to other drugs such as Aspergillosis and *Mucor* infections. In humans it is used for invasive fungal infections, including those caused by *Aspergillus* and *Candida*. It is also active against dermatophytes, *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Coccidioides immitis*, and *Cryptococcus neoformans*. Its advantage over other azole drugs is the activity against *Zygomycetes* and *Mucor*.

Precautionary Information

Adverse Reactions and Side Effects

The use has been relatively infrequent, and information regarding the full range of adverse effects possible from clinical use is not available. In people, similar adverse effects have been observed as with other azole antifungal drugs: headache, diarrhea, nausea, and increased liver enzymes. In toxicity studies, dogs have tolerated 30 mg/kg/day for 1 year without any clinical signs. However, histologically some neuronal vacuolation was observed at this dose. It should not be used during pregnancy because of inhibition of steroidogenesis.

Contraindications and Precautions

No contraindications and precautions have been reported for animals.

Drug Interactions

Drugs that decrease stomach acid (proton pump inhibitors, H₂ blockers) will reduce oral absorption of posaconazole. Like other azole antifungal drugs, posaconazole is a strong inhibitor of cytochrome P450 enzymes (CYP3A4) and may increase concentrations of other drugs metabolized by these enzymes.

Instructions for Use

Use in animals has been based primarily on some isolated case reports (primarily in cats) and extrapolation from human use. No clinical studies for animals have been reported. The treatment regimen in people is approximately 2.5-3 mg/kg three times a day orally.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes in treated animals.

Formulations

Posaconazole is available in a 40-mg/mL oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 5-10 mg/kg PO, q12-24h.

Cats

- 5 mg/kg PO, q24h.

Large Animal Dosage

No doses have been reported.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Potassium Chloride

Trade and Other Names: Generic brands

Functional Classification: Potassium supplement

Pharmacology and Mechanism of Action

Potassium supplement. Potassium is used for treatment of hypokalemia. A dose 1.9 g of potassium chloride is equivalent to 1 g of potassium. One gram of potassium chloride is equal to 14 mEq of potassium. Other potassium supplements include potassium gluconate, potassium acetate, potassium bicarbonate, and potassium citrate.

Indications and Clinical Uses

Potassium supplements are indicated for treating hypokalemia. Hypokalemia may occur with some diseases or as a consequence of diuretic use. Hypokalemia may also occur as a consequence of beta-2 adrenergic agonist overdose. In most patients, potassium chloride is the supplement of choice for hypokalemia. It is better absorbed than other supplements, and the chloride ion may be helpful because hypochloremia may also occur in some patients.

Precautionary Information

Adverse Reactions and Side Effects

Toxicity from high potassium concentrations can be dangerous. Hyperkalemia can lead to cardiovascular toxicity (bradycardia and arrest) and muscular weakness. Oral potassium supplements can cause nausea and stomach irritation.

Contraindications and Precautions

Do not exceed a rate of 0.5 mEq/kg/hr IV infusion. Use cautiously in animals with renal disease. Do not use potassium chloride if metabolic acidosis and hyperchloremia are present. Use another potassium supplement instead. Intravenous use should be done cautiously because of risk of hyperkalemia. Use potassium cautiously in digitalized patients. Do not use with potassium penicillin or potassium bromide (use sodium salts of these drugs instead).

Drug Interactions

Interactions between potassium supplements and the following drugs may occur: digoxin, thiazide diuretics, spironolactone, amphotericin B, corticosteroids, penicillins, angiotensin-converting enzyme (ACE) inhibitors, and laxatives.

Instructions for Use

One gram of potassium chloride provides 13.41 mEq of potassium. It is usually added to fluid solutions. When potassium is supplemented in fluids, do not administer at a rate faster than 0.5 mEq/kg/hr.

Patient Monitoring and Laboratory Tests

Monitor serum potassium levels. Monitor ECG in patients that may be prone to arrhythmias. Normal potassium is 4-5.5 mEq/L (dogs) and 4.3-6.0 mEq/L (cats).

Formulations

Potassium chloride is available in various concentrations for injection (usually 2 mEq/mL). It is available in an oral suspension and oral solution as 10-20 mEq of potassium per packet. One gram potassium chloride contains 14 mEq potassium ion.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Potassium chloride is freely soluble in water.

Small Animal Dosage

Dogs and Cats

- Supplement: 0.5 mEq potassium/kg/day or add 10-40 mEq/500 mL of fluids, depending on serum potassium.
- Acute treatment of hypokalemia: 0.5 mEq potassium/kg/hr.

Large Animal Dosage

Cattle and Horses

- Supplement in intravenous fluids to 20-40 mEq potassium per liter of fluids. Do not exceed a rate of 0.5 mEq/kg/hr IV.

Regulatory Information

No withdrawal times necessary.

Potassium Citrate

Trade and Other Names: Generic and Urocit-K

Functional Classification: Alkalinizing agent

Pharmacology and Mechanism of Action

Potassium citrate ($K_3C_6H_5O_7$) alkalinizes urine and may increase urine citric acid. An increase in urine excretion of citrate and alkaline urine may decrease urinary calcium oxalate crystallization. Urinary excretion of calcium also is decreased. Other potassium supplements include potassium gluconate, potassium acetate, potassium bicarbonate, and potassium chloride.

Indications and Clinical Uses

Potassium citrate is used for prevention of calcium oxalate urolithiasis. It is also used for renal tubular acidosis. In dogs, after administration of 150 mg/kg (of potassium citrate) q12h PO, the urine pH was not significantly increased, but urine concentration of calcium oxalate was decreased.

Precautionary Information

Adverse Reactions and Side Effects

Toxicity from high potassium concentrations can be dangerous. Hyperkalemia can lead to cardiovascular toxicity (bradycardia and arrest) and muscular weakness. Oral potassium supplements can cause nausea and stomach irritation.

Contraindications and Precautions

Use cautiously in animals with renal disease. Do not use with potassium penicillin or potassium bromide.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

One gram of potassium citrate provides 9.26 mEq of potassium. Administer with meals.

Patient Monitoring and Laboratory Tests

Monitor serum potassium levels. Normal potassium is 4-5.5 mEq/L (dogs) and 4.3-6.0 mEq/L (cats). Monitor ECG in patients that may be prone to arrhythmias.

Formulations

Potassium citrate is available in 5-mEq and 10-mEq tablets. Some formulations are in combination with potassium chloride. Potassium citrate tablets in a delayed-released tablet are also available.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage**Dogs and Cats**

- 2.2 mEq/100 kCal of energy/day PO or 0.5 mEq/kg per day, PO. Higher doses have been used safely in some animals. (1000 mg potassium citrate = 9.26 mEq potassium.)

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

No withdrawal times necessary.

Potassium Gluconate

Trade and Other Names: Kaon, Tumil-K, and generic brands

Functional Classification: Potassium supplement

Pharmacology and Mechanism of Action

Potassium supplement. Used for treatment of hypokalemia. Potassium gluconate exists in an anhydrous form and a monohydrate form. Six grams of potassium gluconate anhydrous is equivalent to 1 g potassium; 6.45 g potassium gluconate monohydrate is equivalent to 1 g potassium. One gram potassium gluconate is equal to 4.27 mEq of potassium. Other potassium supplements include potassium chloride, potassium acetate, potassium bicarbonate, and potassium citrate.

Indications and Clinical Uses

Potassium gluconate is used for the treatment of hypokalemia and renal tubular acidosis. Potassium supplements are indicated for treating hypokalemia. Hypokalemia

may occur with some diseases or as a consequence of diuretic use. In most patients, potassium chloride is the supplement of choice for hypokalemia.

Precautionary Information

Adverse Reactions and Side Effects

Toxicity from high potassium concentrations can be dangerous. Hyperkalemia can lead to cardiovascular toxicity (bradycardia and arrest) and muscular weakness. Oral potassium supplements can cause nausea and stomach irritation.

Contraindications and Precautions

Use cautiously in animals with renal disease.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

One gram of potassium gluconate provides 4.27 mEq of potassium.

Patient Monitoring and Laboratory Tests

Monitor serum potassium levels. Normal potassium is 4-5.5 mEq/L (dogs) and 4.3-6.0 mEq/L (cats). Monitor ECG in patients that may be prone to arrhythmias.

Formulations

Potassium gluconate is available in a 2-mEq tablet (equivalent to 500 mg potassium gluconate).

Kaon elixir is 20 mEq potassium/15 mL elixir (containing 4.68 grams potassium gluconate).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Potassium gluconate is soluble in water.

Small Animal Dosage

Dogs

- 0.5 mEq/kg q12-24h PO.

Cats

- 2-8 mEq/day divided twice daily, PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

No withdrawal times are necessary.

Potassium Iodide

Trade and Other Names: Quadrinal

Functional Classification: Antifungal, expectorant

Pharmacology and Mechanism of Action

Potassium iodide is used as an iodide supplement. It also has some antimicrobial properties, although the exact mechanism is uncertain. The antimicrobial activity has

been used as an adjunctive treatment for zygomycosis, conidiobolomycosis, and fungal granuloma. Iodide is also important for thyroid gland function and has been used to treat some thyroid disorders. Potassium iodide also may irritate the respiratory tract and has been used as an expectorant.

Indications and Clinical Uses

Potassium iodide has been used to treat fungal granulomatous disease and infections associated with zygomycetes. In small animals it has been used for sporotrichosis. The antifungal treatment has been questioned for animals because the efficacy is not established. Because it may increase respiratory secretions, it has been used as an expectorant, but the efficacy has not been established. In people, iodide has been used to treat hyperthyroidism, but effectiveness for this use in cats has not been established. Potassium iodide is also used to protect the thyroid gland from radiation injury in the event of a radiation emergency (accidental exposure to radiation) or following administration of radioactive iodide.

Ethylenediamine dihydroiodide (EDDI) is another source of iodide that is used as a nutritional source of iodine in cattle. Sodium iodide also is used, particularly in large animals. See Sodium Iodide and Iodide monograph for more information.

Precautionary Information

Adverse Reactions and Side Effects

High doses can produce signs of iodism, which include lacrimation, irritation of mucous membranes, swelling of eye lids, cough, dry scruffy coat, and hair loss. Potassium iodide has a bitter taste and can cause nausea and salivation. Potassium iodide administration has been associated with cardiomyopathy in cats. Its use may cause abortion in horses or limb deformities in foals.

Contraindications and Precautions

Do not administer to foals or pregnant animals (abortion is possible). Do not administer IV.

Drug Interactions

No known drug interactions.

Instructions for Use

Clinical use in animals is primarily empirical. The doses and indications listed have not been tested in clinical trials. Other, more proven drugs for these indications should be considered as alternatives.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Iodide has been administered as a 1-g/mL potassium iodine saturated solution (SSKI) or as a 65-mg/mL solution. It also has been administered as a 10% potassium iodide/5% iodine solution given orally with food. The saturated solution (1 g/mL) yields 38 mg per drop. A 10% solution of potassium iodide (10%) yields 6.3 mg of iodine per drop. It is also available in tablets of 145 mg of iodine.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze solutions. Inorganic potassium iodide is unstable in light, heat, and excess humidity.

Small Animal Dosage

Dogs and Cats

- Fungal infections: start with 5 mg/kg q8h, PO, and increase gradually to 25 mg/kg q8h, PO.
- Emergency treatment after radiation exposure: 2 mg/kg PO per day.
- Expectorant: 5 mg/kg q8h, PO

Large Animal Dosage

Cattle

- 10-15 g/day (adult cattle) PO, for 30-60 days.
- 5-10 g/day (calves) PO, for 30-60 days.

Feed supplement and other indications: (see Iodide monograph for EDDI doses and Sodium Iodide monograph for other doses).

Horses

- 10-40 mg/kg per day (using inorganic potassium iodide)
- 10-15 g/day (adult horses) PO, for 30-60 days.
- 5-10 g/day (pony) PO, for 30-60 days.

See Iodide monograph for EDDI doses and Sodium Iodide monograph for other doses.

Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

Potassium Phosphate

Trade and Other Names: K-Phos, Neutra-Phos-K, and generic brands

Functional Classification: Phosphate supplement

Pharmacology and Mechanism of Action

Phosphorous supplement. Potassium phosphate if used for severe hypophosphatemia associated with diabetic ketoacidosis. It also acidifies the urine.

Indications and Clinical Uses

Potassium phosphate has been used to reduce calcium urinary secretion in patients prone to calcium urinary calculi and to promote a more acid urine. This drug should not be used to supplement potassium. In most patients, potassium chloride is the supplement of choice for hypokalemia.

Precautionary Information

Adverse Reactions and Side Effects

Intravenous administration can cause hypocalcemia.

Contraindications and Precautions

Use cautiously in animals with renal disease.

Drug Interactions

No drug interactions are reported in animals.

Instructions for Use

Potassium phosphate use in animals is primarily as a urinary acidifier or treatment of hypophosphatemia.

Patient Monitoring and Laboratory Tests

Monitor calcium, potassium, and phosphorus levels in treated animals.

Formulations

Potassium phosphate is currently not available in tablets (previously 500 mg containing 114 mg [3.7 mmol] phosphorus). Oral solutions can be made from powdered concentrate mixed with water for oral administration.

It is also available in 224 mg monobasic potassium phosphate and 236 mg of dibasic potassium phosphate (3 mmol [93 mg] of phosphorus) per mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.03-0.12 mmol/kg/hr IV for acute treatment.
- 0.1 mmol/kg/day IV for daily supplementation.
- 4 mg/kg phosphorus (approximately 0.1 mmol/kg) PO, up to 4 times daily.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

No withdrawal times are necessary.

Pradofloxacin

pray doe-floks'ah-sin

Trade and Other Names: Verafloxx

Functional Classification: Antibacterial

P

Pharmacology and Mechanism of Action

Fluoroquinolone antibacterial drug. Pradofloxacin is of the new generation of fluoroquinolones. This new generation of fluoroquinolones, with substitutions at the C-8 position (e.g., C-8 methoxy), have as their advantage a broader spectrum that includes anaerobic bacteria and gram-positive cocci. The difference in spectrum of activity is largely caused by increased activity against the DNA-gyrase of gram-positive bacteria, rather than activity against topoisomerase IV, which is the target in gram-positive bacteria for the older quinolones (e.g., enrofloxacin, marbofloxacin, orbifloxacin, difloxacin). These newer fluoroquinolones (referred to by some authors as the third-generation fluoroquinolones) include gatifloxacin, gemifloxacin, and moxifloxacin. Susceptibility data indicate that it is more active than other fluoroquinolones against bacterial isolates from dogs and cats, including *Escherichia coli*, *Staphylococcus*, and anaerobes. At the time of this writing (2010) pradofloxacin was approved for small animal use in Europe, but not in the U.S. Another drug with a similar spectrum of activity is the human drug, moxifloxacin, which has been used in clinical situations where pradofloxacin would be a rational choice.

Indications and Clinical Uses

Pradofloxacin has been evaluated in dogs and cats, with efficacy studies published in research abstracts and clinical reports in which it has been used for treating skin and

636 Pradofloxacin

soft tissue infections in dogs and cats, respiratory infections in cats, and urinary tract infections. At a dose of 3 mg/kg orally it was effective for treatment of urinary tract infections in dogs, and at 3 or 5 mg/kg it was effective for canine pyoderma. At a dose of 5 mg/kg in a 2.5% oral suspension it was effective for urinary tract infections in cats. It has been used to effectively treat infections caused by *Chlamydophila felis* or *Mycoplasma* in cats (5 mg/kg q12h, PO, for 28 days), although it was not more effective than doxycycline. It has been used to treat feline rhinitis caused by *Mycoplasma*, *Bordetella*, streptococci, or staphylococci at a dose of 5 mg/kg once daily for 7 doses.

Precautionary Information

Adverse Reactions and Side Effects

A complete range of adverse reactions is not available because of the limited clinical use. It is anticipated that some of the adverse effects seen with other fluoroquinolones may also be possible with pradofloxacin. However, compared to enrofloxacin, pradofloxacin has been safe in cats with respect to ocular lesions.

Contraindications and Precautions

No contraindications or precautions are available. Because it is similar to other fluoroquinolones, use cautiously in young dogs that may be susceptible to articular cartilage injury.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

The uses are based on the clinical reports in dogs and cats currently available. At the time of marketing the drug sponsor may release additional data to guide dosing.

Patient Monitoring and Laboratory Tests

No break points for susceptibility have been established by CLSI for pradofloxacin. In the meantime, use other fluoroquinolones (e.g., moxifloxacin) as a guide to susceptibility for pradofloxacin.

Formulations

Formulations contain pradofloxacin in a 2.5% oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 3-5 mg/kg q24h, PO.

Cats

- 5-10 mg/kg q24h, PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. It should not be used in food-producing animals. Extra-label use of fluoroquinolones in food-producing animals is prohibited.

Pralidoxime Chloride

prah-lih-doks'eem klor'ide

Trade and Other Names: 2-PAM and Protopam chloride

Functional Classification: Antidote

Pharmacology and Mechanism of Action

Pralidoxime chloride is an oxime that is used as an adjunct to atropine for treatment of intoxication. Organophosphate (OP) intoxication results in inactivation of cholinesterase enzymes and excess accumulation of acetylcholine. Pralidoxime (also known as 2-PAM) is used to reactivate acetylcholinesterase by promoting dephosphorylation. Pralidoxime is well absorbed from intramuscular administration, but it does not cross the blood-brain barrier. After absorption, the half-life is short, necessitating repeated administrations.

Indications and Clinical Uses

Pralidoxime chloride is used for treatment of organophosphate toxicosis. Administer promptly after organophosphate intoxication is identified. It also has been used to treat overdoses of other anticholinesterase drugs such as neostigmine, pyridostigmine, and edrophonium.

Precautionary Information

Adverse Reactions and Side Effects

Intramuscular injections cause pain. Rapid intravenous injections may bind calcium and cause muscle spasms. Rapid injections also may cause heart and respiratory problems. Use during pregnancy may produce teratogenic effects.

Contraindications and Precautions

Pralidoxime treatment should not be used for carbamate intoxication. Do not administer rapidly IV or it may cause respiratory depression and other problems.

Drug Interactions

No drug interactions have been reported. However, other drugs should be avoided when treating organophosphate poisoning. These drugs include aminoglycosides, barbiturates, phenothiazine tranquilizers (acepromazine), and neuromuscular blocking agents.

Instructions for Use

Dilute formulation in glucose solution before intravenous administration. Give slowly IV. Administer atropine (0.1 mg/kg) when using pralidoxime. Recovery from organophosphate poisoning may take 48 hours. When treating intoxication, consult a poison control center for precise guidelines.

Patient Monitoring and Laboratory Tests

Monitor for signs of organophosphate poisoning to determine if repeated doses are necessary. Monitor heart rate and rhythm and respiratory rate. It may be possible to monitor cholinesterase activity from a blood sample to confirm organophosphate poisoning (consult local diagnostic laboratory).

Formulations

Pralidoxime chloride is available in a 1-g vial to be reconstituted in 20 mL of water (50-mg/mL injection). pH of solution is 3.5-4.5.

Stability and Storage

Store powder at room temperature and protect from light. Reconstituted solution should be stored below 25°C and protected from light. Discard reconstituted solution after 3 hours.

Small Animal Dosage

- 20 mg/kg, up to 50 mg/kg q8-12h IM or IV (initial dose slow). Dilute solution in glucose and infuse slowly IV.

Large Animal Dosage

Cattle, Sheep, and Pigs

- 20-50 mg/kg q8h (administered as a 10% solution) IM or via slow IV infusion, or as needed. Frequency can be assessed by monitoring clinical signs.

Regulatory Information

Cattle and pig withdrawal times (extralabel): 6 days for milk and 28 days for meat.

Praziquantel

pray-zih-kwon'tel

Trade and Other Names: Droncit and Drontal (combination with febantel)

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic drug. Action on parasites related to neuromuscular toxicity and paralysis via altered permeability to calcium.

Indications and Clinical Uses

Praziquantel is widely used to treat intestinal infections caused by cestodes (*Dipylidium caninum*, *Taenia pisiformis*, and *Echinococcus granulosus*) and removal and control of canine cestode *Echinococcus multilocularis*. In cats it is used for removal of feline cestodes *Dipylidium caninum* and *Taenia taeniaeformis*. In horses it is used to treat tapeworms (*Anoplocephala perfoliata*).

Precautionary Information

Adverse Reactions and Side Effects

Vomiting occurs at high doses. Anorexia and transient diarrhea have been reported. It is safe in pregnant animals and during lactation.

Contraindications and Precautions

Avoid use in cats younger than 6 weeks and dogs younger than 4 weeks. Praziquantel has been safe in pregnancy.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Praziquantel is one of the most common drugs used for tapeworm treatment. It has a wide margin of safety. Some formulations of praziquantel are available in combination (e.g., combination of praziquantel and febantel, combination of ivermectin and praziquantel, moxidectin, and praziquantel).

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Praziquantel is available in 23- and 34-mg tablets and 56.8-mg/mL injection. It is also available in pastes and gels, and they are available in pastes and gels for horses in combination with other drugs (e.g., ivermectin, moxidectin, febantel).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- Dogs <6.8 kg: 7.5 mg/kg once PO.
- Dogs >6.8 kg: 5 mg/kg once PO.
- Dogs <2.3 kg, 7.5 mg/kg, once IM or SQ.
- Dogs 2.7-4.5 kg: 6.3 mg/kg once IM or SQ.
- Dogs >5 kg: 5 mg/kg once IM or SQ.

Cats (all doses given once)

- <1.8 kg: 11.4 mg/cat PO.
- 2.2 kg: 11.4 mg/cat, SQ or IM.
- 2.3 kg to 4.5 kg: 22.7 mg/cat, SQ or IM.
- 2.3 kg to 5 kg: 23 mg/cat, PO.
- >5 kg: 34.5 mg/cat, PO, or 34.1 mg/cat, SQ or IM.

Large Animal Dosage

Horses

- 1.5-2.5 mg/kg PO.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

P

Prazosin

pray'zoe-sin

Trade and Other Names: Minipress

Functional Classification: Vasodilator

Pharmacology and Mechanism of Action

Alpha₁-adrenergic blocker. Prazosin is a vasodilator that is a selective blocker for the alpha₁-adrenergic receptor, but it is not selective for either alpha-1a or alpha-1b. Its action is similar to phenoxybenzamine, but it produces less tachycardia than nonselective alpha-antagonist drugs. Prazosin decreases tension in both arterial and venous vascular smooth muscle. Prazosin relaxes smooth muscle, especially of vasculature. Prazosin is used as a vasodilator and to relax smooth muscle (occasionally urethral muscle). The alpha-1b adrenoreceptors regulate vascular tone and the alpha 1a-adrenoreceptors regulate urethral smooth muscle tone. For specific

urinary smooth muscle relaxation, the drugs tamsulosin (Flomax) and silodosin (Rapaflo) are more specific for the alpha-1a receptor.

Indications and Clinical Uses

Prazosin has been used in people for vasodilation and the management of hypertension that is not responsive to other drugs. Prazosin has been used to a limited extent in veterinary medicine to produce balanced vasodilation. There are no controlled studies to establish efficacy and dose, and indications are derived from anecdotal use and extrapolation from human medicine. It has also been used experimentally in horses to improve digital perfusion in the treatment of laminitis. Long-term administration is not common because tolerance may develop with chronic use.

Precautionary Information

Adverse Reactions and Side Effects

High doses cause vasodilation and hypotension.

Contraindications and Precautions

Use cautiously in animals with compromised cardiac function. It may lower blood pressure and decrease cardiac output.

Drug Interactions

No drug interactions have been reported in animals, but combined with other vasodilators may produce severe lowering of blood pressure.

Instructions for Use

Titrate dose to needs of individual patient. Results of clinical studies in animals have not been reported; therefore, use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

Monitor for hypotension and reflex tachycardia.

Formulations

Prazosin is available in 1-, 2-, and 5-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.5-2 mg/animal (0.07 mg/kg, or approximately 1 mg per 15 kg) q8-12h PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Prednisolone Sodium Succinate

pred-niss-oh'lonə soe'dee-um suk'sih-nate

Trade and Other Names: Solu-Delta-Cortef

Functional Classification: Corticosteroid

Pharmacology and Mechanism of Action

Prednisolone sodium succinate is the same as prednisolone, except that this is a water-soluble formulation intended for acute therapy when high intravenous doses are needed for rapid effect.

Indications and Clinical Uses

Prednisolone sodium succinate has similar uses as prednisolone in other forms, except this is used when prompt response is needed from injection, especially at high doses. Methylprednisolone sodium succinate (Solu-Medrol) has also been used for similar indications. Uses include treatment of immune-mediated diseases (e.g., pemphigus and hemolytic anemia), spinal cord trauma, and adrenocortical insufficiency. Large animal uses include treatment of inflammatory conditions and treatment of recurrent airway obstruction (RAO) in horses. In cattle, corticosteroids have been used in the treatment of ketosis. The use of prednisolone for treatment of shock, snakebites, and head trauma is discouraged because of lack of proven efficacy or high risk of adverse effects.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are not expected from single administration. However, with repeated use, other side effects are possible. Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic–pituitary–adrenal (HPA) axis suppression. Adverse effects include GI ulceration, diarrhea, steroid hepatopathy, diabetes mellitus, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, impaired wound healing, and immunosuppression. In cats, polyuria is less common than in dogs and it has not increased calcium excretion or calcium-containing calculi. With high doses of prednisolone sodium succinate, there is a risk of GI bleeding. In horses, in addition to the previously listed adverse effects, there may be an increased risk of laminitis, although documentation of this effect has been controversial.

Contraindications and Precautions

Use cautiously in patients with a risk of GI ulcers and bleeding or infection or in animals in which growing or healing is necessary. Use prednisolone sodium succinate cautiously in patients with renal disease because it may cause azotemia. Use cautiously in pregnant animals because fetal abnormalities have been reported in laboratory rodents.

Drug Interactions

Administration of corticosteroids with nonsteroidal anti-inflammatory drugs (NSAIDs) will increase the risk of GI injury. Do not mix prednisolone sodium succinate with solutions containing calcium.

Instructions for Use

Doses for prednisolone are based on severity of underlying condition. Use of prednisolone sodium succinate is often at high doses for acute treatment.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an adrenocorticotropic hormone (ACTH) stimulation test to monitor adrenal function. Corticosteroids can increase liver enzymes—especially alkaline phosphatase—without inducing liver pathology. Prednisolone can increase white blood cell count and decrease lymphocyte count. It can increase serum albumin, glucose, triglycerides, and cholesterol. Corticosteroid administration may decrease conversion of thyroid hormones to its active form. Prednisolone and prednisone at high doses for several weeks may produce significant proteinuria and glomerular changes in some dogs.

Formulations

Prednisolone sodium succinate is available in 100- and 500-mg vials for injection (10, 20, and 50 mg/mL). For some indications, methylprednisolone sodium succinate (Solu-Medrol) has been substituted.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Prednisolone sodium succinate should be used immediately after reconstitution. Do not freeze. If solution becomes cloudy, do not administer IV.

Small Animal Dosage

Dogs and Cats

- Shock: (effectiveness of this use is controversial) 15-30 mg/kg IV (repeat in 4-6 hours)
- CNS trauma: 15-30 mg/kg IV, taper to 1-2 mg/kg q12h.
- Anti-inflammatory: 1 mg/kg/day IV.
- Replacement therapy: 0.25-0.5 mg/kg/day IV.
- Intermittent treatment (pulse therapy) of pemphigus foliaceus: 10 mg/kg IV.

Large Animal Dosage

Horses

- 0.5-1 mg/kg q12-24h IM or IV. Intravenous dose should be given slowly over 30-60 seconds.
- Treatment of shock: Although efficacy for treating shock has not been established, recommended doses are 15-30 mg/kg IV; repeat dose in 4-6 hours.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Prednisolone, Prednisolone Acetate

Trade and Other Names: Delta-cortef, PrednisTab, and generic brands

Functional Classification: Corticosteroid

Pharmacology and Mechanism of Action

Glucocorticoid anti-inflammatory drug. Anti-inflammatory effects are complex, but via binding to cellular glucocorticoid receptors, prednisolone acts to inhibit

inflammatory cells and suppresses expression of inflammatory mediators. Prednisolone is approximately four times more potent than cortisol but only one seventh as potent as dexamethasone. Prednisolone is available as the base (usually as a tablet) or as an injectable acetate form, which can be administered IM or intra-articularly.

Indications and Clinical Uses

Prednisolone, like other corticosteroids, is used to treat a variety of inflammatory and immune-mediated disease. The accompanying dosing section lists a range of doses for replacement therapy, anti-inflammatory therapy, and immunosuppressive therapy. Large animal uses include treatment of inflammatory conditions, especially musculoskeletal disorders. In horses prednisolone has been used for treatment of recurrent airway obstruction (RAO), formerly called chronic obstructive pulmonary disease (COPD). In cattle, corticosteroids have been used in the treatment of ketosis. Prednisolone and trimeprazine formulation (Temaril-P) has been effective for treating pruritus in dogs. See Trimeprazine section for further details.

Precautionary Information

Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, behavior changes, and hypothalamic-pituitary-adrenal (HPA) axis suppression. Adverse effects include GI ulceration, steroid hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, increased risk of diabetes, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and UTIs. In horses, in addition to the previously listed adverse effects, there may be an increased risk of laminitis, although documentation of this effect has been controversial.

Contraindications and Precautions

Use cautiously in patients with a risk of GI ulcers and bleeding or infection or in animals in which growing or healing is necessary. Use prednisolone cautiously in patients with renal disease because it may cause azotemia. Use prednisolone cautiously in pregnant animals because fetal abnormalities have been reported in laboratory rodents. Do not administer prednisolone acetate intravenously. In some species—particularly horses and cats—prednisolone (the active form) is preferred for oral treatment (rather than prednisone).

Drug Interactions

Administration of corticosteroids with nonsteroidal anti-inflammatory drugs (NSAIDs) will increase the risk of GI injury. Corticosteroids may inhibit conversion of T4 thyroid hormone to the active form T3.

Instructions for Use

Doses for prednisolone are of a broad range and based on severity of underlying condition. Doses for long-term treatment may eventually be tapered to 0.5 mg/kg q48h, PO.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an adrenocorticotropic hormone (ACTH) stimulation test to monitor adrenal function. Corticosteroids can increase

644 Prednisolone, Prednisolone Acetate

liver enzymes—especially alkaline phosphatase—without inducing liver pathology. Prednisone can increase white blood cell count and decrease lymphocyte count. It can increase serum albumin, glucose, triglycerides, and cholesterol. Corticosteroid administration may decrease conversion of thyroid hormones to active form. Corticosteroid administration may decrease conversion of thyroid hormones to active form. Prednisolone and prednisone at high doses for several weeks may produce significant proteinuria and glomerular changes in some dogs.

Formulations

Prednisolone is available in 5- and 20-mg tablets, 3-mg/mL syrup, and 25-mg/mL acetate suspension injection (10 and 50 mg/mL in Canada). Prednisolone is also available in combination with Trimeprazine (Temaril-P). See Trimeprazine entry for more information.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Prednisolone is slightly soluble in water, but it is more soluble in ethanol. If diluted first in ethanol, it may be compounded into oral liquid formulations with good stability for 90 days. Prednisolone acetate is insoluble in water. Do not freeze.

Small Animal Dosage

Dogs

- Anti-inflammatory: 0.5-1 mg/kg q12-24h IV, IM, or PO initially, then taper to q48h.
- Immunosuppressive: 2.2-6.6 mg/kg/day IV, IM, or PO initially, then taper to 2-4 mg/kg q48h.
- Neurologic disease (steroid responsive): Start with 2 mg/kg q12h, PO for 2 days; followed by gradual tapering to 1 mg/kg, then 0.5 mg/kg, and eventually to 0.5 mg/kg every other day.
- Replacement therapy: 0.2-0.3 mg/kg/day PO.
- Cancer therapy (e.g., COAP protocol): 40 mg/m² q24h for 7 days, then 20 mg/m², every other day, PO.

Cats

Same as for dogs, except that for many conditions they require twice the dog dose.

Large Animal Dosage

Horses

- Prednisolone acetate suspension: 100-200 mg total dosage IM.
- Prednisolone tablets: 0.5-1 mg/kg q12-24h PO. Taper to lower dose for long-term treatment.

Cattle

- Treatment of ketosis: 100-200 mg total dosage IM.

Regulatory Information

Cattle withdrawal times for prednisolone acetate: 5 days for meat, 72 hours for milk (in Canada).

Withdrawal times are not established for animals that produce food in the US.

For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Prednisone

pred'nih-sone

Trade and Other Names: Deltasone, Meticorten, and generic brands

Functional Classification: Corticosteroid

Pharmacology and Mechanism of Action

Glucocorticoid anti-inflammatory drug. The effect of prednisone is attributed to prednisolone. After administration, prednisone is converted to prednisolone. Anti-inflammatory effects are complex, but via binding to cellular glucocorticoid receptors, prednisolone acts to inhibit inflammatory cells and suppresses expression of inflammatory mediators. Prednisolone is approximately four times more potent than cortisol but only one seventh as potent as dexamethasone. Prednisone appears to be well absorbed and converted to active drug in dogs. However, in horses and cats, administration of prednisone results in low systemic levels of the active drug prednisolone, either because of poor absorption of prednisone or because of a deficiency in converting prednisone into prednisolone.

Indications and Clinical Uses

Prednisone, like other corticosteroids, is used to treat a variety of inflammatory and immune-mediated diseases. In cats, prednisone may produce therapeutic failures, and prednisolone (active drug) is preferred. There are several large animal doses cited (similar to prednisolone); however, because of poor activity in horses, the use is discouraged.

Precautionary Information

Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, behavior changes, and hypothalamic-pituitary-adrenal (HPA) axis suppression. Adverse effects include GI ulceration, diarrhea hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and UTIs.

Contraindications and Precautions

Use cautiously in patients with a risk of GI ulcers and bleeding or infection or in animals in which growing or healing is necessary. Use prednisone cautiously in patients with renal disease because it may cause azotemia. Use prednisone cautiously in pregnant animals because fetal abnormalities have been reported in laboratory rodents.

Drug Interactions

Administration of corticosteroids with nonsteroidal anti-inflammatory drugs (NSAIDs) will increase the risk of GI injury. Corticosteroids may inhibit conversion of T4 thyroid hormone to the active form T3.

Instructions for Use

As for prednisolone, the doses vary across a broad range, based on severity of the underlying condition. For long-term treatment, doses can be tapered to 0.5 mg/kg q48h, PO.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an adrenocorticotrophic hormone (ACTH) stimulation test to monitor adrenal function. Corticosteroids can increase liver enzymes—especially alkaline phosphatase—without inducing liver pathology. Corticosteroid administration may decrease conversion of thyroid hormones to active form.

Formulations

Prednisone is available in 1-, 2.5-, 5-, 10-, 20-, 25-, and 50-mg tablets, 1-mg/mL syrup (Liquid Pred in 5% alcohol), 1-mg/mL oral solution (in 5% alcohol), and 10- and 40-mg/mL prednisone suspension for injection (Meticorten; availability has been limited).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Prednisone is slightly soluble in water, and it is soluble in ethanol. Prednisone has been prepared by first dissolving in ethanol, then mixing with syrups and flavorings. No loss occurred, but crystallization is common in aqueous vehicles. Prednisone tablets have been crushed and mixed with syrups and other flavorings, stored for 60 days, and found to produce equal bioavailability as tablets in people.

Small Animal Dosage

Dogs

- Anti-inflammatory: 0.5-1 mg/kg q12-24h IV, IM, or PO initially, then taper to q48h.
- Immunosuppressive: 2.2-6.6 mg/kg/day IV, IM, or PO initially, then taper to 2-4 mg/kg q48h.
- Replacement therapy: 0.2-0.3 mg/kg/day PO.
- Neurologic disease (steroid-responsive): Start with 2 mg/kg q12h, PO for 2 days; followed by gradual tapering to 1 mg/kg, then 0.5 mg/kg, and eventually to 0.5 mg/kg every other day.
- Cancer therapy (e.g., COAP protocol): 40 mg/m² q24h for 7 days, then 20 mg/m², every other day, PO.

Cats

Not recommended for cats because of inability to form active metabolite. However, if use is attempted, higher doses than used in dogs will be needed.

Large Animal Dosage

Horses

- Prednisone suspension (Meticorten) (label dose): 100-400 mg per horse (0.22-0.88 mg/kg) as a single dose, IM, to be repeated every 3-4 days. No oral doses are listed for horses because of inability of oral treatment to produce active prednisolone concentrations.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Pregabalin

Pree ga' bah-lin

Trade and Other Names: Lyrica

Functional Classification: Analgesic, Anticonvulsant

Pharmacology and Mechanism of Action

Analgesic and anticonvulsant. Pregabalin is similar in action to gabapentin, which is an analogue of the inhibitory neurotransmitter GABA. However, like gabapentin, it is not an agonist or antagonist for the GABA receptor. The anticonvulsant effect occurs via inhibition of calcium channels in neurons. Pregabalin inhibits the alpha-2-delta ($\alpha_2 \delta$) subunit of the N-type voltage-dependent calcium channel on neurons. Via inhibition, it reduces calcium influx that is needed for release of neurotransmitters—specifically excitatory amino acids—from presynaptic neurons. Blocking the channels has little effect on normal neurons but may suppress simulated neurons involved in seizure activity and some forms of pain. In humans, pregabalin has better oral absorption and a longer half-life than gabapentin. Pregabalin half-life in dogs is approximately 7 hours, compared to 3-4 hours for gabapentin, and it remained above the estimated effective levels for 11 hours after dosing. In cats, after 4 mg/kg oral, plasma concentrations were above the levels estimated to be effective for over 12 hours, with a half-life of 10 hours. Pregabalin relies on renal excretion, probably to a greater extent than gabapentin.

Indications and Clinical Uses

In people, pregabalin is popular for treating neuropathic pain syndromes associated with diabetes, postherpetic neuralgia, and fibromyalgia. Pregabalin is also used as an anticonvulsant. As an analgesic in animals, it has been used to treat neuropathic pain that does not respond to nonsteroidal anti-inflammatory drugs (NSAIDs) or opiates. It may be combined with those agents. When used to treat epilepsy, pregabalin has reduced seizure frequency in refractory patients when combined with phenobarbital and potassium bromide. Therefore, it is considered when the seizures have become refractory to other drugs in conjunction with other anticonvulsants. For treating pain, regimens have been mostly derived from anecdotal evidence or extrapolation from human medicine.

Precautionary Information

Adverse Reactions and Side Effects

Sedation and ataxia are reported adverse effects that can occur at doses as high as 3-4 mg/kg. As dose increases in dogs sedation is more likely. In people a withdrawal syndrome from abrupt discontinuation has been described, but it is not reported in animals.

Contraindications and Precautions

No known contraindications. Pregabalin, like gabapentin, is excreted in the urine, and liver disease or drug metabolism interactions are not expected to affect the pharmacokinetics. Protein binding is low. In people it has been used with other anticonvulsants and anesthetics without producing a pharmacokinetic drug interaction.

Drug Interactions

There are no reported drug interactions that affect the pharmacokinetics of pregabalin.

Instructions for Use

Pregabalin may be administered with or without food. Pregabalin has been used in some animals with other drugs such as phenobarbital and bromide. It also has been used to treat neuropathic pain syndromes and can be used with NSAIDs and opioids.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. Routine measurement of plasma concentrations is not widely available, but therapeutic concentrations in people (2.8-8.2 mcg/mL) have been used as a guideline. In some dogs, mild increases in liver enzymes may be observed during treatment.

Formulations

Pregabalin is available in 25-, 50-, 75-, 100-, 150-, 200-, 225-, and 300-mg capsules and oral solution of 20 mg/mL.

Stability and Storage

Store in a tightly sealed container, protected from light and humidity. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- Anticonvulsant dose: 2 mg/kg q8h PO. Start with a low dose and gradually increase to the maximum tolerated dose of 3-4 mg/kg PO.
- Neuropathic pain: Start with 4 mg/kg q12h, PO, and increase dose gradually if necessary.

Cats

- Anticonvulsant dose or neuropathic pain dose: start with 2 mg/kg q12h, PO, and increase to 4 mg/kg q12h, PO.

Large Animal Dosage

No doses have been reported.

Regulatory Information

Pregabalin is a Schedule V controlled substance. No withdrawal times are available for food animals. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Primidone

prih'mih-done

Trade and Other Names: Mylepsin, Neurosyn, and Mysoline (in Canada)

Functional Classification: Anticonvulsant

Pharmacology and Mechanism of Action

Anticonvulsant. Primidone is converted to phenylethylmalonamide (PEMA) and phenobarbital, both of which have anticonvulsant activity, but most of the activity (85%) is probably because of the phenobarbital. Phenobarbital acts to potentiate the inhibitory effects of GABA-mediated chloride channels.

Indications and Clinical Uses

Primidone is used for treating seizure disorders in animals, including epilepsy. The effects of primidone are primarily produced by the presence of the active metabolite, phenobarbital. Although it is possible that some patients with epilepsy that are refractory to phenobarbital alone will respond better to primidone, the number of such cases is low. Primidone is approved for use in dogs, but its use has declined in favor of administration of phenobarbital, bromide, or other anticonvulsants.

Precautionary Information

Adverse Reactions and Side Effects

Because primidone is converted to phenobarbital, adverse effects are the same as for phenobarbital. Primidone has been associated with idiosyncratic hepatotoxicity in dogs. Although some labels caution its use in cats, one study in experimental cats determined that it is safe if used at recommended doses.

Contraindications and Precautions

There may be a higher risk of hepatic toxicity with primidone as compared to other anticonvulsants. Primidone should be avoided in animals with liver disease.

Drug Interactions

Primidone is converted to phenobarbital, which is one of the most potent drugs for inducing hepatic microsomal metabolizing enzymes. Therefore, many drugs administered concurrently will have lower (and perhaps subtherapeutic) concentrations because of more rapid clearance. Drugs affected may include theophylline, digoxin, corticosteroids, anesthetics, and many others (see Appendix list for drugs that affect cytochrome P450 enzymes).

Instructions for Use

Recommendations are similar to those for phenobarbital. When monitoring therapy with primidone, phenobarbital plasma concentrations should be measured to estimate anticonvulsant effect. When converting a patient from primidone therapy to phenobarbital, the conversion is as follows: 60 mg phenobarbital is approximately 250 mg of primidone.

Patient Monitoring and Laboratory Tests

Doses should be carefully adjusted via monitoring serum/plasma phenobarbital concentrations. Collect a sample at any time during the dose interval because the timing of the sample is not critical. Avoid the use of plasma separation devices if the tube is to be stored. The therapeutic range in dogs is considered 15-40 mcg/mL (65-180 mmol/L). The optimum range in cats for therapeutic effect is 23-28 mcg/mL. Monitor liver function with bile-acid determinations.

Formulations

Primidone is available in 50- and 250-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 8-10 mg/kg q8-12h as initial dose PO, then is adjusted via monitoring to 10-15 mg/kg q8h.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Procainamide Hydrochloride

proe-kane-ah'mide hye-droe-klor'ide

Trade and Other Names: Pronestyl and generic brands

Functional Classification: Antiarrhythmic

Pharmacology and Mechanism of Action

Class I antiarrhythmic drug. Like other Class I antiarrhythmic drugs (similar to quinidine), procainamide will inhibit sodium influx into the cardiac cell via sodium channel blockade. It will suppress cardiac automaticity and re-entrant arrhythmias, primarily in the ventricle. Procainamide is metabolized in people to n-acetyl procainamide (NAPA), which produces other antiarrhythmic actions (Class III drug: potassium channel–blocking effects). However, dogs do not form this metabolite because of an inability to acetylate some drugs.

Indications and Clinical Uses

Procainamide is used in small animals to suppress ventricular ectopic beats and treat ventricular arrhythmias. Studies in experimental dogs with induced arrhythmias have documented efficacy, but clinical use is based primarily on anecdotal experience. It is used primarily during acute treatment and can be administered by injection or tablet. Rarely is long-term treatment used. Procainamide has occasionally been used in horses to suppress ventricular arrhythmias.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include cardiac arrhythmias, cardiac depression, tachycardia, and hypotension. In people, procainamide produces hypersensitivity effects (lupus-like reactions), but these have not been reported in animals.

Contraindications and Precautions

Procainamide can suppress the heart and produce proarrhythmic effects. Use cautiously in animals receiving digoxin because it may potentiate arrhythmias.

Drug Interactions

Drugs that inhibit cytochrome P450 enzymes (e.g., cimetidine) can potentially increase procainamide concentrations.

Instructions for Use

Because dogs do not produce active metabolite N-acetyl procainamide (NAPA), the dose may be higher compared to dosage for people to control some arrhythmias. In

animals, there is no evidence that slow-release oral formulations produce longer duration of sustained blood concentrations.

Patient Monitoring and Laboratory Tests

Monitor plasma concentrations during chronic therapy. Effective plasma concentrations in experimental dogs are 20 mcg/mL. However, in some references, concentrations as low as 8-10 mcg/mL are cited to be effective. The metabolite, NAPA, is monitored in people, but dogs do not produce this metabolite. ECG should be monitored in treated animals.

Formulations

Procainamide has been available in 250-, 375-, and 500-mg tablets or capsules and a 100- and 500-mg/mL injection. However, because of diminished use in human medicine—in favor of other alternatives—many of the human formulations are no longer available.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Procainamide is soluble in water. When stored, solutions may turn yellow without losing potency. Darker coloration indicates oxidation. Storage of injectable vials in the refrigerator will prevent oxidation. pH of oral compounded products should be 4-6 for maximum stability. Compounded oral products in syrups and flavorings may be stable for 60 days or more, but they should be kept in the refrigerator.

Small Animal Dosage

Dogs

- 10-30 mg/kg q6h PO, to a maximum dose of 40 mg/kg.
- 8-20 mg/kg IV or IM.
- Constant rate infusion (CRI): Initial loading dose of 10 mg/kg, followed by 20 mcg/kg/min IV CRI; the CRI rate can be increased to 25-50 mcg/kg/min if needed for refractory arrhythmias.

Cats

- 3-8 mg/kg q6-8h IM or PO.
- CRI: 1-2 mg/kg IV slowly, then 10-20 mcg/kg/min IV.

Large Animal Dosage

Horses

- 25-35 mg/kg q8h PO.
- Up to 20 mcg/kg IV.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Prochlorperazine Edisylate, Prochlorperazine Maleate

proe-klor-pare'ah-zeen ed-iss'ih-late, proe-klor-pare'ah-zeen mal'ee-ate

Trade and Other Names: Compazine

Functional Classification: Antiemetic, phenothiazine

Pharmacology and Mechanism of Action

Phenothiazine. Central-acting dopamine (D_2) antagonist. Prochlorperazine is related to other phenothiazine antiemetics such as chlorpromazine. Prochlorperazine suppresses dopamine activity in the CNS to produce sedation and prevent vomiting. Antiemetic action also may be related to α_2 - and muscarinic blocking effects. There are two salt formulations of prochlorperazine: prochlorperazine edisylate and prochlorperazine maleate. They are therapeutically equivalent. Other phenothiazines include chlorpromazine, perphenazine, promazine, trifluoperazine, and triflupromazine.

Indications and Clinical Uses

Prochlorperazine is used for sedation, for tranquilization, and as antiemetic. In people it is also used to treat schizophrenia and nonpsychotic anxiety. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Prochlorperazine causes sedation and other side effects attributed to other phenothiazines. It also produces extrapyramidal side effects (involuntary muscle movements) in some individuals. Because of the α -receptor blocking properties it can potentially produce vasodilation and hypotension.

Contraindications and Precautions

Like other phenothiazines it may be contraindicated in some CNS disorders. It may lower seizure threshold in susceptible animals.

Drug Interactions

Prochlorperazine may potentiate other sedatives.

Instructions for Use

Prochlorperazine is used primarily as an antiemetic in animals. Clinical trials are not available; doses are based primarily on extrapolation and anecdotal experience.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Prochlorperazine is available in 5-, 10-, and 25-mg tablets (prochlorperazine maleate), 1-mg/mL oral solution, and 5-mg/mL injection (prochlorperazine edisylate).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Prochlorperazine is slightly soluble in water and soluble in ethanol. However, the maleate form is more insoluble in water. Prochlorperazine edisylate may be mixed with fluids such as water for injection. Some yellow discoloration may not affect potency. However, if milky-white precipitate forms in vial, do not use.

Small Animal Dosage

Dogs and Cats

- 0.1-0.5 mg/kg q6-8h IM, IV, or SQ.
- 0.15-0.35 mg/kg q6-8h PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Prochlorperazine Edisylate + Isopropamide Iodide, Prochlorperazine Maleate + Isopropamide Iodide

Trade and Other Names: Darbazine

Functional Classification: Antiemetic, antidiarrheal

Pharmacology and Mechanism of Action

Combination product. This combination combines either prochlorperazine edisylate (injectable form) or prochlorperazine maleate (oral form) with isopropamide (isopropamide iodide). Chlorpromazine is a central-acting dopamine antagonist (antiemetic); isopropamide is an anticholinergic drug (atropine-like effects).

Indications and Clinical Uses

Prochlorperazine is a phenothiazine used to control vomiting; isopropamide is an anticholinergic used to decrease intestinal motility and GI secretions. Its use is not common because of decreased availability of formulations and lack of proven efficacy.

Precautionary Information

Adverse Reactions and Side Effects

Side effects are attributed to each component. Prochlorperazine produces phenothiazine-like effects described more fully in the prochlorperazine monograph. Isopropamide may produce effects attributed to excess anticholinergic (antimuscarinic) stimulation and include ileus, urine retention, tachycardia, xerostomia (dry mouth), and behavior changes. Treat overdoses with physostigmine.

Contraindications and Precautions

Use of antimuscarinic drugs is contraindicated in animals with gastroparesis and should be used cautiously in animals with diarrhea.

Drug Interactions

Isopropamide will interfere with cholinergic drugs or drugs that promote motility (e.g., metoclopramide). Prochlorperazine will potentiate other sedatives.

Instructions for Use

This combination should be used with caution, especially if considered for repeated doses, in animals with intestinal disease. It can produce ileus.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

654 Promethazine Hydrochloride

Formulations

Prochlorperazine edisylate + isopropamide iodide is available in 3.33-mg prochlorperazine and 1.67-mg isopropamide capsules, and prochlorperazine maleate + isopropamide iodide is available in 4-mg prochlorperazine and 0.28-mg isopropamide per milliliter injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Cats

- 0.14-0.2 mL/kg q12h SQ.

Dogs

- 0.14-0.2 mL/kg q12h SQ.
- 2-7 kg body weight: 1 capsule q12h PO.
- 7-13 kg body weight: 1-2 capsules q12h PO.

Large Animal Dosage

No doses have been reported for large animals. The use is discouraged because isopropamide may decrease GI motility.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Promethazine Hydrochloride

proe-meth'ah-zeen hye-droe-klor-ide

Trade and Other Names: Phenergan

Functional Classification: Antiemetic, phenothiazine

Pharmacology and Mechanism of Action

Phenothiazine with strong antihistamine effects. Promethazine is used mostly for its antiemetic effects, for which it acts either via the antihistamine receptors or by blocking dopamine receptors associated with vomiting.

Indications and Clinical Uses

Promethazine is used for treatment of allergy (antihistamine effect) and as an antiemetic (motion sickness). The efficacy for treating allergies in animals has not been established. Other uses in animals have been derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Promethazine has a risk of producing phenothiazine effects such as sedation and other side effects attributed to other phenothiazines. There also may be

anticholinergic effects produced by the antimuscarinic properties in some individuals.

Contraindications and Precautions

Promethazine may produce antimuscarinic side effects, but these have not been reported from clinical use in animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Results of clinical studies in animals have not been reported. Therefore, the use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Promethazine is available in 6.25- and 25-mg/5 mL syrup; 12.5-, 25-, and 50-mg tablets; and 25- and 50-mg/mL injection.

Stability and Storage

Promethazine hydrochloride is soluble in water. If oxidized it will turn a blue color and should be discarded. It is sensitive to light and should be protected from light.

Small Animal Dosage

Dogs and Cats

- 0.2-0.4 mg/kg q6-8h IV, IM, PO, up to a maximum dose of 1 mg/kg.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Proprantheline Bromide

proe-pan'theh-leen broe'mide

Trade and Other Names: Pro-Banthine

Functional Classification: Antidiarrheal

Pharmacology and Mechanism of Action

Anticholinergic (antimuscarinic) drug. Proprantheline blocks acetylcholine receptor to produce parasympatholytic effects (atropine-like effects). Proprantheline will produce systemic parasympatholytic effects that include decreased GI secretions and motility.

Indications and Clinical Uses

Propantheline is used to decrease smooth muscle contraction and secretion of the gastrointestinal tract. Via the anticholinergic effects, it also has been used to treat vagal-mediated cardiovascular effects, such as bradycardia and heart block. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Because it will produce a profound decrease in gastrointestinal tract motility, its use should be carefully weighed against the potential for adverse effects.

Precautionary Information

Adverse Reactions and Side Effects

Side effects are attributed to excess anticholinergic (antimuscarinic) effects and include ileus, urine retention, tachycardia, xerostomia (dry mouth), and behavior changes. Treat overdoses with physostigmine.

Contraindications and Precautions

Do not use in animals with decreased intestinal motility. Use cautiously in animals with heart disease because it may increase heart rate. Do not use in animals with glaucoma.

Drug Interactions

Propantheline will interfere with cholinergic drugs or drugs that promote motility (e.g., metoclopramide). Bromide concentration in the formulation should be considered for animals also receiving bromide (e.g., potassium bromide) for treatment of epilepsy.

Instructions for Use

Propantheline has not been evaluated in clinical trials in animals, but propantheline is often the drug of choice for oral therapy in cases where an anticholinergic effect is desired.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Propantheline is available in 7.5- and 15-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.25-0.5 mg/kg q8-12h PO.

Large Animal Dosage

No doses have been reported for large animals. The use is discouraged because of adverse effect on GI motility.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Propiopromazine Hydrochloride

proe-pee-oh-prom'ah-zeen hye-droe-klor'ide

Trade and Other Names: Tranvet

Functional Classification: Antiemetic, phenothiazine

Pharmacology and Mechanism of Action

Propiopromazine is a phenothiazine with antihistamine effects. It has actions similar to other systemic phenothiazine drugs. Propiopromazine is used mostly for its antiemetic and sedative effects, for which it acts either via the antihistamine receptors or by blocking dopamine receptors. This drug was once registered for human use, but the only formulations currently available are veterinary forms. A related drug is promazine.

Indications and Clinical Uses

Propiopromazine has been used for its antiemetic and sedative effects, for which it acts either via the antihistamine receptors or by blocking dopamine receptors. It also has sedative and tranquilizing effects and has been used in cats and dogs to facilitate handling difficult, excited, or unruly animals. It has also been used as a preanesthetic. The approved label use indicates that it is “intended for administration to dogs as a tranquilizer. It is used as an aid in handling difficult, excited, and unruly dogs, and in controlling excessive kennel barking, car sickness, and severe dermatitis. It is also indicated for use in minor surgery and prior to routine examinations, laboratory procedures, and diagnostic procedures.” Despite this labeling, some of these indications are outdated and there are better treatments to manage these conditions.

Precautionary Information

Adverse Reactions and Side Effects

Phenothiazines can cause sedation as a common side effect. Propiopromazine produces extrapyramidal side effects in some individuals.

Contraindications and Precautions

It may lower blood pressure via alpha-adrenergic blockade.

Drug Interactions

Do not use with other phenothiazines, organophosphates, or procaine.

Instructions for Use

Results of clinical studies in animals have not been reported, despite indications listed on the product label. Use in animals (and doses) is based on anecdotal experience in animals and product label.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Propiopromazine is available as a 20-mg chewable tablet and a 5- or 10-mg/mL injection. Similar human drugs (e.g., promazine) have been discontinued.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 1.1-4.4 mg/kg q12-24h, PO.
- 0.1-1.1 mg/kg IV, IM (range of injectable doses depends on level of sedation needed).

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Propofol

proe'poe-fole

Trade and Other Names: Rapinovet, Propoflo (veterinary preparations), and Diprivan (human preparation)

Functional Classification: Anesthetic

Pharmacology and Mechanism of Action

Anesthetic. Mechanism of action is not well-defined but may be barbiturate-like. Propofol produces a short-acting (10 minutes) anesthesia, followed by a rapid and smooth recovery. The original formulation contained propofol in castor oil and other formulations containing soybean oil, glycerol, and purified egg phosphatide. The newest formulation contains 1% propofol in an emulsion mixture of medium- and long-chain triglycerides that produces greater encapsulation and lower concentration of free propofol.

Indications and Clinical Uses

Propofol is used as a short-term injectable anesthetic. It may be used as an induction agent followed by inhalation with halothane or isoflurane. The advantage of propofol over other agents is smooth, rapid recovery. It can be used with acepromazine, diazepam, alpha-2 agonists (e.g., dexmedetomidine), butorphanol, and inhalant anesthetics. An additional use of propofol is treatment of status epilepticus. It has been used safely and effectively for short-term induction and surgical procedures. It is also appropriate for procedures that require repeated anesthetic episodes in dogs and cats without producing adverse effects.

Precautionary Information

Adverse Reactions and Side Effects

Apnea and respiratory depression are the most common adverse effects, which are more likely when the dose is increased. Propofol can induce a dose-dependent cardiovascular depression, but the severity of cardiac adverse events is generally low. However, propofol can induce vasodilation, which can be minimized by supplementing with intravenous fluids. Propofol can cause spontaneous muscle movements (padding, tremors, muscle rigidity), panting, nystagmus, salivation,

and retraction of tongue in some animals (incidence 3%-7%). Less frequent adverse reactions include vomiting during recovery and pain. Pain upon injection occurs in people but is less common in dogs. The pain from injection is caused by the free propofol in the formulation and is decreased with newer formulations. Phenolic drugs such as propofol may potentially cause oxidative damage to hemoglobin in cats because of higher concentration of oxidizable sulphhydryl groups in feline RBCs (leading to Heinz-body formation and methemoglobinemia). However, this has not been a consistent problem with routine clinical use, and repeated anesthetic episodes have been performed safely in cats.

Contraindications and Precautions

Propofol can induce apnea, hypoxia, and cyanosis upon induction. Supplemental oxygen should be available to prevent adverse effects. Do not administer to hypotensive animals. When propofol has been used to sedate animals for intradermal skin testing, it may produce a greater number of positive reactions.

Drug Interactions

Propofol can be used with several other anesthetics and adjuncts safely. Propofol has been mixed with thiopental sodium (2.5%) in a 1:1 mixture without loss of effectiveness. However, it should not be mixed in a syringe with other anesthetics unless compatibility is known.

Instructions for Use

Shake well before using. Use strict aseptic technique for administration. Propofol may be diluted in 5% dextrose, lactated Ringer's solution, and 0.9% saline but not to less than 2 mg/mL concentration. Delay in penetration to brain is approximately 3 minutes; therefore there is a delayed CNS effect during injection. When using with other drugs, (acepromazine, barbiturates, opiates, etc.) lower doses should be administered. A mixture of 1:1 thiopental (2.5%) and propofol can be used in dogs and results in a smooth induction.

Patient Monitoring and Laboratory Tests

Monitor respiration rate and character during anesthesia with propofol.

Formulations

Propofol is available in 1% (10 mg/mL) injection in 20-mL ampules.

Stability and Storage

Shake well before use. Once an ampule has been opened, discard within 6 hours. Use careful technique to prevent microbial contamination of vial. Propofol has been mixed with thiopental sodium in a 1:1 mixture, and they are physically and chemically compatible. However, do not mix with other drugs unless compatibility is known. Propofol has a pH of 7-8.5. Protect from light. Store at 40°F to 72°F (4°C-22°C). Do not freeze.

Small Animal Dosage

Dogs

- 6.6 mg/kg IV slowly over 60 seconds. If necessary, an additional dose can be given at 0.5-1 mg/kg for intubation. Although the typical range needed for induction is 5-7 mg/kg IV, most inductions can be performed with 3.7 (± 1.5) mg/kg. If premedicated with alpha-2 agonists (e.g., dexmedetomidine), a lower dose of 3 mg/kg can be used.

660 **Propranolol Hydrochloride**

- Constant rate infusion (CRI): 5 mg/kg slowly IV, followed by 100-400 mcg/kg/min (or 6-24 mg/kg/hour).
- Status epilepticus: 1-6 mg/kg IV (to effect), followed by CRI of 0.1-0.6 mg/kg/min.

Cats

- Anesthesia induction: 7 mg/kg IV slowly. (If combined with midazolam, the propofol requirement listed can be reduced by as much as 25%.)
- CRI: 6 mg/kg slowly IV, followed by 200-300 mcg/kg/min (0.2-0.3 mg/kg) IV. For short-term procedures the total dose is 15 mg/kg for 30-minute protocol.
- CRI infusion with ketamine in cats: 0.025 mg/min/kg + ketamine 23-46 mcg/kg/min.
- Short-term surgery: 10 mg/kg IV dose delivered over 1 minute (duration of anesthesia 10-20 min).

Large Animal Dosage

Small Ruminants

- 4 mg/kg IV.

Pigs

- 2-5 mg/kg IV.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Propranolol Hydrochloride

proe-pran'oh-lole hye-droe-klor'ide

Trade and Other Names: Inderal and generic brands

Functional Classification: Beta blocker

Pharmacology and Mechanism of Action

Beta-adrenergic blocker. Nonselective for beta₁- and beta₂-adrenergic receptors. Class II antiarrhythmic. Propranolol is a lipophilic beta blocker and relies on the liver for clearance. Lipophilic beta blockers such as propranolol undergo high first-pass clearance, which reduces oral bioavailability and causes high interpatient variability in plasma concentrations and effects. Drug concentrations may be higher when there is impaired liver blood flow.

Indications and Clinical Uses

Propranolol is used primarily to decrease heart rate, decrease cardiac conduction, control tachyarrhythmias, and decrease blood pressure. Propranolol is effective in controlling the response from adrenergic stimulation. Beta blockers such as propranolol are among the most effective drugs for slowing heart rate.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects related to beta₁-blocking effects on heart. Propranolol causes cardiac depression and decreases cardiac output. Beta₂-blocking effects can cause bronchoconstriction and decrease insulin secretion. Weakness and fatigue can be caused by beta blockers, which can indicate that a reduction in dose is needed.

Contraindications and Precautions

Do not administer to animals with low cardiac reserve, bradycardia, or poor systolic function. Use cautiously in animals with respiratory problems; bronchoconstriction can occur from beta₂ effects. Hyperthyroid cats may have reduced clearance and increased risk of toxicity.

Drug Interactions

Lipophilic beta blockers, such as propranolol, rely on the liver for clearance. These drugs are subject to interactions from drugs that affect liver blood flow and interact with hepatic enzymes. Decreased liver blood flow will reduce propranolol clearance.

Instructions for Use

Usually dose is titrated according to patient's response. Start with low dose and increase gradually to desired effect. Clearance relies on hepatic blood flow; use cautiously in animals with impaired hepatic perfusion. In cats with hyperthyroidism, consider reducing the dose to prevent adverse effects. Cats with hyperthyroidism may have decreased clearance or increased oral absorption compared to other cats.

Patient Monitoring and Laboratory Tests

Monitor heart rate during treatment. Monitor respiratory function in patients prone to bronchoconstriction.

Formulations

Propranolol is available in 10-, 20-, 40-, 60-, 80-, and 90-mg tablets; 1-mg/mL injection; and 4- and 8-mg/mL oral solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Propranolol is soluble in water and ethanol. Suspensions prepared in various syrups and flavorings were stable for 4 months, but some settling may occur (shake before administration). pH of formulations should be kept at 2.8-4 for maximum stability. In alkaline solutions it will decompose.

Small Animal Dosage

Dogs

- 20-60 mcg/kg over 5-10 min IV (titrate dose to effect).
- 0.2-1 mg/kg q8h PO (titrate dose to effect).

Cats

- 0.4-1.2 mg/kg (2.5-5 mg/cat) q8h PO.

Large Animal Dosage

Horses

- 0.1 mg/kg IV, slowly. Repeat in 6-8 hours if necessary. If low dose is not effective, administer 0.5 mg/kg and increase dose to 2 mg/kg IV gradually until desired response.
- 0.4-0.8 mg/kg, q8h, PO.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Propylthiouracil

pro-pil-thye-oh-yoo'rah-sil

Trade and Other Names: Propyl-Thyracil, PTU, and generic brands

Functional Classification: Antithyroid

Pharmacology and Mechanism of Action

Antithyroid drug. Propylthiouracil inhibits synthesis of thyroid hormones; specifically, it interferes with conversion of T₄ to T₃.

Indications and Clinical Uses

Propylthiouracil has been used for the treatment of feline hyperthyroidism. Because of adverse effects, use of propylthiouracil in most cats has been replaced with methimazole or carbimazole. The only remaining indication for propylthiouracil in animals is to treat an acute “thyroid storm” because it rapidly inhibits conversion of T₃ to T₄, which methimazole does not.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects in cats include hepatopathy, hemolytic anemia, thrombocytopenia, and other signs of immune-mediated disease. If these signs are observed, the medication should be changed to another antithyroid agent.

Contraindications and Precautions

Do not use in cats with low platelet counts or bleeding problems.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Avoid the use of propylthiouracil because of the frequency of adverse effects. Other drugs can be used as a replacement such as methimazole or carbimazole.

Patient Monitoring and Laboratory Tests

Monitor CBC to look for evidence of hematologic abnormalities. Monitor T₄ levels to assess therapy.

Formulations

Propylthiouracil is available in 50- and 100-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Propylthiouracil is slightly soluble in water and soluble in ethanol.

Small Animal Dosage

Cats

- 11 mg/kg q12h PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Prostaglandin F₂ Alpha

pross-teh-glan'din

Trade and Other Names: Lutalyse, Dinoprost, and PGF₂ alpha

Functional Classification: Prostaglandin

Pharmacology and Mechanism of Action

Prostaglandin F₂ (PGF₂) alpha simulates the action of endogenous PGF₂ alpha in animals. It induces luteolysis and will terminate pregnancy. It is also called Dinoprost.

Indications and Clinical Uses

PGF₂ alpha has been used to treat open pyometra in animals. In cattle, Dinoprost has been used for treatment of chronic endometritis. Use for inducing abortion in small animals has been questioned and other drugs are usually used instead. However, in large animals, Dinoprost is used to induce abortion in the first 100 days of gestation. Dinoprost is used for estrous synchronization in cattle and horses by causing luteolysis. In pigs, Dinoprost is used to induce parturition when given within 3 days of farrowing.

Precautionary Information

Adverse Reactions and Side Effects

PGF₂ alpha causes increased smooth muscle tone, resulting in diarrhea, abdominal discomfort, bronchoconstriction, and an increase in blood pressure. In small animals, other side effects include vomiting. Induction of abortion may cause retained placenta.

Contraindications and Precautions

Do not administer IV. PGF₂ alpha induces abortion in pregnant animals. Use caution when handling this drug. It should not be handled by pregnant women. Absorption through the intact skin is possible. People with respiratory problems also should not handle Dinoprost because absorption across the skin may lead to bronchoconstriction.

Drug Interactions

According to the label, dinoprost should not be used with nonsteroidal anti-inflammatory drugs (NSAIDs) because these drugs inhibit synthesis of

prostaglandins. However, NSAIDs should not affect concentrations of PGF₂ alpha after administration with this product. When using oxytocin concurrently, it should be used cautiously because there is a risk of uterine rupture.

Instructions for Use

Use in treating pyometra should be monitored carefully.

Patient Monitoring and Laboratory Tests

Monitor for signs of estrus after treatment.

Formulations

PGF₂ is available in a 5-mg/mL solution for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It should be stored in a manner to avoid skin contact with humans.

Small Animal Dosage

Dogs

- Pyometra: 0.1-0.2 mg/kg once daily for 5 days SQ.
- Termination of pregnancy: 0.025-0.05 mg (25-50 mcg)/kg q12h IM.

Cats

- Pyometra: 0.1-0.25 mg/kg once daily for 5 days SQ.
- Termination of pregnancy: 0.5-1 mg/kg IM for 2 injections.

Large Animal Dosage

Cattle

- Termination of pregnancy: 25 mg total dosage, administered once IM.
- Estrus synchronization: 25 mg once IM or twice at 10-12 day intervals.
- Pyometra: 25 mg IM administered once.

Horses

- Estrus synchronization: 1 mg/100 pounds (1 mg/45 kg) IM or 1-2 mL administered once IM. Mares should return to estrus within 2-4 days and ovulate 8-12 days after treatment.

Pigs

- Induction of parturition: 10 mg administered once IM. Parturition occurs within 30 hours.

Regulatory Information

No withdrawal time required for meat or milk.

Pseudoephedrine Hydrochloride

soo-doh-eh-fed'rin hye-droe-klor'ide

Trade and Other Names: Sudafed and generic brands

Functional Classification: Adrenergic agonist

Pharmacology and Mechanism of Action

Adrenergic agonist. Pseudoephedrine is a sympathomimetic. It nonselectively acts as an agonist for the alpha-adrenergic and beta-adrenergic receptors. These receptors are found throughout the body, such as on sphincters, blood vessels, smooth muscle, and heart. Pseudoephedrine produces a similar effect as ephedrine and phenylpropranolamine. However, compared to ephedrine it may have fewer CNS effects.

Indications and Clinical Uses

Pseudoephedrine has been used as a decongestant, as a mild bronchodilator, and to increase tone of urinary sphincter. Pseudoephedrine, phenylpropranolamine, and ephedrine have similar alpha-receptor and beta-receptor effects. The most common use in animals is for treating urinary incontinence. The mechanism for this action appears to be via stimulating receptors on the sphincter. In people, it has been used as a decongestant. However, because pseudoephedrine is easily diverted to manufacture of methamphetamine, the availability in human medicine has diminished unless available by prescription. Most of the over-the-counter forms and combination products for people have been removed. For animals, phenylpropranolamine will produce similar effects and may be substituted.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are attributed to adrenergic effects. These include excitement, rapid heart rate, increased blood pressure, and arrhythmias.

Contraindications and Precautions

Pseudoephedrine may cause some effects that are similar to phenylpropranolamine. Use cautiously in patients with cardiovascular disease. Use cautiously, or not at all, with monoamine oxidase inhibitors (MAOIs; e.g., selegiline). Beta agonists such as pseudoephedrine may increase blood glucose. Pseudoephedrine has been used in clandestine laboratories to illegally manufacture methamphetamine. Therefore, the availability of pseudoephedrine has been limited in most states.

Drug Interactions

Pseudoephedrine, like other sympathomimetic agents, is expected to potentiate other alpha- and beta-receptor agonists. It may cause increased vasoconstriction and changes in heart rate. Use cautiously with other vasoactive drugs. Use cautiously with other drugs that may lower seizure threshold. Use of inhalant anesthetics with PPA may increase cardiovascular risk. Do not use with tricyclic antidepressants (TCAs) or MAOIs (e.g., selegiline or amitraz).

Instructions for Use

Although clinical trials have not been conducted for comparison, it is believed that the action and efficacy of pseudoephedrine is similar to ephedrine and phenylpropranolamine.

Patient Monitoring and Laboratory Tests

Monitor heart rate in patients. If possible, monitor blood pressure and ECG in patients that may be susceptible to cardiovascular problems.

Formulations Available

Pseudoephedrine is available in 30- and 60-mg tablets, 120-mg capsules, and 6-mg/mL syrup. (Some combination formulations have other ingredients such as antitussives or antihistamines.)

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Pseudoephedrine is soluble in water and ethanol. Keep compounded formulations at a low pH for maximum stability. Protect from freezing.

Small Animal Dosage

Dogs

- 0.2-0.4 mg/kg (or 15-60 mg/dog) q8-12h PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Psyllium

sill'ee-um

Trade and Other Names: Metamucil and generic brands

Functional Classification: Laxative

Pharmacology and Mechanism of Action

Bulk-forming laxative. The action of psyllium is to absorb water and expand to provide increased bulk and moisture content to the stool, which encourages normal peristalsis and bowel motility. Psyllium also may have antilipidemia effects.

Indications and Clinical Uses

Psyllium is administered orally for treatment of constipation and bowel evacuation. In horses, it has been used for treating sand colic, but the effectiveness for this indication has not been shown.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. Intestinal impaction can occur with overuse or in patients with inadequate fluid intake. In horses, it may be difficult to administer via stomach tube because it is prone to forming a gel when mixed with water.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

Psyllium may lower serum cholesterol measurements.

Formulations

- Psyllium is available as powder, usually 3.4 g/tsp.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 1 teaspoon/5-10 kg (added to each meal).

Large Animal Dosage

Horses

- Up to 1000 mg/kg per day PO, via stomach tube or added to feed.

Regulatory Information

No withdrawal times are necessary.

Pyrantel Pamoate, Pyrantel Tartrate

pye-ran'tel

Trade and Other Names: Nemex, Strongid, Priex, Pyran, and Pyr-A-Pam

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic drug. Pyrantel is in the class of tetrahydropyrimidines. Others in this class include morantel. Pyrantel acts to interfere with ganglionic neurotransmission via blocking with acetylcholine receptors and other sites. This causes paralysis of the parasites. Paralyzed worms are expelled from the intestinal lumen by peristalsis. Pyrantel is poorly water soluble and not absorbed systemically in ruminants, although some absorption occurs in monogastric animals. Most of the activity is confined to the intestinal lumen.

Indications and Clinical Uses

Pyrantel is indicated for treatment of intestinal nematodes. In horses, pyrantel is used for treatment and prevention of nematodes, including pinworms (*Oxyuris equi*), large roundworms (*Parascaris equorum*), large strongyles (*Strongylus edentatus*, *S. equinus*, and *S. vulgaris*), and small strongyles. When added to medicated feed it is used to control nematodes, including pinworms (*O. equi*), large roundworms (*P. equorum*), large strongyles (*S. edentatus*, *S. vulgaris*, and *Triodontophorus* species), and small strongyles. In pigs it is used for prevention of large roundworm (*Ascaris suum*) and prevention of the nodular worm, *Oesophagostomum* species. In dogs and cats, it is used for treatment of nematodes, including hookworms (*Ancylostoma* species) and roundworms (*Toxocara cati*, *T. canis* and *Toxascaris leonina*). There is some evidence that it is effective for control of some tapeworms, but ordinarily other drugs should be used for tapeworms.

Precautionary Information**Adverse Reactions and Side Effects**

No adverse effects reported.

Contraindications and Precautions

No contraindications in animals. It may be used in all ages and in lactating and pregnant animals.

Drug Interactions

CNS toxicity may be more likely when coadministered with levamisole, but this is not reported from clinical use in animals.

Instructions for Use

Shake suspension prior to use. Doses listed are for single dose, but they may be repeated as part of a parasite management program. Lower doses may be added to daily feed for prevention of parasites.

Patient Monitoring and Laboratory Tests

Monitor fecal samples for presence of intestinal parasites.

Formulations

Pyrantel is available in 171-, 180-, and 226-mg (base) per mL paste; 22.7- and 113.5-mg (base) tablets; and 2.27-, 4.54-, and 50-mg (base) per mL suspension. Equine paste is 19.31%. It is also available in 10.6-, 12.6-, and 21.1-g/kg of pellets for medicated feed.

Pyrantel pamoate is a salt and contains 34.7% pyrantel base. Doses are based on the amount of pyrantel base. Pyrantel tartrate contains 57.9% pyrantel base. Many of the formulations contain other antiparasitic drugs (e.g., praziquantel).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Protect from freezing.

Small Animal Dosage**Dogs**

- 5 mg/kg once PO, repeat in 7-10 days.

Cats

- 20 mg/kg once PO.
Doses may be mixed with food.

Large Animal Dosage**Horses**

- Nematodes: 6.6 mg/kg PO.
- Cestodes: 13.2 mg/kg.
- Medicated feed: 12.5 mg/kg as a single dose or 2.6 mg/kg/day for prevention.

Pigs

- 22 mg/kg administered in feed, as a single treatment.

Regulatory Information

Pigs: 1-day withdrawal (US); 7 days (Canada).

Withdrawal times for other species are not established. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Pyridostigmine Bromide

peer-id-oh-stig'meen broe'mide

Trade and Other Names: Mestinon and Regonol

Functional Classification: Anticholinesterase, antimyasthenic

Pharmacology and Mechanism of Action

Cholinesterase inhibitor and antimyasthenic drug. This drug inhibits the enzyme that breaks down acetylcholine. Therefore it prolongs the action of acetylcholine at the synapse. The major difference between physostigmine and neostigmine or pyridostigmine is that physostigmine crosses the blood-brain barrier and the others do not. Compared to neostigmine, pyridostigmine has a longer duration of action.

Indications and Clinical Uses

Pyridostigmine is used as an antidote for anticholinergic intoxication and treatment (antidote) for neuromuscular blockade. It is also used as a treatment of myasthenia gravis, ileus, and retention of urine (such as postoperative) by increasing tone of bladder smooth muscle. Most often, pyridostigmine is the first drug of choice for myasthenia gravis and is preferred over neostigmine.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are caused by the cholinergic action resulting from inhibition of cholinesterase. These effects can be seen in the GI tract as diarrhea and increased secretions. Other adverse effects can include miosis, bradycardia, muscle twitching or weakness, and constriction of bronchi and ureters. Pyridostigmine may be associated with fewer adverse effects than neostigmine, but the effects of pyridostigmine may persist longer. If adverse effects are observed, treat with anticholinergic drugs such as 0.125 mg of hyoscyamine sulfate. Atropine also may be used.

Contraindications and Precautions

Do not use in these conditions: urinary obstruction, intestinal obstruction, asthma or bronchoconstriction, pneumonia, and cardiac arrhythmias. Do not use in patients sensitive to bromide. Consider the amount of bromide in dose in any patient also receiving bromide (KBr) for treatment of seizures.

Drug Interactions

Bromide concentration in the formulation should be considered for animals also receiving bromide (e.g., potassium bromide) for treatment of epilepsy. (Sodium bromide may be used as an alternative.)

Instructions for Use

Pyridostigmine is used for treatment of myasthenia gravis. Neostigmine and pyridostigmine have fewer side effects than physostigmine. When used, frequency of dose may be increased based on observation of effects. After administration, pyridostigmine benefits should be observed in approximately 15-30 minutes. The duration of action may be 3-4 hours.

Patient Monitoring and Laboratory Tests

Monitor GI effects. Monitor cardiac rate and rhythm.

Formulations

Pyridostigmine is available in 12-mg/mL oral syrup, 60-mg tablets (scored), and 5-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Pyridostigmine is soluble in water. Store in acid solutions; it may decompose in alkaline vehicles.

Small Animal Dosage

Dogs and Cats

- Antimyasthenic: 0.02-0.04 mg/kg q2h IV or 0.5-3 mg/kg q8-12h PO.
- Antidote for muscle blockade: 0.15-0.3 mg/kg IM or IV, as needed.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Pyrimethamine

peer-ih-meth'ah-meen

Trade and Other Names: Daraprim

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Antibacterial and antiprotozoal drug. Pyrimethamine blocks the dihydrofolate reductase enzyme, which inhibits synthesis of reduced folate and nucleic acids.

Activity of pyrimethamine is more specific against protozoa than bacteria.

Pyrimethamine is often combined with a sulfonamide to produce a synergistic effect.

Indications and Clinical Uses

Pyrimethamine is used to treat protozoal infections in animals. It is most often combined with a sulfonamide, either separately, or in a combined formulation. See pyrimethamine + sulfadiazine monograph for additional information.

Precautionary Information

Adverse Reactions and Side Effects

There is a risk of folic acid anemia when pyrimethamine and sulfonamide combinations are administered. This has been observed in 12% of treated horses in a field trial. Folic or folinic acid (preferably folinic acid) has been supplemented to prevent anemia, but benefit of this treatment is unclear. Bone marrow suppression usually resolves after discontinuation of treatment. Diarrhea may

occur after oral administration. Multiple adverse effects have been documented from administration of sulfonamides. These include allergic reactions, Type II and III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites.

Contraindications and Precautions

Do not administer to animals sensitive to sulfonamides.

Drug Interactions

Drug interactions are not reported for animals. However, a combination of pyrimethamine with trimethoprim/sulfonamides will enhance the bone marrow toxicity.

Instructions for Use

Pyrimethamine is used either alone or in combination with sulfonamides. (See pyrimethamine + sulfadiazine combination for further details.)

Patient Monitoring and Laboratory Tests

Monitor CBC periodically in animals receiving treatment.

Formulations

Pyrimethamine is available in 25-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Pyrimethamine is poorly soluble in water, but it is more soluble in ethanol. Tablets have been crushed to make extemporaneous suspensions in syrups and other flavorings. These formulations have been stable for 7 days and up to 90 days, depending on the formulation.

Small Animal Dosage

Dogs

- 1 mg/kg q24h PO for 14-21 days (5 days for *Neospora caninum*).

Cats

- 0.5-1 mg/kg q24h PO for 14-28 days.

Large Animal Dosage

- Horses, equine protozoal myeloencephalitis (EPM), caused by *Sarcocystis neurona*: 1 mg/kg q24h PO in combination with a sulfonamide (see details on pyrimethamine + sulfadiazine).

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Pyrimethamine + Sulfadiazine

peer-ih-meth'ah-meen + sul-fa-dye'ah-zeen

Trade and Other Names: ReBalance

Functional Classification: Antiprotozoal

Pharmacology and Mechanism of Action

Antibacterial, antiprotozoal drug, and sulfonamide combination. Pyrimethamine blocks dihydrofolate reductase enzyme, which inhibits synthesis of reduced folate and nucleic acids. Activity of pyrimethamine is more specific against protozoa than bacteria. Sulfadiazine provides a false PABA substrate for synthesis of dihydrofolic acid by bacteria and protozoa. Together the combination is synergistic against protozoa.

Indications and Clinical Uses

Pyrimethamine + sulfadiazine is used to treat horses with equine protozoal myeloencephalitis (EPM). Although not registered for use to treat other animals, the equine formulation has been administered to small animals to treat protozoal infections caused by *Toxoplasma*, *Neospora*, and *Sarcocystis* species.

Precautionary Information

Adverse Reactions and Side Effects

When administered with trimethoprim sulfonamide combinations, anemia has been observed. Folic or folinic acid has been supplemented to prevent anemia, but benefit of this treatment is unclear.

Contraindications and Precautions

Do not administer to animals that may be prone to anemia or in which a CBC cannot be monitored.

Drug Interactions

Drug interactions are not reported for animals. However, a combination of pyrimethamine with trimethoprim/sulfonamides will enhance the bone marrow toxicity.

Instructions for Use

Use of pyrimethamine sulfadiazine has been primarily for treatment of protozoal infections in horses. However, there is anecdotal evidence that pyrimethamine + sulfadiazine may be indicated for treatment of some protozoa (e.g., *Toxoplasma*, *Neospora*, or *Sarcocystis*) in small animals.

Patient Monitoring and Laboratory Tests

Monitor CBC periodically in animals receiving treatment. A CBC should be performed at least monthly in treated animals.

Formulations

Pyrimethamine + sulfadiazine is available in an oral suspension that is 250 mg sulfadiazine and 12.5 mg pyrimethamine per mL.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze.

Small Animal Dosage

Dogs and Cats

- 1 mg/kg pyrimethamine and 20 mg/kg sulfadiazine once daily PO. (Equivalent to one-third milliliter of the equine formulation—0.33 mL—per 4 kg of body weight.)

Large Animal Dosage

- EPM caused by *S. neurona*: 1 mg/kg pyrimethamine, 20 mg/kg sulfadiazine q24h PO (4 mL per 110 pounds). Treatment duration in horses varies from 90-270 days.

Regulatory Information

Do not administer to animals intended for food.

Quinacrine Hydrochloride

kwin'eh-krin hye-droe-klor'ide

Trade and Other Names: Atabrine (No longer available in the US.)

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Antimalarial drug. Quinacrine is an outdated antimalarial drug. It inhibits nucleic acid synthesis in parasites.

Indications and Clinical Uses

Quinacrine is used occasionally for treatment of protozoa (*Giardia*), but other drugs (e.g., metronidazole and tinidazole) are used more often. Although it is not commercially available, veterinarians have obtained quinacrine through compounding pharmacies.

Precautionary Information

Adverse Reactions and Side Effects

Side effects are common. Vomiting occurs after oral administration.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Doses listed are for treatment of giardiasis. Effects for other organisms are not reported.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Quinacrine is available in 100-mg tablets. Quinacrine may no longer be marketed in the US, but it may be available from some pharmacies in a compounded formulation.

Stability and Storage

Store in a tightly closed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

• 6.6 mg/kg q12h PO for 5 days.

Cats

• 11 mg/kg q24h PO for 5 days.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Quinidine, Quinidine Sulfate

kwin-ih-deen

Trade and Other Names: Quinidine gluconate: Quiniglute, Duraquin and Quinidine polygalacturonate: Cardioquin, and Quinidine sulfate: Cin-Quin, and Quinora

Functional Classification: Antiarrhythmic

Pharmacology and Mechanism of Action

Antiarrhythmic drug. Class I antiarrhythmic. Like other Class I antiarrhythmic drugs, its action is to inhibit sodium influx via blockade of sodium channels. Therefore it suppresses cardiac Phase 0 action potential and decreases ectopic arrhythmic foci.

Indications and Clinical Uses

Quinidine is used to treat ventricular arrhythmias and occasionally to convert atrial fibrillation to sinus rhythm. In small animals it is rarely used because there are other more effective and safer alternatives available. In horses and cattle, quinidine has been the drug of choice to treat atrial fibrillation. However, other alternatives are considered because of frequency of adverse effects in horses and decreased availability of commercial forms of quinidine. Alternatives include diltiazem and electrical cardioversion.

Precautionary Information

Adverse Reactions and Side Effects

Side effects with quinidine are more common than procainamide and include nausea and vomiting. Adverse effects include hypotension and tachycardia (because of vagolytic effect). With intravenous dosing, adverse effects such as hypotension and tachyarrhythmias are common in cattle. In horses, adverse effects are common, which include hypotension, gastrointestinal problems, and supraventricular tachycardia. Sudden cardiac death is possible but uncommon in horses.

Contraindications and Precautions

Quinidine may increase heart rate. Use cautiously in animals with heart disease.

Drug Interactions

Quinidine is a well-known multidrug resistance (MDR1) membrane pump (p-glycoprotein) inhibitor. It will interfere with membrane channels and increase concentrations of some coadministered drugs. Coadministration with digoxin may increase digoxin concentrations. See Appendix for list of potential p-glycoprotein substrates.

Instructions for Use

Quinidine has a rapid clearance in cattle (half-life is 2.25 hours), which results in the need for frequent administration. Equine doses are usually administered orally via stomach tube. Because of decreased availability of commercial forms and frequency of adverse effects, quinidine is not used as commonly as other Class I antiarrhythmic drugs. If quinidine is administered, calculate the dose to the amount of quinidine base in each formulation: 324 mg of quinidine gluconate has a 202-mg quinidine

676 Quinidine, Quinidine Sulfate

base; 275 of mg quinidine polygalacturonate has a 167-mg quinidine base; 300 mg of quinidine sulfate has a 250-mg quinidine base.

Patient Monitoring and Laboratory Tests

Quinidine can be hypotensive and vagolytic. Monitor patient's ECG for arrhythmias and monitor blood pressure.

Formulations

In some countries, quinidine is being discontinued and may be difficult to obtain. Older formulations include quinidine gluconate 324-mg tablets and 80-mg/mL injection; quinidine polygalacturonate in 275-mg tablets; and quinidine sulfate in 100-, 200-, and 300-mg tablets, 200- and 300-mg capsules, and 200-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Quinidine is slightly soluble in water. Quinidine salts may form a dark color when exposed to light and should not be used. Quinidine has been compounded for oral use in syrups (e.g., Ora-Sweet) and is stable for 60 days.

Small Animal Dose

Dogs

- Quinidine gluconate: 6-20 mg/kg q6h IM or 6-20 mg/kg q6-8h PO (of base).
- Quinidine polygalacturonate: 6-20 mg/kg q6h PO (of base).
- Quinidine sulfate: 6-20 mg/kg q6-8h PO (of base) or 5-10 mg/kg q6h IV.

Large Animal Dosage

Cattle

- Treatment of atrial fibrillation: Quinidine is poorly absorbed orally in cattle and must be given IV. A loading dose of 49 mg/kg (given over 4 hours) to be followed by 42 mg/kg IV maintenance dose. Or give 40 mg/kg diluted in 4 L of fluid slowly at a rate of 1 L/hr until fibrillation is converted.

Horses

- Atrial fibrillation treatment: 5 grams per 450 kg BW (per 1000 pounds) for the first treatment; thereafter give 10 grams per 450 kg every 2 hours until the sinus rate is achieved. IV dose is 1-1.5 mg/kg every 10-15 min to a total dose of 10 mg/kg or until sinus rate conversion.

Regulatory Information

Withdrawal times are not established for animals that produce food. Because of rapid elimination, short withdrawal times can be used. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Racemethionine

rah-see'meth-eye'oh-neen

Trade and Other Names: Urozeze, Methio-Form, and generic brands and Pedameth, Uracid, and generic brands (human preparations)

Functional Classification: Acidifier

Pharmacology and Mechanism of Action

Urinary acidifier. Methionine lowers urinary pH. Racemethionine also has been used to protect against acetaminophen overdose in people by restoring hepatic concentrations of glutathione.

Indications and Clinical Uses

It is used as a urinary acidifier. In people it also is used to treat dermatitis caused by urinary incontinence (reduces urine ammonia).

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported.

Contraindications and Precautions

Do not use in animals with metabolic acidosis. Do not use in young cats. Do not use in animals with hepatic disease.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Use for acetaminophen toxicity has been replaced by acetylcysteine.

Patient Monitoring and Laboratory Tests

Monitor CBC and hepatic enzymes if used to treat toxicity.

Formulations

Racemethionine is available in 500-mg tablets, 75-mg/5-mL pediatric oral solution, 200-mg capsules, and powders to add to an animal's food.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 150-300 mg/kg/day PO.

Cats

- 1-1.5 g per cat PO (added to food each day).

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Ramipril

ram'ih-pril

Trade and Other Names: Vasotop**Functional Classification:** Vasodilator, angiotensin-converting enzyme (ACE) inhibitor

Pharmacology and Mechanism of Action

Like other ACE inhibitors, ramipril inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and will stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. The ability of aldosterone to cause sodium and water retention contributes to congestion. Ramipril, like other ACE inhibitors, will cause vasodilation and decrease aldosterone-induced congestion. ACE inhibitors also contribute to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins. There is evidence for a cardioprotective effect when used to treat dogs with heart disease caused by cardiomyopathy or valvular disease.

Indications and Clinical Uses

Ramipril is used to treat hypertension and congestive heart failure (CHF). It has not been studied as much as other ACE inhibitors in animals (e.g., enalapril or benazepril), but it is expected to have similar pharmacodynamic effects. It has been primarily used in dogs. It has also been used safely in cats to control hypertension but has not been effective for treating hypertrophic cardiomyopathy.

Precautionary Information

Adverse Reactions and Side Effects

It has not been used as often as other drugs in this class; therefore, a full range of potential adverse effects has not been reported. Ramipril was well tolerated in clinical studies in dogs.

Contraindications and Precautions

Studies performed in experimental dogs indicated that dose adjustments are not necessary when administering ramipril in dogs with impaired renal function. Discontinue use of ACE inhibitors in pregnant animals; they cross the placenta and have caused fetal malformations and death of the fetus.

Drug Interactions

Use cautiously with other hypotensive drugs and diuretics. Nonsteroidal anti-inflammatory drugs (NSAIDs) may decrease vasodilating effects.

Instructions for Use

Clinical efficacy has been demonstrated in dogs with dilated cardiomyopathy. Other drugs used for treatment of heart failure may be used concurrently. Dogs also may receive pimobendan, digoxin and/or furosemide with ramipril.

Patient Monitoring and Laboratory Tests

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

Formulations

Ramipril is available in 1.25-, 2.5-, 5-, and 10-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 0.125-0.25 mg/kg daily PO.

Cats

- 0.125 mg/kg, q24h, PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Ranitidine Hydrochloride

rah-nit'ih-deen hye-droe-klor'ide

Trade and Other Names: Zantac

Functional Classification: Antiulcer agent

Pharmacology and Mechanism of Action

Histamine₂ antagonist (H₂ blocker). Ranitidine, like other H₂ blockers, suppresses histamine stimulation of gastric parietal cell to decrease gastric acid secretion. Ranitidine will increase stomach pH. Ranitidine is longer acting and 4 to 10 times more potent than cimetidine. The half-life of ranitidine is longer than cimetidine, which results in decreased frequency of administration for ranitidine. When adjusting doses, ranitidine hydrochloride is 89% ranitidine.

Indications and Clinical Uses

Ranitidine is used to treat ulcers and gastritis. It does not produce as much of a sustained increase in stomach pH as proton pump inhibitors (omeprazole). Ranitidine (6.6 mg/kg PO) in foals suppressed acid for 6 hours, but omeprazole suppressed acid for 22 hours at 4 mg/kg. It is used to prevent nonsteroidal anti-inflammatory drug (NSAID)-induced ulcers in animals, although efficacy has not been demonstrated for this effect. In horses, ranitidine did not improve healing of ulcers induced by NSAIDs, and it was not as effective as omeprazole for treating ulcers. Ranitidine may stimulate stomach emptying and colon motility via anticholinesterase action. In horses, the effect on gastric emptying is minimal.

R

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are usually seen only with decreased renal clearance. In people, CNS signs may occur with high doses. Ranitidine may have fewer effects on endocrine function and drug interactions compared to cimetidine.

Contraindications and Precautions

Fewer drug interactions are possible with ranitidine compared to cimetidine because ranitidine does not inhibit cytochrome P450 enzymes.

Drug Interactions

Ranitidine and other H₂-receptor blockers block secretion of stomach acid. Therefore, they will interfere with oral absorption of drugs dependent on acidity, such as ketoconazole, itraconazole, and iron supplements. Unlike cimetidine, ranitidine is not known to inhibit microsomal P450 enzymes.

Instructions for Use

Pharmacokinetic information in dogs suggests that ranitidine may be administered less often than cimetidine to achieve continuous suppression of stomach acid secretion. Use in horses and foals is based on experimental studies and pharmacokinetic data.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Ranitidine is available in 75-, 150-, and 300-mg tablets; 50- and 300-mg capsules; and 25-mg/mL injection. Some forms are available over the counter (OTC).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Ranitidine hydrochloride is soluble in water. Tablets have been crushed and mixed with water and syrup and were stable for 7 days. Protect from freezing.

Small Animal Dosage

Dogs

- 2 mg/kg q8h IV or PO.

Cats

- 2.5 mg/kg q12h IV, or 3.5 mg/kg q12h PO.

Large Animal Dosage

Horses

- 2.2-6.6 mg/kg q6-8h PO. The higher dose (6.6 mg/kg) is more effective at suppressing stomach acid.
- 2 mg/kg q6-8h IV.

Calves

- 50 mg/kg q8h PO in milk-fed calves.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 5

Remifentanyl Hydrochloride

Rem-i-fen' ta-nil

Trade and Other Names: Ultiva

Functional Classification: Anesthetic, analgesic, opioid

Pharmacology and Mechanism of Action

Remifentanyl is a potent opioid similar in potency and activity to fentanyl. Like fentanyl, remifentanyl has activity primarily at the mu-opiate receptor. The difference between remifentanyl and other opioids is that it has an ultrashort action. The rapid onset and peak effect and short duration of action are attributed to its unique disposition. Remifentanyl is quickly metabolized by hydrolysis of the propanoic acid-methyl ester by blood and tissue esterases. Therefore it is rapidly metabolized in the blood, does not depend on liver metabolism, and can be used safely in patients with liver or kidney disease. It also is rapidly delivered to tissues with an octanol:water partition coefficient of 17.9 at pH 7.3. However, it does not accumulate in tissues or blood even after prolonged IV infusions. Because of the rapid metabolism and quick equilibration between plasma and tissues, remifentanyl has a fast onset of activity after IV injection. The half-life in dogs is approximately 3-6 minutes and does not change with increasing doses. Recovery occurs rapidly (within 5 to 10 minutes), and when using constant rate infusions, new steady-state concentrations can be achieved within 5 to 10 minutes after changes in infusion rate. Because of rapid equilibration with tissues, it can be easily titrated to the desired depth of anesthesia/analgesia by changing the continuous infusion rate or by administering an IV bolus injection.

Indications and Clinical Uses

Remifentanyl is used as an anesthetic agent, often in combination with other agents. Because of its rapid metabolism and short half-life, it should be administered via constant rate infusion (CRI) to maintain a balanced anesthetic effect. It is used for induction and maintenance of anesthesia. It can be administered with other drugs, including inhalant anesthetics, alpha-2 agonists, sedatives, and tranquilizers. Because it does not require hepatic metabolism or renal elimination, it can be administered safely to patients that have liver or kidney disease. Remifentanyl use in dogs is limited to a few studies and case reports. Doses in animals have been extrapolated from humans (human starting dose is 0.1 mcg/kg/min CRI). Remifentanyl has been infused safely in cats, and over a wide range of doses (0.06-16 mcg/kg/min) IV it did not affect isoflurane MAC.

Precautionary Information

Adverse Reactions and Side Effects

Like other opioids and opiates, remifentanyl has adverse effects that are attributed to the binding to opiate receptors. These effects include reduced heart rate and sedation. In people at rates greater than 0.2 mcg/kg/min, respiratory depression occurs. In cats, remifentanyl induced dysphoria at high infusion rates (>8 mcg/kg/min). Adverse effects will quickly dissipate when the infusion is discontinued because of the drug's rapid metabolism in the plasma and tissues. The opioid activity of remifentanyl is antagonized by opioid antagonists such as naloxone.

Contraindications and Precautions

Remifentanyl will potentiate the effects of other anesthetics. Use cautiously in animals sensitive to opiates.

Drug Interactions

Other anesthetics will be potentiated when used with remifentanyl. Lower doses of other anesthetic agents may be used when combined with remifentanyl.

Instructions for Use

Administer IV as a constant rate infusion (CRI).

Patient Monitoring and Laboratory Tests

Monitor patients during anesthetic protocol. Monitor ECG, heart rate, and breathing character.

Formulations

Remifentanyl is available in a 1-mg/mL solution and in vials of 1, 2, or 5 mg of remifentanyl base. Add 1 mL of diluent per milligram of remifentanyl to produce a solution of 1 mg/mL. This solution can be further diluted for intravenous use to a concentration of 20, 25, 50, or 250 mcg/mL.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Remifentanyl HCl has a pKa of 7.07, but the pH of reconstituted solutions ranges from 2.5 to 3.5. The pH of solutions should be considered when combining with other drugs or fluid solutions. Remifentanyl is compatible with sterile water, lactated Ringer's solution, 5% dextrose, 0.9% sodium chloride, and 0.45% sodium chloride. Once mixed in solution, it is stable for 4 hours at room temperature. It can be mixed in solution with propofol. Because of the presence of plasma esterases, it should not be mixed with blood products. Therefore, administration with IV blood transfusions is not recommended.

Small Animal Dosage

Dogs

- CRI: 0.20 mcg/kg/min, up to 1 mcg/kg/min. Infusion rate can be adjusted to achieve desired effect, but 0.30 mcg/kg/min was optimum to achieve desired effects in anesthetized dogs, and higher rates did not produce increased benefit.

Cats

- Similar infusion rates have been used as in dogs, but optimum doses have not been determined for cats.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Remifentanyl is a Schedule II controlled substance. Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Riboflavin (Vitamin B₂)

rye'boe-flay-vin

Trade and Other Names: Vitamin B₂

Functional Classification: Vitamin

Pharmacology and Mechanism of Action

Vitamin B₂ supplement. Thiamine is commonly included as an ingredient in vitamin B complex aqueous solutions for injection. In these formulations it is available as 5' phosphate sodium riboflavin. Vitamin B complex often contains thiamine (B₁), riboflavin, niacinamide, and cyanocobalamin B₁₂.

Indications and Clinical Uses

Riboflavin is used as a vitamin B₂ supplement. It is usually administered for maintenance in patients who are vitamin B₂ deficient.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are rare because water-soluble vitamins are easily excreted. Riboflavin may discolor the urine.

Contraindications and Precautions

Do not administer injectable solution IV rapidly if it contains thiamine (vitamin B₁₂) because this may cause an anaphylactic reaction.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

It is not necessary to supplement in animals with well-balanced diets.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Riboflavin is available in various-sized tablets in increments from 10 to 250 mg. Riboflavin is most commonly formulated with other vitamins in a "vitamin B complex" aqueous solution for injection (2 and 5 mg/mL of riboflavin).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 10-20 mg/day PO.
- 1-4 mg/dog q24h SQ.

Cats

- 5-10 mg/day PO.
- 1-2 mg/cat q24h SQ.

Large Animal Dosage

Lambs

- 2-4 mg q24h IM, or SQ.

Cattle and Horses

- 20-40 mg q24h IM or SQ.

Calves and Foals

- 6-10 mg q24h IM or SQ.

Sheep and Pigs

- 10-20 mg q24h IM or SQ.

Regulatory Information

Because of the low risk of harmful residues in animals intended for food, no withdrawal time is necessary.

Rifampin

rih-fam'pin

Trade and Other Names: Rifadin, Rimactane, and Rifampicin

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Antibacterial. Action of rifampin is to inhibit bacterial RNA synthesis. Rifampin is a semisynthetic antibiotic derived from rifamycin B to produce rifampin (US and Canadian name), also known as rifampicin in Europe. Rifampin has a high activity against gram-positive bacteria (*Staphylococcus* spp.), *Mycobacterium* spp., *Haemophilus* spp., *Neisseria* spp., and *Chlamydia* spp. but more limited activity against the gram-negative bacteria because it penetrates the gram-positive organism cell wall more easily than the gram-negative organism cell wall. Rifampin is highly lipid soluble and has the characteristic of entering cells to concentrate in leukocytes to inhibit intracellular bacteria. This is a therapeutic advantage for treating intracellular organisms (*Brucella*, *Mycobacterium*, *Rhodococcus*, *Chlamydia*) and chronic granulomatous diseases. Rifampin enters the microbial cell and forms stable complexes with the beta subunit of DNA-dependent RNA polymerases of microorganisms. This binding results in inactive enzymes and inhibition of RNA synthesis by preventing chain initiation. Resistance occurs via a single mutation of the amino acid sequence of the beta subunit of the DNA-dependent RNA polymerase enzyme. Rifampin is rapidly absorbed from the GI tract after oral administration in humans, dogs, calves, horses, and foals. Pharmacokinetics in adult horses shows rapid oral absorption of rifampin and a half-life of approximately 5-7 hours and a volume of distribution (VD) of 0.7 L/kg, but the half-life is longer in foals at approximately 18 hours. The half-life in dogs is approximately 8 hours.

Indications and Clinical Uses

Rifampin is used in people primarily for treatment of tuberculosis. In veterinary medicine, rifampin has been used to treat susceptible gram-positive and intracellular bacteria, including *Staphylococcus* species (including methicillin-resistant strains); *Streptococcus* spp.; *Rhodococcus equi*; *Corynebacterium pseudotuberculosis*; and most strains of *Bacteroides* spp., *Clostridium* spp., *Neisseria* spp., and *Listeria* spp. Gram-negative organisms are not affected at typical doses. In small animals, it is occasionally used to treat staphylococcal infections, particularly methicillin-resistant strains. Resistance among bacteria (e.g. *Staphylococcus* spp.) has been reported to develop rapidly, but this has not been well-documented among veterinary isolates. Nevertheless, to prevent the emergence of resistance, many clinicians advise using rifampin in conjunction with another antibiotic to decrease the emergence of resistant strains. One of the most common uses of rifampin is for treating infections caused by *Rhodococcus equi* in horses. For this treatment, it is frequently combined with erythromycin, azithromycin, or clarithromycin. Rifampin also may have activity against bacteria in biofilms. However, there are insufficient reports to confirm the clinical effectiveness for treating biofilm bacteria.

Precautionary Information

Adverse Reactions and Side Effects

In people, hypersensitivity and flulike symptoms are reported. Hepatotoxicity is seen more commonly in dogs when high doses are administered (10 mg/kg and higher). Hepatic enzyme elevations may be observed. Urine will be colored orange to reddish-orange in treated patients. It will also discolor saliva, tears, feces, sclera, and mucous membranes to a reddish-orange color. Rifampin is unpalatable and may be difficult to administer to some animals. Pancreatitis has been associated with rifampin administration.

Contraindications and Precautions

When administered with other drugs, consideration for more rapid elimination of other drugs should be considered. Use cautiously in animals that are at risk for pancreatitis. Because of risk of hepatitis, use cautiously with any other drug that may be potentially hepatotoxic (e.g., sulfonamides, anticonvulsants, acetaminophen). Avoid use in pregnant animals.

Drug Interactions

Multiple drug interactions are possible. Rifampin is a potent inducer of cytochrome P450 hepatic enzymes. Drugs that may have decreased levels when administered with rifampin include barbiturates, chloramphenicol, progestins, digitalis, warfarin, corticosteroids, and potentially many other drugs concurrently administered with rifampin. Rifampin is also an inducer of membrane efflux pump (P-glycoprotein), which may have the consequence of decreasing oral absorption of other drugs.

Instructions for Use

Most of the documented clinical experience has been in horses when rifampin was combined with a macrolide antibiotic for use in foals. When selecting a dose, the 10 mg/kg PO dose was adequate for susceptible gram-positive infections in the adult horse. Use in small animals (and doses) is based on experience in people or anecdotal experience in animals. It is often administered in combination with other drugs to decrease emergence of resistance. Administer on an empty stomach whenever possible.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is ≤ 1.0 mcg/mL. MICs for gram-positive organisms generally occur at 0.1 mcg/mL, whereas gram negatives have MIC values ranging from 8 to 32 mcg/mL.

Formulations

Rifampin is available in 150-mg and 300-mg capsules and 600-mg Rifadin IV injectable solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Rifampin is slightly soluble in water and ethanol. It is more soluble at acidic pH. Acid should be added to solutions (e.g., ascorbic acid) to prevent oxidation and improve solubility. Rifampin has been mixed with syrups and flavorings for oral administration and was stable for 4-6 weeks. The injectable solution is prepared by adding 10 mL of saline to a 600-mg vial and mixing (60 mg/mL). It may be

686 Ringer's Solution

infused with 0.9% saline or 5% dextrose solution. Reconstituted injectable solution is stable for 24 hours.

Small Animal Dosage

Dogs and Cats

- 5 mg/kg q12h PO or 10 mg/kg q24h, PO.

Large Animal Dosage

Horses

- 10 mg/kg q24h PO.
- Foals for treatment of *R. equi*: 5 mg/kg q12h PO, combined with erythromycin (25 mg/kg q8h PO).

Cattle

- 20 mg/kg q24h PO.

Regulatory Information

No regulatory information is available. Withdrawal times have not been established for animals that produce food. For extra label use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Ringer's Solution

Trade and Other Names: Generic brands

Functional Classification: Fluid replacement

Pharmacology and Mechanism of Action

Intravenous solution for fluid replacement. Ringer's solution contains 147 mEq/L sodium, 4 mEq/L potassium, 155 mEq/L chloride, and 4 mEq/L calcium.

Indications and Clinical Uses

Ringer's solution is used as a fluid replacement and for maintenance. It has a balanced electrolyte concentration, but it does not contain any bases (see Lactated Ringer's for solutions that contain bases).

Precautionary Information

Adverse Reactions and Side Effects

Ringer's solution is considered an acidifying solution because with prolonged administration the chloride will increase renal excretion of bicarbonate. Fluid overload occurs at high infusion rates.

Contraindications and Precautions

Do not exceed fluid rates of 80 mL/kg/hr. Consider supplementing with potassium because this fluid will not meet maintenance potassium needs.

Drug Interactions

Ringer's solution contains calcium; do not mix with drugs that may bind to calcium.

Instructions for Use

When administering intravenous fluid solution, monitor rate and electrolyte concentrations carefully. Add bicarbonate to fluids, if necessary, based on calculation of base deficit.

Fluid administration rates are as follows: normal maintenance rates: 40-65 mL/kg/24 hr (approximately 2-2.5 mL/kg/hr). For replacement fluid use the following calculation:

$$\text{Liters needed} = \% \text{ dehydration} \times \text{body weight (kg)}$$

or

$$\text{mL needed} = \% \text{ dehydration} \times \text{body weight (kg)} \times 1000$$

Patient Monitoring and Laboratory Tests

Monitor pulmonary pressure when infusing high doses. Monitor electrolyte balance, especially potassium during treatment.

Formulations

Ringer's solution is available in 250-, 500-, and 1000-mL bags for infusion.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 55-65 mL/kg day (2.5 mL/kg/hr) IV, SQ, or IP (intraperitoneal), for maintenance.
- 15-30 mL/kg/hr IV for moderate dehydration.
- 50 mL/kg/hr IV for severe dehydration.

Large Animal Dosage

Large Animals

- 40-50 mL/kg day IV, SQ, or IP (intraperitoneal) for maintenance.
- 15-30 mL/kg/hr IV for moderate dehydration.
- 50 mL/kg/hr IV for severe dehydration.

Calves

- Moderate dehydration: 45 mL/kg given at a rate of 30-40 mL/kg/hr.
- Severe dehydration: 80-90 mL/kg given at a rate of 30-40 mL/kg/hr or as fast as 80 mL/kg/hr, if necessary.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Romifidine Hydrochloride

roe-mif"ih-deen hye-droe-klor'ide

Trade and Other Names: Sedivet

Functional Classification: Analgesic, alpha₂-agonist

Pharmacology and Mechanism of Action

Alpha₂-adrenergic agonist. Alpha₂-agonists decrease release of neurotransmitters from the neuron. The proposed mechanism whereby they decrease transmission is via

binding to presynaptic α_2 receptors (negative feedback receptors). The result is decreased sympathetic outflow, analgesia, sedation, and anesthesia. Romifidine is structurally similar to clonidine. Other drugs in this class include xylazine, detomidine, dexmedetomidine, and medetomidine. Medetomidine, dexmedetomidine, romifidine, and detomidine are more specific for the α_2 -receptor than xylazine. Romifidine has an onset of effect of 2 minutes and a duration of 1-1.5 hours.

Indications and Clinical Uses

Romifidine, like other α_2 -agonists, is used as a sedative, anesthetic adjunct, and for analgesia. Romifidine produces the longest duration of sedative effects, followed by detomidine, medetomidine, and xylazine. Its use is primarily limited to horses in which it is used as a sedative and analgesic to facilitate handling, clinical examinations, clinical procedures, and minor surgical procedures and for use as a preanesthetic prior to the induction of general anesthesia.

Precautionary Information

Adverse Reactions and Side Effects

Romifidine, like other α_2 -agonists, decreases sympathetic output. Bradycardia is common and cardiovascular depression may occur. Cardiac effects can include sinoatrial block, first-degree and second-degree AV block, bradycardia, and sinus arrhythmia. In horses it causes effects similar to other α_2 -agonists, including ataxia, head drooping, sweating, and bradycardia. Facial edema is common, especially with higher doses. Even at high doses in experimental horses (up to 600 mcg/kg), there were no deaths.

Contraindications and Precautions

Romifidine, like other α_2 -agonists, should be used cautiously in animals with heart disease. Use may be contraindicated in older animals with pre-existing cardiac disease. Xylazine causes problems in pregnant animals, and this also should be considered for other α_2 -agonists. Use cautiously in animals that are pregnant; it may induce labor. In addition, it may decrease oxygen delivery to the fetus in late gestation. In case of overdose, reverse with atipamezole or yohimbine.

Drug Interactions

Do not use with other drugs that may cause cardiac depression. It may be used in horses with diazepam or ketamine. Do not mix in vial or syringe with other anesthetics. Use with opioid analgesic drugs will greatly enhance the CNS depression. Consider lowering doses if administered with opioids.

Instructions for Use

Romifidine, like other α_2 -agonists, can be administered with ketamine or benzodiazepines. It can be reversed with α_2 -antagonists such as atipamezole or yohimbine. A range of doses is used in horses for romifidine; 40 and 120 mcg/kg IV have been compared, which showed that sedation, cardiac effects, and analgesia are all dose-dependent effects. Deeper sedation occurs with higher doses. Each dose produced effects for at least 60 minutes, and some were observed for 180 minutes. Duration of 180 minutes is more likely with higher doses.

Patient Monitoring and Laboratory Tests

Monitor vital signs during anesthesia. Monitor heart rate, blood pressure, and ECG if possible during anesthesia.

Formulations

Ronidazole is available in a 1% injection (10 mg/mL).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

Doses not established for small animals.

Large Animal Dosage

Horses

- Sedation and analgesia: 40 to 120 mcg/kg IV.
- Preanesthetic: 100 mcg/kg IV.

Regulatory Information

Do not administer in animals intended for food.

Ronidazole

roe'nid'ah-zole

Trade and Other Names: Generic

Functional Classification: Antibacterial, antiparasitic

Pharmacology and Mechanism of Action

Antibacterial and antiprotozoal drug. It is a nitroimidazole in which the activity involves generation of free nitroradicals via metabolism within protozoa and bacteria. Ronidazole disrupts DNA in an organism via reaction with intracellular metabolite. Its action is specific for anaerobic bacteria and protozoa. Like other nitroimidazoles, it is active against some protozoa, including *Trichomonas*, and *Giardia*, and intestinal protozoal parasites. After oral administration in cats, it was rapidly and completely absorbed. The half-life in cats is approximately 10 hours.

Indications and Clinical Uses

Ronidazole is currently not a registered drug, but it has been used in cats to treat intestinal protozoal parasites. Studies for treatment of other organisms are not available. For treatment of feline *Tritrichomonas foetus* intestinal infections, it has been administered orally at a dose of 30 mg/kg twice daily for 2 weeks. Pharmacokinetic data indicate that 30 mg/kg, once daily, may be equally effective, but this dose has not been tested for efficacy. Efficacy for long-term remission has not been established, but temporary resolution of feline *Tritrichomonas foetus* intestinal infections has been observed.

Precautionary Information

Adverse Reactions and Side Effects

Like other nitroimidazoles, the most severe adverse effect is caused by toxicity to CNS. High doses may cause lethargy, CNS depression, ataxia, tremors, hyperesthesia, seizures, vomiting, and weakness. The CNS signs are related to inhibition of action of GABA and are responsive to benzodiazepines (diazepam). Adverse CNS effects are dose related. Dogs show neurotoxicity at doses of

50-200 mg/kg (seizures, tremors, ataxia). Avoid doses that exceed 60 mg/kg per day in cats. Like other nitroimidazoles, it has the potential to produce mutagenic changes in cells, but this has not been demonstrated in vivo. Like other nitroimidazoles, it has a bitter taste and can cause vomiting and anorexia.

Contraindications and Precautions

Fetal abnormalities have not been demonstrated in animals with recommended doses, but use cautiously during pregnancy.

Drug Interactions

Like other nitroimidazoles, it may potentiate the effects of warfarin and cyclosporine via inhibition of drug metabolism.

Instructions for Use

Ronidazole is currently not a marketed drug but has been prepared from bulk powder in compounding pharmacies.

Patient Monitoring and Laboratory Tests

Monitor for neurologic adverse effects.

Formulations

No available formulation exists; it is compounded from bulk chemical. Intravenous formulations have been prepared by dissolving ronidazole pure powder in 5% dextrose in water (D5W) to a concentration of 3.2 mg/ml. This formulation has been safely administered to research animals.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- No dose has been reported.

Cats

- 30 mg/kg q12-24h PO for 2 weeks. Clinical studies were performed with 30 mg/kg q12h, but longer intervals of q24h may also be effective.

Large Animal Dose

No doses have been reported for large animals.

Regulatory Information

Do not administer to animals that produce food. Administration of nitroimidazoles to animals intended for food is prohibited. Treated cattle must not be slaughtered for food.

S-Adenosylmethionine (S-AdoMet)

ess'ah-den'oh-sill-meh-thye'oh-noon

Trade and Other Names: Denosyl, Denamarin, and S-AdoMet

Functional Classification: Nutritional supplement

Pharmacology and Mechanism of Action

Nutritional supplement. S-Adenosylmethionine, usually abbreviated as S-AdoMet, is found naturally and is formed from methionine and ATP. It has been associated with improvement in acetaminophen-induced hepatotoxicity in humans and has been beneficial according to isolated reports in veterinary medicine. It serves as a methyl donor, catalyzed by methyltransferase. It also is a substrate for a transsulfuration reaction in which demethylated S-AdoMet is metabolized to glutathione (GSH). Glutathione may conjugate certain drug metabolites to enhance excretion. Cats and dogs have low levels of GSH, and S-AdoMet may help restore GSH in animals that have been intoxicated and perhaps in animals that have liver disease. It is a methyl donor for neurotransmitter metabolism in the synthesis and turnover of biogenic monoamines (CNS neurotransmitters such as serotonin, dopamine, and norepinephrine). In dogs, the half-life after oral administration is approximately 2 hours.

Indications and Clinical Uses

S-AdoMet has been used as a dietary supplement to support patients with hepatic disease. It may help restore hepatic GSH concentrations in deficient animals. It also has been administered to treat liver injury caused by intoxication of acetaminophen and other drugs that produce hepatotoxic oxidative drug injury. Another dietary supplement, silymarin (see monograph for silymarin), also known as “milk thistle” and silybin, has hepatic antioxidant properties and has been combined with S-AdoMet for treatment in dogs in cats (Denamarin). Via the effect on neurotransmitter synthesis, S-AdoMet has been used to improve cognitive function in dogs. In dogs older than 8 years, S-AdoMet (18 mg/kg/day) improved age-related mental impairment compared to placebo. It has been used to treat arthritis in dogs, but there are no studies that have demonstrated effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

It may produce a self-limiting transient gastric upset. No other adverse effects are reported.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

Reactions of S-AdoMet with tricyclic antidepressants (TCAs) have been reported, although the mechanism is not known. In laboratory animals, administration with clomipramine has caused serotonin syndrome.

Instructions for Use

S-AdoMet is a dietary supplement widely available without a prescription (OTC). Potency of formulations may vary. Absorption is decreased when given with a meal. Administer 30 minutes to 1 hour before feeding. To ensure passage into the

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stomach of cats, administer with water. Coated tablets (such as Denosyl) protect the active ingredient from moisture during storage and destruction by stomach acid. Do not break tablets or disrupt coating.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes in animals being treated for toxicity.

Formulations

SAME is widely available OTC in tablets and powder. The brand Denosyl is available in 90-, 225-, and 425-mg tablets. Veterinary formulations (e.g., Denamarin) may also contain silymarin (silybin) and vitamin E.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not disrupt coating on tablet.

Small Animal Dosage

Dogs

- 20 mg/kg per day, PO, or 90 mg (small dogs); 225 mg (medium dogs); and 425 mg (large dogs).

Cats

- 90 mg/cat/day PO, for cats up to 5 kg body weight.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Because of low risk of harmful residues in food animals, no withdrawal time is suggested.

Selamectin

sel-ah-mek'tin

Trade and Other Names: Revolution

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic. Microfilaricide for heartworm prevention in dogs and cats. Selamectin is a semisynthetic avermectin. Avermectins (ivermectin-like drugs) and milbemycins (milbemycin, doramectin, and moxidectin) are macrocyclic lactones. Avermectins and macrocyclic lactones share similarities, including mechanism of action. These drugs are neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in parasites. Paralysis and death of the parasite are caused by increased permeability to chloride ions and hyperpolarization of nerve cells. These drugs also potentiate other chloride channels, including ones gated by GABA. Mammals ordinarily are not affected because they lack glutamate-gated chloride channels, and there is a lower affinity for other mammalian chloride channels. Because these drugs ordinarily do not penetrate the blood-brain barrier, GABA-gated channels in the CNS of mammals are not affected. After topical application selamectin has high affinity for sebaceous glands and skin. The terminal half-life of selamectin is 11 days in dogs and 8 days in cats.

Indications and Clinical Uses

Selamectin is approved for prevention of heartworms; control of fleas, mites, and ticks in dogs; and prevention of heartworms, control of fleas, mites, hookworms, and roundworms in cats.

Precautionary Information

Adverse Reactions and Side Effects

Transient, localized alopecia with or without inflammation at or near the site of application was observed in approximately 1% of treated cats. Other adverse effects included nausea, lethargy, salivation, tachypnea, and muscle tremors.

Contraindications and Precautions

Do not use in dogs younger than 6 weeks of age. Do not use in cats younger than 8 weeks of age.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Apply as indicated on product label to skin of dogs and cats.

Patient Monitoring and Laboratory Tests

Monitor heartworm status in animals.

Formulations

Selamectin is available in 60- and 120-mg/mL topical solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- Heartworm prevention: 6-12 mg/kg applied topically every 30 days. (This dose also may be applied for treatment and prevention of ear mites and fleas.)
- Sarcoptic mange treatment: 6-12 mg/kg twice 30 days apart. (However, many dermatologists administer it at 2 to 3-week intervals.)

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Selegiline Hydrochloride

se-leh'jeh-leen hye-droe-klor'ide

Trade and Other Names: Anipryl (also known as deprenyl and l-deprenyl), Eldepryl (human preparation), and Emsam transdermal patch

Functional Classification: Dopamine agonist

Pharmacology and Mechanism of Action

Dopamine agonist. Selegiline has been known by many names. Selegiline hydrochloride is the official USP drug name, but most clinicians know it by the older name, l-deprenyl. (l-deprenyl is distinguished from its stereoisomer d-deprenyl.) A related drug is rasagiline. Selegiline has been used in humans for treatment of Parkinson's disease and occasionally for Alzheimer's disease with the trade name *Eldepryl*. (Efficacy for Alzheimer's disease has not been established.)

The veterinary formulation is approved for treatment of Cushing's disease in dogs and canine cognitive dysfunction. The action of selegiline is to inhibit MAO type B (and other MAOs at higher doses). The proposed mechanism of action is to inhibit the metabolism of dopamine in the central nervous system. The action for pituitary-dependent hyperadrenocorticism may be through increased dopamine levels in the brain, which decreases ACTH release, resulting in lower cortisol levels. Secondary effects are related to inhibition of the metabolism of phenylethylamine. (Phenylethylamine in laboratory animals produces amphetamine-like effects.) Two active metabolites are l-amphetamine and l-methamphetamine, but it is not known to what extent these contribute to pharmacologic effects. In horses, the metabolism to amphetamine-like metabolites is low.

Indications and Clinical Uses

In dogs, selegiline is approved to control clinical signs of pituitary-dependent hyperadrenocorticism (PDH; Cushing's disease) and to treat cognitive dysfunction in older dogs. However, the efficacy for Cushing's disease may not be as high as for other drugs such as mitotane or trilostane. Selegiline effects may be limited PDH caused by lesions of the pars intermedia and may not be effective for other forms of PDH (most cases of canine PDH have lesions of the pars distalis). It may improve some clinical signs without lowering cortisol levels in dogs with PDH administered 1.0 mg/kg once daily. For canine cognitive dysfunction (dementia) in old dogs, treatment with selegiline inhibits MAO type B and increases dopamine concentrations in the brain, which restores dopamine and balance and may improve cognitive ability. It has been administered to some older cats with age-related behavior problems, but clinical results in cats have not been reported. It does not appear to produce any clinical effects in horses from oral administration.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are rare in dogs but have included vomiting, diarrhea, and hyperactive and restless behavior. Amphetamine-like signs can be produced in experimental animals. At high doses in dogs, hyperactivity has been observed (doses >3 mg/kg) that included salivation, panting, repetitive movements, decreased weight, and changes in activity level. At doses of 30 mg per horse IV or oral, there were no behavior effects.

Two active metabolites are l-amphetamine and l-methamphetamine. Even though there were increases in amphetamine concentrations in dogs, they were not high enough to produce adverse effects. However, at high doses (>3 mg/kg) it may produce behavioral changes. The l-isomer metabolites are not as active as their d-forms, and studies have not supported a potential for amphetamine-like abuse or dependency from selegiline compared with other amphetamine-like drugs.

Contraindications and Precautions

Not indicated for adrenal tumors. Use cautiously with other drugs. (See the following list of interactions.)

Drug Interactions

Do not use with other monoamine oxidase inhibitors (MAOIs). Do not use with tricyclic antidepressants (TCAs), such as clomipramine and amitriptyline, or with selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine. Do not administer with meperidine, dobutamine, or amitraz. Use cautiously with sympathetic amines such as phenylpropanolamine, linezolid, and tramadol.

Instructions for Use

Dose titration to effect. Start with low dose and increase gradually until clinical effect is observed. The transdermal patch for humans has not been evaluated for animals.

Patient Monitoring and Laboratory Tests

No specific monitoring is required. Serum cortisol testing is not valuable for evaluating efficacy.

Formulations

Selegiline is available in 2-, 5-, 10-, 15-, and 30-mg tablets for animals; 5-mg tablets or capsules for humans; and 20-, 30-, and 40-cm² transdermal patch (EmSam) for humans.

Stability and Storage

Stable if stored in manufacturer's original formulation.

Small Animal Dosage

Dogs

- Begin with 1 mg/kg q24h PO. If there is no response within 2 months, increase dose to maximum of 2 mg/kg q24h PO.

Cats

- 0.25-0.5 mg/kg q12-24h PO.

Large Animal Dosage

No dose has been reported for large animals. In preliminary studies in which selegiline was administered at a dose of 30 mg/horse PO or IV, there were no observed effects on behavior or locomotor activity.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 2

Senna

sen'na

Trade and Other Names: Senokot

Functional Classification: Laxative

Pharmacology and Mechanism of Action

Laxative. Senna acts via local stimulation or via contact with intestinal mucosa.

Indications and Clinical Uses

Senna is indicated for treatment of constipation.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects not reported for animals. However, excessive doses are expected to cause fluid and electrolyte loss.

Contraindications and Precautions

Do not administer to animals with GI obstruction. Do not administer to dehydrated animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Doses and indications are not well established for veterinary medicine. Use is strictly based on anecdotal experience.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Senna is available in granules in concentrate or syrup.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- Syrup: 5-10 mL/dog/day PO.
- Granules: 1/2 to 1 tsp/dog/day PO.

Cats

- Syrup: 5 mL/cat q24h.
- Granules: 1/2 tsp/cat q24h (with food).

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Sevoflurane

see-voe-floo'rane

Trade and Other Names: Aerrane

Functional Classification: Anesthetic

Pharmacology and Mechanism of Action

Inhalant anesthetic. Like other inhalant anesthetics, the mechanism of action is uncertain. Sevoflurane produces a generalized, reversible depression of the CNS. The inhalant anesthetics vary in their solubility in blood, their potency, and the rate

of induction and recovery. Those with low blood/gas partition coefficients are associated with the most rapid rates of induction and recovery. Sevoflurane has a vapor pressure of 160 mm Hg (at 20°C), a blood/gas partition coefficient of 0.65, and a fat/blood coefficient of 48. Sevoflurane is similar to isoflurane in many respects, except that it has lower solubility, resulting in faster induction and recovery times.

Indications and Clinical Uses

Sevoflurane is used as an inhalant anesthetic. There are not any significant advantages over the use of isoflurane and it is more expensive than isoflurane. It has a minimum alveolar concentration (MAC) value of 2.58%, 2.36%, and 2.31% in cats, dogs, and horses, respectively. Sevoflurane, like other inhalant anesthetics, can be used with preanesthetics, opioids, alpha-2 agonists, and tranquilizers.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are related to anesthetic effects (e.g., cardiovascular and respiratory depression). Sevoflurane can produce byproducts of fluoride ions and Compound A, which can be toxic to the kidneys.

Contraindications and Precautions

Do not use unless there is an adequate facility to monitor patients.

Drug Interactions

No drug interactions have been reported for animals.

Instructions for Use

Use of inhalant anesthetics requires careful monitoring. Dose is determined by depth of anesthesia.

Patient Monitoring and Laboratory Tests

Carefully monitor patient's heart rate and rhythm and respiratory rate during use.

Formulations

Sevoflurane is available in a 100-mL bottle.

Stability and Storage

Sevoflurane is highly volatile and should only be stored in approved containers.

Small Animal Dosage

- Induction: 8%; maintenance: 3%-6%

Large Animal Dosage

Horses

MAC value: 2.31.

Regulatory Information

No withdrawal times are established for animals intended for food. Clearance is rapid and short withdrawal times are suggested. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Sildenafil Citrate

sill-den'-ah-fil

Trade and Other Names: Viagra, Revatio

Functional Classification: Vasodilator

Pharmacology and Mechanism of Action

Vasodilator. Sildenafil is a vasodilator, specific for phosphodiesterase V. Sildenafil and similar drugs act to increase cyclic GMP by inhibiting its breakdown by phosphodiesterase-V (PDE-V). There are two important locations of phosphodiesterase V: (1) vascular smooth muscle of the lungs, and (2) corpus cavernosum. The second effect produces the desired clinical effects that have caused the popularity in human medicine. The effect on vascular smooth muscle of the lungs produces vasodilation of the pulmonary vascular bed in patients with pulmonary hypertension. Other drugs that have been used for this effect are tadalafil (Cialis) at a dose of 1-2 mg/kg q12h PO in dogs.

Indications and Clinical Uses

Sildenafil and related drugs are used in people for treating erectile dysfunction via the effect on the corpus cavernosum. This effect has not been explored in veterinary medicine. The use in veterinary medicine has been limited to the treatment of pulmonary arterial hypertension. In dogs sildenafil produced improvement in patients with pulmonary hypertension.

Precautionary Information

Adverse Reactions and Side Effects

Cutaneous flushing of the inguinal area has been observed in dogs. Otherwise, adverse effects have not been reported with clinical use in dogs. Potential effects are attributed to the vasodilator action. If high doses or other vasodilators are administered—especially those that increase cyclic-GMP levels—hypotension can occur.

Contraindications and Precautions

Use cautiously in conjunction with other vasodilator drugs.

Drug Interactions

No drug interactions reported for animals, but in people there are precautions about use with other vasodilators such as alpha blockers and nitrates.

Instructions for Use

The use in veterinary medicine has been based on studies in dogs with pulmonary hypertension. The dosages and clinical use are based on these limited reports.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary, but monitor the patient's cardiovascular function (blood pressure and heart rate) in animals at risk for cardiovascular complications.

Formulations

Sildenafil is available as 20-, 25-, 50-, and 100-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 2 mg/kg q12h, PO. Dose interval may range from 8 to 24 hours, and doses as high as 3 mg/kg have been administered to some dogs.

Cats

- 1 mg/kg q8h, PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No withdrawal times are established for animals intended for food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Silymarin

sill-ih-mare'in

Trade and Other Names: Silybin, Marin, Milk Thistle, and generic brands

Functional Classification: Hepatic protectant

Pharmacology and Mechanism of Action

Silymarin contains silybin as the most active ingredient. It is also known as milk thistle, from which it is derived. Silymarin is a mixture of antihepatotoxic flavonolignans (derived from the plant silybum). Silymarin has three components that are considered flavonolignans: silidianin, silcristin, and silybin (which is the major component and also called silymarin and silibinin). Silymarin has been used for the treatment of a variety of liver disorders in humans. The mechanism of silymarin's action is thought to be as an antioxidant inhibiting both peroxidation of lipid membranes and glutathione oxidation. Experimental data have supported the hepatoprotective properties of silymarin as an antioxidant and a free radical scavenger.

Indications and Clinical Uses

Silymarin has been used to treat hepatic disease, including hepatotoxic reactions in people and animals. In cats it may provide antioxidant activity. Silymarin is used as a complementary treatment in canine and feline liver disease. However, there is no scientific information on the oral absorption, correct dose, or evidence of efficacy of silymarin treatment. Silymarin can be used with S-adenosylmethionine (SAME). There are preparations that include both silymarin and SAME (Denamarin).

Precautionary Information

Adverse Reactions and Side Effects

No adverse reactions have been reported.

Contraindications and Precautions

No contraindications have been reported for animals.

Drug Interactions

No drug interactions have been reported.

Instructions for Use

Silymarin is a dietary supplement, and forms available may vary in potency and stability.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes in animals being treated for toxicity.

Formulations

Silymarin tablets are widely available OTC. Commercial veterinary formulations (Marin) also contain zinc and vitamin E in a phosphatidylcholine complex in tablets for dogs and cats. The combination of Denamarin contains both silymarin and SAMe.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 5-15 mg/kg PO, once daily. Some sources recommend a higher dose of a minimum of 30 mg/kg PO per day.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Sodium Bicarbonate

Trade and Other Names: Baking soda, Soda mint, Citrocarbonate, and Arm & Hammer pure baking soda

Functional Classification: Alkalinizing agent

Pharmacology and Mechanism of Action

Alkalinizing agent. Antacid. It increases plasma and urinary concentrations of bicarbonate. One gram sodium bicarbonate is equal to 12 mEq sodium and bicarbonate ions; 3.65 g sodium bicarbonate is equal to 1 g sodium.

Indications and Clinical Uses

Sodium bicarbonate is a typical alkalinizing solution. It is the most frequent alkalinizing solution used for intravenous therapy of systemic acidosis and to treat severe hyperkalemia. When adding to fluid therapy, the goal is to maintain PaCO₂ within 37-43 mm Hg. It also has been administered to alkalinize urine.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have been attributed to alkalinizing activity. Hypokalemia may occur with excessive administration. Hyperosmolality, hypernatremia, paradoxical CNS, and intracellular acidosis may occur.

Contraindications and Precautions

Do not administer to animals with hypocalcemia (may exacerbate tetany). Do not administer to animals with excessive chloride loss because of vomiting. Do not administer to animals with alkalosis. Administration of sodium bicarbonate may increase risk of hypernatremia, paradoxical CNS acidosis, and hyperosmolality.

Drug Interactions

Sodium bicarbonate should not be mixed with drugs that require an acidic medium for stability and solubility. Such drugs may include solutions containing hydrochloride (HCl) salts. When mixing intravenous solutions, do not mix bicarbonate with solutions containing calcium (chelation may result). When administered orally, interaction may occur to decrease absorption of other drugs (partial list includes anticholinergic drugs, ketoconazole, fluoroquinolones, and tetracyclines).

Instructions for Use

When used for systemic acidosis, doses should be adjusted on the basis of blood gas measurements or assessment of acidosis. The following equation may be used to estimate requirement:

$$\text{mEq Bicarbonate} = \text{body weight (kg)} \times \text{base deficit (mEq/L)} \times 0.3.$$

Initially, administer 25%-50% of this dose in intravenous fluids over 20-30 minutes. In calves or neonates, use a factor of 0.5 instead of 0.3. Twelve mEq of bicarbonate = 1 g of sodium bicarbonate. Note: 1.4% solution = 0.17 mEq/mL and provides 13 g of bicarbonate per L. 8.5 % solution = 1 mEq/mL of NaHCO_3 . One teaspoon of baking soda is approximately 2 g of NaHCO_3 . When used during cardiac resuscitation, caution is advised because of risk of hyperosmolality, hypernatremia, and paradoxical CNS acidosis.

Patient Monitoring and Laboratory Tests

Monitor acid-base status.

Formulations

Sodium bicarbonate is available in 325-, 520-, and 650-mg tablets. Per teaspoonful (3.9 g) of Citrocarbonate, there is 780 mg sodium bicarbonate and 1.82 grams sodium citrate. It is also available in injections of various strengths: 4.2% is 0.5 mEq/mL (11.5 mg/mL sodium) and 8.4% is 1 mEq/mL (23 mg/mL sodium).

Stability and Storage

Store in a tightly sealed container at room temperature. Alkaline solution with pH of 7-8.5. Do not mix with acid solutions. Sodium bicarbonate is soluble in water. If exposed to air, it may decompose to sodium carbonate, which is more alkaline.

Small Animal Dosage

Dogs and Cats

- Metabolic acidosis: 0.5-1 mEq/kg IV.
- Renal failure: 10 mg/kg q8-12h PO.
- Alkalinization of urine: 50 mg/kg q8-12h PO.
- Antacid: 2-5 g mixed with water PO.
- CPR: 1 mEq/kg with additional doses of 0.5 mEq/kg at 10-minute intervals.

Large Animal Dosage

- Metabolic acidosis: 0.5-1 mEq/kg IV slowly. Other doses should be calculated based on base deficits. Oral doses vary. Ten to 12 grams of sodium bicarbonate may be given orally to adult large animals (horses and cattle) and 2-5 grams to calves, foals, and pigs.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Sodium Chloride 0.9%

Trade and Other Names: Normal saline and generic brands

Functional Classification: Fluid replacement

Pharmacology and Mechanism of Action

Sodium chloride is used for intravenous infusion as replacement fluid. It is not a suitable maintenance solution. Sodium chloride (0.9%) contains 154 mEq/L sodium and 154 mEq/L chloride. See Appendix for comparison to other fluid solutions.

Indications and Clinical Uses

Sodium chloride is used for intravenous fluid supplementation. However, it is not a balanced electrolyte solution and should not be used for maintenance. It also is frequently used as a vehicle to deliver intravenous medications via constant rate infusion (CRI).

Precautionary Information

Adverse Reactions and Side Effects

It is not a balanced electrolyte solution. Long-term infusion may cause electrolyte imbalance. Saline solution is not balanced and it may cause acidemia because it will increase renal elimination of bicarbonate. Prolonged use may cause hypokalemia.

Contraindications and Precautions

Do not exceed maximum dose rate of 80 mL/kg/hr. This solution does not contain electrolyte balance for maintenance.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

When administering intravenous fluid solution, monitor rate and electrolyte concentrations carefully.

Fluid administration rates are as follows:

Replacement fluid: calculate as liters needed = % dehydration × body weight (kg)
or

Milliliters needed = % dehydration × body weight (kg) × 1000.

Add bicarbonate to fluids if necessary based on calculation of base deficit.

Patient Monitoring and Laboratory Tests

Monitor hydration status and serum electrolytes, particularly potassium.

Formulations

Sodium chloride 0.9% is available in a 500- and 1000-mL infusion.

Stability and Storage

Store in a tightly sealed container at room temperature.

Small Animal Dosage

Dogs and Cats

- Maintenance administration (no deficits): 1.5-2.5 mL/kg/hr (caution; this is not a balanced maintenance solution).
- Moderate dehydration: 15-30 mL/kg/hr IV.
- Severe dehydration: 50 mL/kg/hr IV.

Large Animal Dosage

- 40-50 mL/kg day IV, IP, or SQ maintenance.
- Moderate dehydration: 15-30 mL/kg/hr IV.
- Severe dehydration: 50 mL/kg/hr IV.

Calves

- Moderate dehydration: 45 mL/kg given at a rate of 30-40 mL/kg/hr.
- Severe dehydration: 80-90 mL/kg given at a rate of 30-40 mL/kg/hr or as fast as 80 mL/kg/hr if necessary.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Sodium Chloride 7.2%

Trade and Other Names: Hypertonic saline solution and HSS

Functional Classification: Fluid replacement

Pharmacology and Mechanism of Action

Concentrated sodium chloride used for acute treatment of hypovolemia. Hypertonic saline solution causes rapid expansion of plasma volume and may improve microvascular blood flow. Hypertonic saline solution contains 2566 mOsm/L, 1232 mEq/L sodium, and 1232 mEq/L chloride.

Indications and Clinical Uses

Hypertonic saline is used to treat hypovolemic shock in animals. The duration of its benefit is short lived. There may be benefits for combination with colloids such as Dextran 70. It has been used at doses of 4 mL/kg IV to dogs during a 5-minute infusion to be effective for treatment of septic shock.

Precautionary Information

Adverse Reactions and Side Effects

This is not a balanced electrolyte solution. Long-term infusion may cause electrolyte imbalance.

Contraindications and Precautions

Do not administer to hypernatremic animals. Do not administer solutions high in sodium to animals with renal insufficiency.

Drug Interactions

No drug interactions have been reported in animals.

704 Sodium Iodide (20%)

Instructions for Use

Hypertonic saline is used for short-term infusion for rapid replacement of vascular volume.

Patient Monitoring and Laboratory Tests

Monitor hematocrit and blood pressure in treated animals.

Formulations

Sodium chloride 7.2% is available as an infusion.

Stability and Storage

Store in a tightly sealed container at room temperature.

Small Animal Dosage

Dogs and Cats

- 3-8 mL/kg IV of 7.2% solution. (Rate of administration should not exceed 1 mL/kg/min.)

Large Animal Dosage

- 4-8 mL/kg of 7.2% solution IV at a rate of 1 mL/kg/min.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Sodium Iodide (20%)

Trade and Other Names: Iodopen and generic brands

Functional Classification: Iodine replacement

Pharmacology and Mechanism of Action

Sodium iodide is used to treat iodine deficiency.

Indications and Clinical Uses

Sodium iodide is used to treat fungal infections and is preferred over potassium iodide. It has been used for bacterial, actinomycete, and fungal infections, primarily in horses and cattle. In cattle it has been used for actinomycosis (lumpy jaw) and actinobacillosis (wooden tongue and necrotic stomatitis). In small animals it has been used for sporotrichosis. Proof of efficacy for these indications has not been established. See section on Iodide (EDDI) and Potassium Iodide for additional information on use and formulations available.

Precautionary Information

Adverse Reactions and Side Effects

High doses can produce signs of iodism, which include lacrimation, irritation of mucous membranes, swelling of eye lids, cough, dry and scruffy coat, and hair loss. Potassium iodide has a bitter taste and can cause nausea and salivation.

Contraindications and Precautions

Do not use in pregnant animals; it may cause abortion.

Drug Interactions

No drug interactions have been reported.

Instructions for Use

For treatment in cattle, administer slowly IV. Be careful not to inject outside the vein or tissue necrosis may occur. Clinical use in animals is primarily empirical. The doses and indications listed have not been tested in clinical trials. Other, more proven drugs for these indications should be considered as alternatives.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Sodium iodide is available in a 20-g/100 mL (20%) injection, and there is 100 mcg elemental iodide (118 mcg sodium iodide) per mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

Consult oral dose for potassium iodide.

Large Animal Dosage

Horses

- 125 mL of a 20% solution IV daily for 3 days, then 30 g/horse daily injection for 30 days.

Cattle

- 67 mg/kg IV (15 mL per 100 pounds) slowly, and repeat weekly.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Sotalol Hydrochloride

soe'tah-lole hye-droe-klar'ide

Trade and Other Names: Betapace

Functional Classification: Beta blocker, antiarrhythmic

Pharmacology and Mechanism of Action

Nonspecific beta-receptor (Beta₁ and Beta₂) adrenergic blocker (Class II antiarrhythmic). Action is similar to propranolol (one-third potency); however, its beneficial effect may be caused more by the other antiarrhythmic effects. In addition to being a Class II antiarrhythmic drug, sotalol may have some Class III (potassium-channel-blocking) activity. The Class III activity prolongs the refractory period by decreasing potassium conduction in delayed rectifier currents. Sotalol is a water-soluble beta blocker and relies less on the liver for clearance than other beta blockers. Plasma levels and interindividual differences in clearance are expected to be less than other beta blockers.

Indications and Clinical Uses

Sotalol is indicated for control of refractory ventricular arrhythmias. It has also been used for refractory atrial fibrillation. Although sotalol is commonly administered to small animals, particularly dogs, the use and doses are derived primarily from anecdotal and clinical experience.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported for animals but are expected to be similar to propranolol. Like many antiarrhythmics, sotalol may have some proarrhythmic activity. Negative inotropic effects may cause concern in some animals with poor cardiac contractility.

Contraindications and Precautions

Administer cautiously to patients with heart failure or atrioventricular block. Use cautiously in patients with poor cardiac reserve.

Drug Interactions

Use cautiously with other drugs that may decrease cardiac contractility or lower heart rate.

Instructions for Use

The beta-blocking effects occur at low doses; Class III antiarrhythmic effects occur at higher doses. In people, it may be a more effective maintenance agent for controlling arrhythmias than other drugs.

Patient Monitoring and Laboratory Tests

Monitor heart rate during treatment.

Formulations

Sotalol is available in 80-, 120-, 160-, and 240-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Sotalol is soluble in both water and ethanol. It has been mixed with syrups and flavorings and is stable for 12 weeks, but it should be stored in the refrigerator.

Small Animal Dosage

Dogs

- 1-2 mg/kg q12h PO. (For medium- to large-breed dogs, begin with 40 mg/dog q12h, then increase to 80 mg, if no response.)

Cats

- 1-2 mg/kg q12h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Spectinomycin, Spectinomycin Dihydrochloride Pentahydrate

spek-tih-noe-mye'sin

Trade and Other Names: Spectam, Spectogard, Prospec, and Adspec

Functional Classification: Antibiotic, aminocyclitol

Pharmacology and Mechanism of Action

Spectinomycin is an aminocyclitol antibiotic, which shares similar features with an aminoglycoside. However, it differs in that it does not contain amino sugars or glycosidic bonds. It has a broad spectrum of activity. It is highly water soluble and is easily mixed in aqueous solutions. Spectinomycin, like aminoglycosides, inhibits protein synthesis via a 30S ribosomal target. It is a broad-spectrum drug with activity against gram-positive and some gram-negative bacteria, and mycoplasma but little anaerobic activity. It is not absorbed orally but is administered either in drinking water for treatment of enteritis or by injection for other infections. After injection the half-life in animals is 1-2 hours.

Indications and Clinical Uses

Spectinomycin has *in vitro* activity against some gram-negative bacteria and has also been administered orally for treatment of bacteria enteritis caused by *E. coli* and as an injection for treatment of respiratory infections. Spectinomycin has been used in cattle to treat respiratory infections caused by *Pasteurella*, *Mannheimia*, and *Histophilus somni* (formerly *Haemophilus somnus*). It also has activity against *Mycoplasma*. It has been used in dogs but not commonly. Spectinomycin has been withdrawn by the original drug sponsor and may not be commercially available.

Precautionary Information

Adverse Reactions and Side Effects

Injection site lesions may occur from administration to cattle.

Contraindications and Precautions

The powder intended to be used in drinking water should not be formulated with water or saline for intravenous injection. This solution has produced severe pulmonary edema and death.

Drug Interactions

No drug interactions are reported.

Instructions for Use

Injections in cattle should be made in the neck muscle.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Spectinomycin is available in an oral solution, powder for drinking water, and injection for cattle. Spectinomycin injectable was discontinued by the drug sponsor and may not be available. It was previously available in a 100-mg spectinomycin sulfate/mL solution (Adspec). The lincomycin-spectinomycin combination contains 50 mg lincomycin with 100 mg spectinomycin ("Linco-Spectam") per milliliter. Formulations for poultry include 500 mg per gram water-soluble powder.

Stability and Storage

Store at room temperature. Protect from freezing. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 22 mg/kg q12h PO for 4 days.
- 5.5-11 mg/kg q12h IM for 4 days.

Large Animal Dosage

Pigs

- 6.6-22 mg/kg, q12-24h, IM; or 50-100 mg/pig PO.

Cattle

- 10-15 mg/kg q24h SQ (in neck) for 3-5 days.

Regulatory Information

Cattle withdrawal time (meat): 11 days. (Discoloration at meat injection may persist for 15 days.)

Pig withdrawal time (meat): 21 days. At doses of 20 mg/kg the withdrawal time is 30 days.

Do not administer to calves to be slaughtered for veal. A milk discard time has not been established. Do not administer to dairy cattle 20 months of age or older.

Spinosad

Spin-oh'-sad

Trade and Other Names: Comfortis

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Spinosad is a member of the spinosyns class of insecticides. These resemble tetracycline macrolides but are not antibacterial. Spinosad is a combination of spinosyn A and spinosyn D, derived from bacteria (*Saccharopolyspora spinosa*). The action of spinosad in fleas is activation of nicotinic acetylcholine receptors but not other nicotinic receptors or GABA receptors. The actions in insects treated with spinosad are muscle contractions and tremors in motor neurons, paralysis, and flea death. It does not affect mammals because of differences in the susceptibility of nicotinic acetylcholine receptors.

Indications and Clinical Uses

Spinosad is used as a monthly treatment for flea infestations. After administration, spinosad can kill fleas within 30 minutes and has complete kill within 4 hours.

Precautionary Information

Adverse Reactions and Side Effects

In safety studies, administration of high doses (100 mg/kg once daily for 10 days) did not produce any serious adverse effects other than vomiting and mild elevation of liver enzymes. Oral administration of spinosad (300 mg/kg) to Collie dogs with the MDR gene mutation (p-glycoprotein deficient) did not

cause signs of toxicosis. Occasional vomiting may be observed with routine use (see Instructions for Use section about dosing after vomiting.)

Contraindications and Precautions

It can be used safely with heartworm preventatives, including ivermectin, but do not administer with high-dose ivermectin for treatment of *Demodex*. Use cautiously in pregnant and breeding animals. Some adverse effects on puppies have been reported from safety studies on pregnant dogs. Adverse effects in puppies nursing from dams administered spinosad also have been reported.

Drug Interactions

Spinosad has been used with many other drugs, including heartworm preventatives, safely. No drug interactions have been reported.

Instructions for Use

Spinosad should be administered with food for maximum absorption. If vomiting occurs within an hour of administration, redose with another full dose. If a dose is missed, administer Comfortis chewable tablets with food and resume a monthly dosing schedule. Treatment with spinosad may begin at any season of the year, preferably started before fleas emerge. It can also be used year-round.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Spinosad is available in five chewable tablet sizes containing 140, 270, 560, 810, or 1620 mg.

Stability and Storage

Store in blister packs and at room temperature.

Small Animal Dosage

Dogs

- 30 mg/kg (13.5 mg/pound), PO, administered once per month.

Cats

No dose has been reported for cats.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Spironolactone

speer-one-oh-lak'tone

Trade and Other Names: Aldactone

Functional Classification: Diuretic

Pharmacology and Mechanism of Action

Potassium-sparing diuretic. Action of spironolactone is to interfere with sodium reabsorption in distal renal tubule by competitively inhibiting the action of aldosterone. It binds directly to the aldosterone receptor, but at usual doses it does not block the action of other steroid receptors. It is more properly referred to as an *aldosterone antagonist* rather than a diuretic. It does not produce a significant diuretic action. There are minor antiandrogenic effects produced, but in animals these have not been clinically relevant. A related drug, eplerenone (Inspra) has been used in people because it produces fewer antiandrogenic effects compared to aldosterone.

Indications and Clinical Uses

Spironolactone is used for treating high blood pressure and congestion caused by heart failure. It is approved in Europe (Prilactone) for dogs, to be used with standard therapy for the treatment of congestive heart failure caused by valvular disease. Spironolactone may be used with angiotensin-converting enzyme (ACE) inhibitors to achieve a synergistic effect for treatment of heart failure in animals. The proposed benefit is via aldosterone antagonism and can be used to inhibit the renin–angiotensin–aldosterone system (RAAS) activation that occurs from diuretic administration (e.g., furosemide) or with some diseases that produce congestion. Spironolactone has also been used for managing hepatic cirrhosis because it will inhibit ascites formation caused by excess aldosterone. It has not been beneficial for treatment in cats with hypertrophic cardiomyopathy (see also Adverse Reactions and Side Effects section for cats).

Precautionary Information

Adverse Reactions and Side Effects

Spironolactone can produce hyperkalemia in some patients. High doses and long-term use may produce some steroid-like side effects. There are concerns about adverse effects that have been reported from spironolactone use in cats. Facial dermatitis has been reported from administration to cats. The mechanism of these reactions is not known. In humans, treatment with spironolactone has been associated with antiandrogenic effects such as gynecomastia, hirsutism, and impotence. Antiandrogenic effects have not been reported from its use in animals, except that prostatic atrophy has been observed in some male dogs.

Contraindications and Precautions

Do not use in patients that are dehydrated. Nonsteroidal anti-inflammatory drugs (NSAIDs) may interfere with action. Avoid concurrent use of supplements that are high in potassium. Do not administer to patients with gastric ulcers or who may be prone to GI disease such as gastritis or diarrhea.

Drug Interactions

Spironolactone is often used together with ACE inhibitors, such as enalapril. It acts synergistically with those drugs. Risk of hyperkalemia may increase when used with an ACE inhibitor, but this has not been a clinical problem in dogs. Use cautiously with other drugs that can increase potassium concentrations such as trimethoprim and NSAIDs.

Instructions for Use

Spironolactone usually is administered with other drugs (e.g., ACE inhibitors, inotropic agents, vasodilators) for treating congestive heart failure.

Patient Monitoring and Laboratory Tests

Monitor serum potassium concentration when administering with an ACE inhibitor (e.g., enalapril maleate). Administration of spironolactone may cause a slightly false-positive result for digoxin assay.

Formulations

Spironolactone is available in 25-, 50-, and 100-mg tablets. Tablets can be split easily.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Spironolactone is insoluble in water, but it is slightly more soluble in ethanol. It has been mixed with syrups for an oral suspension (after first mixing with ethanol) and found to be stable for 90-160 days.

Small Animal Dosage

Dogs

- 2-4 mg/kg/day (or 1-2 mg/kg q12h) PO. In dogs, start with 2 mg/kg/day and increase gradually, not to exceed 4 mg/kg/day. In Europe, the approved dose for dogs is 2 mg/kg per day.

Cats

- Use in cats is controversial because it may produce dermatitis and because the efficacy is questionable. However, doses in the range of 2-4 mg/kg/day (or 1-2 mg/kg q12h) PO have been administered for some conditions.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Stanozolol

stan-oh'zoe-lole

Trade and Other Names: Winstrol-V

Functional Classification: Hormone, anabolic agent

S

Pharmacology and Mechanism of Action

Anabolic steroid. Stanozolol is a derivative of testosterone. Anabolic agents are designed to maximize anabolic effects while minimizing androgenic action. Other anabolic agents include boldenone, nandrolone, oxymetholone, and methyltestosterone.

Indications and Clinical Uses

Anabolic agents, such as stanozolol, have been used for reversing catabolic conditions, increasing weight gain, increasing muscling in animals, and stimulating erythropoiesis. It has been used in horses during training. Stanozolol has been used

in animals with chronic renal failure and there is some evidence of an improvement in the nitrogen balance in dogs with renal disease treated with stanozolol. Use in cats is associated with toxicity.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects from anabolic steroids can be attributed to the pharmacologic action of these steroids. Increased masculine effects are common. Increased incidence of some tumors has been reported in people. Some 17-alpha-methylated oral anabolic steroids (oxymetholone, stanozolol, and oxandrolone) are associated with hepatic toxicity. Stanozolol administration in cats with renal disease has been shown to consistently produce increased hepatic enzymes and hepatic toxicosis.

Contraindications and Precautions

Do not administer to cats with renal disease. Use cautiously in dogs that have other pre-existing disease such as liver failure. Do not administer to pregnant animals. Stanozolol, like other anabolic steroids, has a high potential for abuse in humans. This drug is abused by humans to enhance athletic performance.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

However, for many indications, use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes for signs of hepatic injury (cholestatic) during treatment.

Formulations

Stanozolol is available in a 50-mg/mL injection as a sterile suspension and 2-mg tablets. However, there has been limited availability of veterinary injectable formulations. Commercial forms have been withdrawn from the market, but some compounding sources still persist.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 2 mg/dog (or range of 1-4 mg/dog) q12h PO.
- 25-50 mg/dog/week IM.

Cats

- 1 mg/cat q12h PO.
- 25 mg/cat/week IM (use cautiously in cats).

Large Animal Dosage

Horses

- 0.55 mg/kg (5 mL per 1000 pounds) IM, once a week for up to 4 weeks.

Regulatory Information

Stanozolol is a Schedule III controlled drug and should not be administered to animals that produce food.

RCI Classification: 4

Streptozocin

strep-toe-zoe'sin

Trade and Other Names: Streptozotocin and Zanosar

Functional Classification: Antihyperglycemic agent

Pharmacology and Mechanism of Action

Streptozocin (also known as streptozotocin) is an agent with specific effects on pancreatic beta cells. It is a nitrosourea alkylating agent with a specific cytotoxic effect on the pancreatic cells. There is selective uptake into pancreatic beta cells. It can produce diabetes mellitus in normal animals, but it is used primarily for treating insuloma tumors in animals. Occasionally it has been used as a cytotoxic agent for treating other tumors in humans (e.g., lymphoma, sarcomas), but these uses are not reported for animals. Streptozocin has a rapid half-life in animals but metabolites may be active. Metabolites rapidly cross the blood–brain barrier.

Indications and Clinical Uses

In animals, streptozocin is used primarily for treating insulin-secreting tumors (insulinoma). It has been used in experimental animals to create models of diabetes mellitus.

Precautionary Information

Adverse Reactions and Side Effects

Diabetes mellitus is anticipated in treated animals. In humans the major adverse effect is renal injury caused by tubular necrosis. Renal injury has been reported in dogs at doses of >700 mg/m². Other adverse effects include vomiting, nausea, and diarrhea. Increases in hepatic enzymes and hepatic injury have been reported in dogs; however, hepatotoxicity appears to be reversible. Bone marrow suppression is rare in animals. Local phlebitis may occur from intravenous administration.

Contraindications and Precautions

Streptozocin may produce diabetes mellitus in treated animals. In addition, there may be a sudden release of insulin after intravenous administration and intravenous dextrose should be available to treat acute hypoglycemia. Monitor animals for evidence of renal and hepatic injury. Do not administer to pregnant animals.

Drug Interactions

No specific drug interactions are reported for animals; however, use with any other nephrotoxic, hepatotoxic, or myelotoxic drug will exacerbate toxicity.

Instructions for Use

Risk of renal toxicosis caused by streptozocin may be decreased with administration of fluid diuresis. The diuresis should consist of administration of fluids (e.g., 0.9% saline) IV prior to drug administration. Antiemetics should be administered with each infusion because vomiting is common. Treatment is continued every 3 weeks until signs of tumor recurrence occur or until toxicosis limits the continuation of treatments. Reconstitute vial prior to use by adding 9.5 mL of 5% dextrose or 0.9% saline to vial. Resulting solution is 100 mg per mL. Further dilute this vial with 5% dextrose or 0.9% saline for intravenous infusion.

Patient Monitoring and Laboratory Tests

Monitor serum glucose in treated animals. Monitor serum creatinine, urea nitrogen, and hepatic enzymes for evidence of hepatotoxicity and renal injury. Although myelotoxicity is unusual, monitor CBC before each treatment.

Formulations

Streptozocin is available in 1-g vials for injection.

Stability and Storage

Store vial between 2°C and 8°C. Use vial within 12 hours after reconstitution at room temperature. Formulation also contains citric acid. Do not use if color changes from pale yellow to a darker brown color because this indicates degradation.

Small Animal Dosage

Dogs

- 500 mg/m² IV, infused over 2 hours, every 3 weeks.

Cats

A safe dose has not been reported for cats.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals that produce food.

Succimer

suks'ih-mer

Trade and Other Names: Chemet

Functional Classification: Antidote

Pharmacology and Mechanism of Action

Chelating agent. Succimer chelates lead and other heavy metals such as mercury and arsenic and increases their elimination from the body. Succimer is an analog to British anti-Lewisite (BAL),

Indications and Clinical Uses

Succimer is used for treatment of metal toxicosis, primarily toxicosis caused by lead. Other chelators that have been used for lead toxicity include calcium-EDTA, British anti-Lewisite (BAL), and penicillamine. Calcium-EDTA is often the preferred drug for initial treatment. The advantages of succimer over other chelators are that it is better tolerated with fewer GI adverse effects and it is not associated with nephrotoxicosis. It also does not bind other minerals such as copper, zinc, calcium, and iron.

Precautionary Information

Adverse Reactions and Side Effects

No adverse effects have been reported in dogs. However, renal injury has been associated with succimer treatment in cats.

Contraindications and Precautions

No contraindications have been reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Doses cited are based on studies in dogs. In cats, succimer has been used at 10 mg/kg q8h PO for 2 weeks.

Patient Monitoring and Laboratory Tests

Monitor patient's blood lead levels during treatment. Monitor renal function during treatment because renal failure has been associated with succimer administration in cats.

Formulations

Succimer is available in 100-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage**Dogs**

- 10 mg/kg q8h PO for 5 days, then 10 mg/kg q12h PO for 2 more weeks. It has also been administered rectally in vomiting dogs.

Cats

- 10 mg/kg q8h PO for 2 weeks.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Sucralfate

soo-krahlfate

Trade and Other Names: Carafate and Sulcrate (in Canada)

Functional Classification: Antiulcer agent

Pharmacology and Mechanism of Action

Gastric mucosa protectant. Antiulcer agent. Sucralfate dissociates in the stomach to form sucrose octasulfate and aluminum hydroxide. Sucrose octasulfate polymerizes to a viscous, sticky substance that creates a protective effect by binding to ulcerated mucosa. It has an affinity for negatively charged injured tissue. It protects the mucosa by preventing back diffusion of hydrogen ions and inactivates pepsin and adsorbs bile acid. There is some evidence that sucralfate may act as a cytoprotectant

(via increasing prostaglandin synthesis), but it is not certain that this is relevant to the clinical effects in dogs and cats.

Indications and Clinical Uses

Sucralfate is used to prevent and treat gastric ulcers. However, in clinical use, there is little evidence that it will prevent ulcers from nonsteroidal anti-inflammatory drugs (NSAIDs), although experimental evidence is available for horses. Sucralfate is administered orally and may protect ulcerated tissue and promote healing. Dosage regimens for sucralfate have been extrapolated from human dosages.

Precautionary Information

Adverse Reactions and Side Effects

Because sucralfate is not absorbed, it is virtually free of adverse effects. The most common side effect associated with its use in people has been constipation.

Contraindications and Precautions

No contraindications have been listed for animals.

Drug Interactions

Sucralfate may decrease absorption of other drugs administered orally via chelation with aluminum (such as fluoroquinolones and tetracyclines). Administer these other drugs at least 30 minutes before sucralfate. If mixed with other drugs (antimicrobials), inactivation may occur.

Instructions for Use

Dosing recommendations are based largely on empiricism. There are no clinical studies to demonstrate efficacy in animals with sucralfate. Sucralfate may be administered concurrently with histamine Type 2 inhibitors (H_2 blockers) (e.g., cimetidine) without causing an interaction.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Sucralfate is available in 1-g tablets and a 200-mg/mL oral suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Sucralfate is insoluble in water, unless exposed to strong acid or alkaline conditions. The tablets may be crushed and suspended in water to a concentration of 200 mg/mL and stored in the refrigerator for 14 days. Shake this suspension before using.

Small Animal Dosage

Dogs

- 0.5-1 g q8-12h PO.

Cats

- 0.25 g (one fourth tablet) q8-12h PO.

Large Animal Dosage

Foals

- 1 g q8h PO.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Sufentanil Citrate

soo-fen'tah-nil sih'trate

Trade and Other Names: Sufenta

Functional Classification: Analgesic, opioid

Pharmacology and Mechanism of Action

Opioid agonist. Action of fentanyl derivatives is via mu-opiate receptor. Sufentanil is five to seven times more potent than fentanyl, and in some studies it is as much as 10 times more potent than fentanyl. Doses of 13 to 20 mcg of sufentanil produce analgesia equal to 10 mg of morphine.

Indications and Clinical Uses

Sufentanil, like other opiate derivatives, is used for sedation, general anesthesia, and analgesia. It can be used as part of a regimen for balanced general anesthesia. It can be used with other agents or as a primary agent in patients intubated and delivered oxygen. Sufentanil has a rapid onset of effect and rapid recovery. It does not accumulate in tissues; therefore recovery is rapid following an anesthetic procedure. It can also be administered by the epidural route. The use of sufentanil, compared to other opiates, has been limited in animals.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are similar to morphine. Like all opiates, side effects are predictable and unavoidable. Side effects include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses.

Contraindications and Precautions

Use cautiously in animals with respiratory disease. Because of its high potency compared with morphine and other opiates, calculate dose carefully.

Drug Interactions

Like other opiates, sufentanil may potentiate other sedatives and anesthetics.

Instructions for Use

When used for anesthesia, animals are often premedicated with acepromazine or a benzodiazepine.

Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

Formulations

Sufentanil is available in a 50-mcg/mL injection in ampules of 1, 2, and 5 mL.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Sufentanil is a Schedule II drug and should be stored in a locked compartment.

718 Sulfachlorpyridazine

Small Animal Dosage

Dogs and Cats

- 2 mcg/kg IV (0.002 mg/kg), up to a maximum dose of 5 mcg/kg (0.005 mg/kg).

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Schedule II controlled drug.

Avoid use in animals intended for food. Withdrawal times are not established. However, for extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 1

Sulfachlorpyridazine

sul-fah-klor-peer-id'ah-zeen

Trade and Other Names: Vetsulid

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Sulfonamide antibacterial. Sulfonamides compete with para-aminobenzoic acid (PABA) for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic with trimethoprim. Bacteriostatic. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

Indications and Clinical Uses

Sulfachlorpyridazine is used as a broad-spectrum antimicrobial to treat or prevent infections caused by susceptible organisms. Infections treated may include pneumonia, intestinal infections (especially coccidia), soft tissue infections, and UTIs. However, resistance is common. The use of sulfachlorpyridazine has not been reported for small animals. It is used primarily for pigs and cattle. However, other drugs may be equally effective.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides (primarily in dogs) include allergic reactions, Type II and Type III hypersensitivity, hepatotoxicity, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions.

Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides.

Drug Interactions

There are several interactions reported for sulfonamide administration in small animals. (See sulfonamide manuscripts.) However, these interactions have not been relevant for its use in cattle and pigs.

Instructions for Use

The most common use of sulfachlorpyridazine is for treatment of enteritis in pigs and calves.

Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease thyroxine (T₄) concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI break point for sensitive organisms is ≤ 256 mcg/mL. One sulfonamide can be used as a marker for susceptibility to other sulfonamides. According to CLSI, susceptibility tests for sulfonamides can be used to interpret urinary bacteria isolates only.

Formulations

Sulfachlorpyridazine is available in a 2-g bolus and a 200-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

No doses reported for dogs and cats.

Large Animal Dosage

Cattle

- 33-50 mg/kg q12h PO or IV.

Pigs

- 22-39 mg/kg q12h PO or 44-77 mg/kg/day PO in the drinking water.

Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age.

Cattle withdrawal time (meat): 7 days.

Pig withdrawal time (meat): 4 days.

Sulfadiazine

sul-fa-dye'a-zeen

Trade and Other Names: Generic brands and combined with trimethoprim as Tribrisen

Functional Classification: Antibacterial

S

Pharmacology and Mechanism of Action

Sulfonamide antibacterial. Sulfonamides compete with para-aminobenzoic acid (PABA) for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic with trimethoprim. Bacteriostatic. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

Indications and Clinical Uses

Sulfadiazine is used occasionally alone; however, efficacy is not established for many infections. Most often, it is used with trimethoprim to treat a variety of infections,

including UTIs and skin infections. (See section on trimethoprim-sulfonamides for a more complete description.)

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other, more toxic metabolites may persist.

Contraindications and Precautions

Do not administer to animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed.

Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde that may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for intravenous forms of trimethoprim-sulfonamides.

Instructions for Use

Usually, sulfonamides are combined with trimethoprim or ormetoprim in a 5:1 ratio, and sulfonamides are rarely used alone in small animals and horses. There is no clinical evidence that one sulfonamide is more or less toxic or efficacious than another sulfonamide.

Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease thyroxine (T4) concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI break point for sensitive organisms is ≤ 256 mcg/mL. One sulfonamide can be used as a marker for susceptibility to other sulfonamides. According to CLSI, susceptibility tests for sulfonamides can be used to interpret urinary bacteria isolates only.

Formulations

Sulfadiazine is available in 500-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 100 mg/kg IV PO (loading dose), followed by 50 mg/kg q12h IV or PO (see also Trimethoprim).

Large Animal Dosage

For horses, see dosing for Trimethoprim combinations.

Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age. No withdrawal times are established. However, for extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Sulfadimethoxine

sul-fah-dye-meth-oks'een

Trade and Other Names: Albon, Bactrovet, and generic brands

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Sulfonamide antibacterial. Sulfonamides compete with para-aminobenzoic acid (PABA) for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic with trimethoprim. Bacteriostatic. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

Indications and Clinical Uses

Sulfadimethoxine is used as a broad-spectrum antimicrobial to treat or prevent infections caused by susceptible organisms. Infections treated may include pneumonia, intestinal infections (especially coccidia), soft tissue infections, and UTIs. However resistance is common, unless combined with ormetoprim (see Primor).

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other, more toxic metabolites may persist.

Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed.

Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapson, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde that may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for intravenous forms of trimethoprim-sulfonamides.

Instructions for Use

Usually, sulfonamides are combined with trimethoprim or ormetoprim in 5:1 ratio, and sulfonamides are rarely used alone in small animals and horses. There is no clinical evidence that one sulfonamide is more or less toxic or efficacious than another sulfonamide. Sulfadimethoxine has been combined with ormetoprim in Primor.

Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease thyroxine (T₄) concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI break point for sensitive organisms is ≤ 256 mcg/mL. One sulfonamide can be used as a marker for susceptibility to other sulfonamides. According to CLSI, susceptibility tests for sulfonamides can be used to interpret urinary bacteria isolates only.

Formulations

Sulfadimethoxine is available in 125-, 250-, and 500-mg tablets; 400-mg/mL injection; and 50-mg/mL suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 55 mg/kg PO (loading dose), followed by 27.5 mg/kg q12h PO. (For doses of combination with ormetoprim, see Primor.)

Large Animal Dosage

Cattle

- Treatment of pneumonia and other infections: 55 mg/kg as initial dose, followed by 27 mg/kg q24h PO for 5 days.
- Sustained-release bolus (Albon-SR): 137.5 mg/kg PO, as a single dose.

Regulatory Information

Cattle withdrawal time (meat): 7 days.

Cattle withdrawal time (milk): 60 hours.

Withdrawal time for sustained-released bolus 21 days.

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age. Currently, sulfadimethoxine is the only sulfonamide with approved indications in dairy cattle.

Sulfamethazine

sul-fah-meth'ah-zeen

Trade and Other Names: Sulmet and generic brands

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Sulfonamide antibacterial. Sulfonamides compete with para-aminobenzoic acid (PABA) for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic

with trimethoprim. Bacteriostatic. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

Indications and Clinical Uses

Sulfamethazine is used as a broad-spectrum antimicrobial to treat or prevent infections caused by susceptible organisms. Infections treated may include pneumonia, intestinal infections (especially coccidia), soft tissue infections and UTIs. However, resistance is common.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other, more toxic metabolites may persist.

Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed.

Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapson, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde, which may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for intravenous forms of trimethoprim-sulfonamides.

Instructions for Use

Usually, sulfonamides are combined with trimethoprim or ormetoprim in 5:1 ratio, and sulfonamides are rarely used alone in small animals and horses that have other pre-existing disease such as liver failure. There is no clinical evidence that one sulfonamide is more or less toxic or efficacious than another sulfonamide.

Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease thyroxine (T₄) concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI break point for sensitive organisms is ≤ 256 mcg/mL. One sulfonamide can be used as a marker for susceptibility to other sulfonamides. According to CLSI, susceptibility tests for sulfonamides can be used to interpret urinary bacteria isolates only.

Formulations

Sulfamethazine is available in a 30-g bolus.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

724 Sulfamethoxazole

Small Animal Dosage

Dogs and Cats

- 100 mg/kg PO (loading dose), followed by 50 mg/kg q12h PO.

Large Animal Dosage

Cattle

- Treatment of pneumonia and other infections: 220 mg/kg as initial dose, followed by 110 mg/kg q24h PO.
- Use of soluble powder as a drench or in drinking water: 237 mg/kg as initial dose, followed by 119 mg/kg q24h PO.
- Sustained-release bolus: 350-400 mg/kg PO as a single dose.

Pigs

- Use of soluble powder as a drench or in drinking water: 237 mg/kg as initial dose, followed by 119 mg/kg q24h PO.

Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle greater than 20 months of age.

Cattle withdrawal time (meat): 10 or 11 days.

Cattle withdrawal time (meat; soluble powder): 10 days.

Pig withdrawal time (meat; soluble powder): 15 days.

Cattle withdrawal time (meat; sustained-release bolus): 8-18 days, depending on the product.

Sulfamethoxazole

sul-fah-meth-oks'ah-zole

Trade and Other Names: Gantanol

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Sulfonamide antibacterial. Sulfonamides compete with para-aminobenzoic acid (PABA) for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic with trimethoprim. Bacteriostatic. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

Indications and Clinical Uses

Sulfamethoxazole is used as a broad-spectrum antimicrobial to treat or prevent infections caused by susceptible organisms. Infections treated may include pneumonia, intestinal infections (especially coccidia), soft tissue infections, and UTIs. However, resistance is common, unless combined with trimethoprim.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca,

and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other, more toxic metabolites may persist.

Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed.

Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde, which may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for intravenous forms of trimethoprim-sulfonamides.

Instructions for Use

Usually, sulfonamides are combined with trimethoprim or ormetoprim in 5:1 ratio, and sulfonamides are rarely used alone in small animals and horses. There is no clinical evidence that one sulfonamide is more or less toxic or efficacious than another sulfonamide.

Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease thyroxine (T₄) concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI break point for sensitive organisms is ≤ 256 mcg/mL. One sulfonamide can be used as a marker for susceptibility to other sulfonamides. According to CLSI, susceptibility tests for sulfonamides can be used to interpret urinary bacteria isolates only.

Formulations

Human formulations of sulfamethoxazole have been removed from the market. Usually it is combined with trimethoprim. Some older forms of sulfamethoxazole may still be available from pharmacies. Sulfamethoxazole is combined with trimethoprim in Bactrim, Septra, and generic products (see Trimethoprim).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 100 mg/kg PO (loading dose), followed by 50 mg/kg q12h PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age. Withdrawal times are not established. However, for extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Sulfaquinoxaline

sul-fah-kwin-ok's'ah-leen

Trade and Other Names: Sulfa-Nox

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Sulfonamide antibacterial. Sulfonamides compete with para-aminobenzoic acid (PABA) for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic with trimethoprim. Bacteriostatic. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

Indications and Clinical Uses

Sulfaquinoxaline is used as a broad-spectrum antimicrobial to treat or prevent infections caused by susceptible organisms. Infections treated may include pneumonia, intestinal infections (especially coccidia), soft tissue infections, and UTIs. However, resistance is common.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other, more toxic metabolites may persist.

Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides. Avoid contact with skin or mucous membranes when mixing in water.

Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde that may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for intravenous forms of trimethoprim-sulfonamides.

Instructions for Use

Mix in the drinking water. Make fresh solutions daily. The most common use of sulfaquinoxaline is for treatment of enteritis caused by coccidia in calves, sheep, and poultry.

Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease thyroxine (T₄) concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI break point for sensitive organisms is ≤ 256 mcg/mL. One sulfonamide can be used as a marker for susceptibility to

other sulfonamides. According to CLSI, susceptibility tests for sulfonamides can be used to interpret urinary bacteria isolates only.

Formulations

Sulfaquinoxaline is available in 34.4-, 128.5-, 192-, 200-, 286.2-, and 340-mg/mL solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

No doses reported for dogs and cats.

Large Animal Dosage

Calves

- 13.2 mg/kg/day PO (usually administered in the drinking water as a 0.015% solution for 5 days).

Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle greater than 20 months of age.

Cattle withdrawal time: 10 days.

Sheep withdrawal time: 10 days.

Poultry withdrawal time: 10 days.

Rabbit withdrawal time: 10 days.

Sulfasalazine

sul-fah-sal'ah-zeen

Trade and Other Names: Azulfidine and Salazopyrin (in Canada)

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Sulfonamide combined with an anti-inflammatory drug. Sulfasalazine has little effect and salicylic acid (mesalamine) has anti-inflammatory effects. (See manuscript for mesalamine for more details on mesalamine use.) When administered as the combination of salicylic acid and the sulfonamide, sulfapyridine, the salicylic acid is released by colonic bacteria to produce an anti-inflammatory effect. The anti-inflammatory effect is believed to be through antiprostaglandin action, antileukotriene activity, or both.

Indications and Clinical Uses

Sulfasalazine is used in small animals for the treatment of idiopathic colitis and other inflammatory intestinal diseases. It is often the first drug of choice for treatment when dietary therapy has been unsuccessful. Although sulfasalazine has been commonly used in small animals, use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. The section on mesalamine has additional information on clinical use.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are all attributed to sulfonamide component. Adverse effects are associated with sulfonamides and include allergic reactions, Type II and Type III hypersensitivity, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Keratoconjunctivitis sicca has been reported in dogs that received sulfasalazine for chronic treatment. The amount of salicylate absorbed appears to be small in cats; therefore adverse effects from salicylate in cats are unlikely.

Contraindications and Precautions

Do not administer to animals that are sensitive to sulfonamides. Drug interactions are possible but have not been reported in animals, probably because low systemic drug levels are achieved. Mesalamine can potentially interfere with thiopurine methyltransferase and, therefore, increase the risk of toxicity from azathioprine.

Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde, which may form a complex and precipitate with sulfonamides.

Instructions for Use

Usually used for treatment of idiopathic colitis, often in combination with dietary therapy. For animals sensitive to sulfonamides, consider other forms of mesalamine (see mesalamine section for more details).

Patient Monitoring and Laboratory Tests

Monitor tear production in dogs that receive chronic therapy.

Formulations

Sulfasalazine is available in 500-mg tablets, and has been compounded as an oral suspension for smaller animals.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 10-30 mg/kg q8-12h PO.

Cats

- 20 mg/kg q12h PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age.

RCI Classification: 4

Tacrolimus

tak-roe-lih'mus

Trade and Other Names: Protopic, FK506

Functional Classification: Immunosuppressant

Pharmacology and Mechanism of Action

Tacrolimus is a microbial product isolated from the organism *Streptomyces tsukubaensis*. Tacrolimus binds to an intracellular receptor and subsequently binds to calcineurin and inhibits the calcineurin pathway that stimulates the nuclear factor, NFAT. The action resembles that of cyclosporine (both drugs are calcineurin inhibitors), although the cellular receptors differ. By inhibiting the action of NFAT, tacrolimus decreases synthesis of inflammatory cytokines. In particular, synthesis of IL-2 is inhibited, which results in decreased activation of T lymphocytes. It is 10-100 times more potent than cyclosporine. Tacrolimus inhibits release of mast cell and basophil mediators and decreases inflammatory mediator expression.

Indications and Clinical Uses

Tacrolimus is used as an immunosuppressive drug to treat autoimmune disease, prevent organ transplant rejection, and treat atopic dermatitis. Most use in animals is with a topical formulation. It has been applied topically (ointment) for localized areas of atopic dermatitis. In some cases after resolution of lesions with systemic treatment with cyclosporine, isolated skin lesions are managed topically with tacrolimus ointment. There has been limited use for preventing renal transplant rejection in cats because the pharmacokinetics have been highly variable. A related drug, pimecrolimus, also has been used topically.

Precautionary Information

Adverse Reactions and Side Effects

There may be a slight burning or pruritic sensation with initial topical application. These reactions are mild and decrease as the skin heals. With systemic administration, dogs may show GI signs, which include diarrhea, intestinal discomfort, vomiting, intestinal intussusception, and intestinal injury. Tacrolimus is minimally absorbed systemically from topical application.

Contraindications and Precautions

Tacrolimus is a potent immunosuppressant. Use cautiously in animals prone to infection. Pet owners should be cautioned about skin contact when handling the medication for their pets.

Drug Interactions

No drug interactions have been identified from topical administration.

Instructions for Use

There are no reports of safe systemic doses used in dogs. Most use is topical. It can be used topically for immune-mediated skin lesions where local treatment can be used (e.g., on the bridge of the nose). It has also been applied topically for perianal fistula in addition to systemic prednisolone.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary with topical use.

730 Tegaserod Maleate

Formulations Available

Tacrolimus is available in 0.1% and 0.03% topical ointment in 30-, 60-, and 100-g tubes.

Stability and Storage

Ointment is stable if stored in manufacturer's original formulation. Compounded formulations of tacrolimus have been available from pharmacists, but the stability and potency of these formulations have not been evaluated. It is practically insoluble in water. When prepared in a suspension, it was stable for several weeks.

Small Animal Dosage

Dogs and Cats

Apply topical ointment (0.1%) to localized lesions on affected areas of skin. It has been used in dogs twice daily. For perianal fistula it has been applied twice daily.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Tegaserod Maleate

teg-ah-ser'-odd mal'-ee-ate

Trade and Other Names: Zelnorm

Functional Classification: Gastrointestinal stimulant

Pharmacology and Mechanism of Action

Tegaserod maleate is an intestinal simulant that produces a prokinetic action to stimulate motility. It acts by binding to serotonin type-4 (5-HT₄) receptors and triggers the release of neurotransmitters that stimulate smooth muscle motility. Activation of 5-HT₄ receptors in the GI tract stimulates peristaltic reflex and intestinal secretion. In horses it has increased motility in the equine pelvic flexure and accelerated GI transit. In horses it has a 55% oral absorption rate and a half-life of approximately 2.7 hours.

Indications and Clinical Uses

Tegaserod has been withdrawn from the human market because of adverse effects but is still available from some sources. In people it was associated with an increased risk of cardiovascular adverse events, including heart attack, chest pain, and stroke. It had been used in people with irritable bowel syndrome (IBS) whose primary symptom is constipation. The only reported use in animals has been in horses to stimulate intestinal motility. It has increased GI transit in horses and stimulated motility in the large colon. The use in small animals is primarily anecdotal, and clinical use is not established.

Precautionary Information

Adverse Reactions and Side Effects

Adverse cardiovascular events have been responsible for its withdrawal in humans. However, adverse effects have not been reported in animals.

Contraindications and Precautions

Do not use in animals with intestinal obstruction. Tegaserod is not absorbed from rectal administration in horses.

Drug Interactions

No drug interactions have been identified in animals.

Instructions for Use

Use in animals is based primarily from reports of use in horses.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations Available

Tegaserod melete has been available in 2- and 6-mg tablets. However, after discontinuation from the human market, the availability has become more difficult. It is practically insoluble in water, but crushed tablets may be used in a suspension for oral administration to horses. It has also been dissolved in acetic acid and further diluted for IV administration.

Stability and Storage

Crushed tablets in water have been stable if administered shortly after mixing for horses.

Small Animal Dosage**Dogs and Cats**

No doses have been reported for small animals. (Doses have been extrapolated from humans.)

Large Animal Dosage

0.27 mg/kg, PO, q12h.

Regulatory Information

Do not administer to animals intended for food.

Tamoxifen Citrate

tah-moks'ih-fen sih'trate

Trade and Other Names: Nolvadex

Functional Classification: Antiestrogen

Pharmacology and Mechanism of Action

Nonsteroidal estrogen receptor blocker. Tamoxifen also has weak estrogenic effects. Tamoxifen also may increase release of gonadotropin-releasing hormone (GnRH).

Indications and Clinical Uses

Tamoxifen is used as adjunctive treatment for certain tumors, especially estrogen-responsive tumors. The most common use in animals is adjunctive treatment for mammary neoplasia. In women it has been used to induce ovulation by stimulating release of GnRH from the hypothalamus.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been thoroughly documented in animals. However, in people, tamoxifen has been reported to cause increased tumor pain.

Contraindications and Precautions

Do not use in pregnant animals.

Drug Interactions

Tamoxifen is a potent cytochrome P450 enzyme inhibitor.

Instructions for Use

Tamoxifen is often used with other anticancer drug protocols.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations Available

Tamoxifen is available in 10- and 20-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Veterinary dose not established but has been extrapolated from the human dose. Human dose is 10 mg q12h PO (approximately 0.14 mg/kg q12h).

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Taurine

tore'een

Trade and Other Names: Generic brands

Functional Classification: Nutritional supplement

Pharmacology and Mechanism of Action

Nutritional supplement. Taurine is a naturally occurring amino acid considered essential for cats. Deficiencies in animals may lead to blindness and heart disease. Taurine may have some cardiac inotropic effects.

Indications and Clinical Uses

Taurine is used in the prevention and treatment of ocular and cardiac disease (dilated cardiomyopathy) caused by taurine deficiency. Although current commercial diets have adequate amounts of taurine, it has been supplemented in dogs and cats with heart disease.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Routine supplementation with taurine may not be necessary in animals that are receiving a balanced diet. However, supplementation may be necessary in animals with diseases associated with taurine deficiency.

Patient Monitoring and Laboratory Tests

Taurine concentrations can be measured in some laboratories to detect deficiencies. Normal levels in plasma are 60-120 nmol/mL in dogs and cats or 200-350 nmol/mL in whole blood. Levels below 40 nmol/mL in plasma and 150 nmol/mL in whole blood are considered deficient.

Formulations Available

Taurine is available in powder or supplemented in some diets. Consult a compounding pharmacy for availability.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 500 mg/dog q12h PO.

Cats

- 250 mg/cat q12h PO.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Tepoxalin

tep-oks'ah-lin

Trade and Other Names: Zubrin

Functional Classification: Anti-inflammatory

Pharmacology and Mechanism of Action

Tepoxalin is a nonsteroidal anti-inflammatory drug (NSAID). Like other drugs in this class, tepoxalin produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. However, tepoxalin also inhibits the action of lipoxygenase (LOX) to decrease synthesis of inflammatory leukotrienes in dogs. This produces a “dual action” in dogs by inhibiting both prostaglandins and leukotrienes.

Tepoxalin, using in vitro assays, is more cyclo-oxygenase-1 (COX-1) selective than COX-2 selective. It has not been established if the specificity for COX-1 or COX-2 is related to efficacy or safety. Tepoxalin forms an active metabolite after administration to dogs, cats, and horses. In dogs, tepoxalin has a half-life of 2 hours and the acid-metabolite has a half-life of 13 hours. It is highly protein bound. Feeding increases oral absorption in dogs.

Indications and Clinical Uses

Tepoxalin is used to decrease pain and inflammation. It has been used for the acute and chronic treatment of pain and inflammation in dogs. One of the most common uses is osteoarthritis, but it also has been used for pain associated with surgery. There is evidence that it was more effective than carprofen or meloxicam for reducing intra-articular inflammation in dogs and controlling synthesis of intra-articular PgE₂. Because of the dual action of tepoxalin, it has been investigated for treating other inflammatory conditions in dogs and cats. Studies available thus far to investigate the beneficial effect of dual inhibition by tepoxalin for other inflammatory diseases (for example, ocular inflammation, respiratory disease, or dermatitis) have had mixed results. Tepoxalin has been more effective than other drugs for ocular inflammation, but only partially effective for dermatitis, and not effective for respiratory disease. Use in large animals has not been reported.

Precautionary Information

Adverse Reactions and Side Effects

GI problems are the most often adverse effects associated with tepoxalin and can include vomiting, diarrhea, nausea, ulcers, and erosions of the GI tract. Both acute and long-term safety and efficacy have been established for dogs. In field trials, vomiting was the most often reported adverse effect. In studies performed in dogs, dogs have tolerated 10 times and 30 times the labeled dose. Renal effects and bleeding studies have been performed on healthy dogs. Tepoxalin in these studies was not shown to adversely affect bleeding times or renal function. Nevertheless, renal toxicity, especially in dehydrated animals or animals with preexisting renal disease, has been shown for some NSAIDs. Toxicity studies have not been performed in cats, but single doses of 10 mg/kg to a small group of cats did not produce adverse effects.

Contraindications and Precautions

Dogs and cats with preexisting GI problems or renal problems may be at a greater risk of adverse effects from NSAIDs. Safety in pregnancy is not known, but adverse effects have not been reported.

Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors. However, in experimental studies in dogs, tepoxalin combined with an ACE inhibitor did not produce adverse renal effects.

Instructions for Use

Rapidly dissolving tablets can be administered with or without food. In some animals, it is helpful to wet the tablet before placing on the animal's tongue. Long-term studies have not been completed in cats; only single-dose studies have been reported in which a dose of 10 mg/kg did not produce adverse effects.

Patient Monitoring and Laboratory Tests

Monitor GI signs for evidence of diarrhea, GI bleeding, or ulcers. Because of risk of renal injury, monitor renal parameters (water consumption, BUN, creatinine, and urine-specific gravity) periodically during treatment.

Formulations

Topoxalin is available in 30-, 50-, 100-, and 200-mg tablets (rapidly dissolving).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Shelf life is 2 years if maintained in manufacturer's original packaging.

Small Animal Dosage

Dogs

- 10 mg/kg q24h PO. It is safe to start with 20 mg/kg initially and use a dose of 10-20 mg/kg because of its wide safety margin.

Cats

- Cats have tolerated 10 mg/kg as a single dose, but long-term safety has not been evaluated.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Do not administer to animals that produce food.

Terbinafine Hydrochloride

ter-bin'ah-feen hye-droe-klor'ide

Trade and Other Names: Lamisil

Functional Classification: Antifungal

Pharmacology and Mechanism of Action

Antifungal drug. Terbinafine belongs to the allylamine group of antifungal drugs. It acts on ergosterol biosynthesis by targeting fungal squalene epoxidase (SE). SE is a membrane-bound enzyme and is involved in the conversion of squalene into squalene 2,3-epoxide, which is subsequently converted into lanosterol and ergosterol. Terbinafine is selective for fungal SE. Terbinafine is active against dermatophytes. After administration, concentrations persist in hair for much longer than in plasma or other body fluids. For example, concentrations were maintained in cat hair for more than 5 weeks after treatment.

Indications and Clinical Uses

Terbinafine is indicated for treatment of dermatophyte infections in dogs, cats, birds, and some exotic animals. For dermatophytes in animals, the doses necessary for efficacy are much higher than those used in people. Although there has been experience with using terbinafine in animals—primarily for dermatophytes—there is no evidence that terbinafine is more effective than other oral antifungal agents. In dogs it has been used for *Malassezia* yeast infections. Treatment of infections in horses with terbinafine has not been successful probably because of poor absorption.

Precautionary Information

Adverse Reactions and Side Effects

Vomiting has been the most common adverse effect. Nausea and anorexia also are possible. Liver enzymes may be elevated in some animals. Hepatotoxicity is possible, but it has not been reported from use in animals. Facial pruritus has been observed in some treated cats. In people, a persistent taste disturbance, gastrointestinal problems, and headache have been reported.

Contraindications and Precautions

No contraindications have been reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Treatment of dogs and cats requires much higher doses compared to doses used in people.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Terbutaline is available in 250-mg tablets, 1% topical solution, and 1% topical cream.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Terbutaline is slightly soluble in water and alcohol. When suspensions have been prepared from crushed tablets in a vehicle (Ora-Sweet) it was stable for 42 days.

Small Animal Dosage

Dogs

- 30-40 mg/kg q24h PO (with food) for 2-3 weeks.

Cats

- 30-40 mg/kg/day PO for at least 2 weeks.

Large Animal Dosage

There are no effective doses reported for large animals. It is not effective for horses.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Terbutaline Sulfate

ter-byoo'tah-leen sul'fate

Trade and Other Names: Brethine and Bricanyl

Functional Classification: Bronchodilator, beta agonist

Pharmacology and Mechanism of Action

Beta₂-adrenergic agonist. Bronchodilator. Stimulates beta₂ receptors to relax bronchial smooth muscle. Terbutaline is more beta₂ specific than drugs such as isoproterenol. Other beta₂-specific drugs include albuterol and metaproterenol. In addition to the beta₂ effects to relax bronchial smooth muscle and relieve bronchospasm, the beta₂-agonists also may inhibit release of inflammatory mediators, especially from mast cells.

Indications and Clinical Uses

Terbutaline, like other beta₂-agonists, is indicated in animals with reversible bronchoconstriction, such as cats with bronchial asthma. It also has been used in dogs to relieve bronchoconstriction and in animals with bronchitis and other airway diseases. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Albuterol injection may be used as an alternative for terbutaline injection (4 mcg/kg bolus, up to 8 mcg/kg as needed). Terbutaline is not absorbed by the oral route in horses; therefore, it is not effective in horses for oral administration. Clenbuterol usually is the drug of choice for horses.

Precautionary Information

Adverse Reactions and Side Effects

Excessive beta-adrenergic stimulation from terbutaline at high doses results in tachycardia and muscle tremors. Arrhythmias are possible with high doses. All beta₂-agonists will inhibit uterine contractions at the end of gestation in pregnant animals. High doses of beta₂-agonists can lead to hypokalemia because they stimulate Na⁺-K⁺-ATPase and increase intracellular K⁺, while decreasing serum K⁺ and producing hyperglycemia. Treatment consists of KCl supplement at a rate of 0.5 mEq/kg/hr.

Contraindications and Precautions

Administer cautiously to animals with cardiac disease, particularly animals that may be susceptible to tachyarrhythmias. Do not use late in gestation unless the intended effect is to delay uterine contractions.

Drug Interactions

Use cautiously with other drugs that may stimulate the heart and cause tachycardia.

Instructions for Use

May be administered PO, IM, or SQ. Terbutaline (and other beta₂-agonists) have also been used in people to delay labor (dose in people is 2.5 mg q6h PO). Other beta₂-agonists used in animals for relief of bronchoconstriction include albuterol and salmeterol. Animals with acute bronchoconstriction also may benefit from corticosteroid treatment and oxygen therapy. Caution should be used when administering repeated subcutaneous doses. The maximum subcutaneous dose in people is 500 mcg/person (0.5 mg) within a 4-hour period.

Patient Monitoring and Laboratory Tests

Monitor heart rate in animals during treatment. Monitor potassium concentration if high doses are administered.

Formulations

Terbutaline is available in 2.5- and 5-mg tablets and 1-mg/mL (equivalent to 0.82 mg/mL) injections.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Terbutaline sulfate is soluble in water. Solutions may be subject to degradation. Observe for color change, and discard if solution turns a dark color. Suspensions have been prepared from tablets in syrup and stable for 55 days.

Small Animal Dosage

Dogs

- 1.25-5 mg/dog q8h PO.
- 3-5 mcg/kg (0.003-0.005 mg/kg) SQ, usually as a single dose in an emergency. If necessary repeat in 4-6 h.

Cats

- 0.1 mg/kg q8h PO.
- 0.625 mg/cat (1/4 of 2.5 mg tablet) q12h PO.
- 5-10 mcg/kg (0.005-0.01 mg/kg) q4h SQ or IM.

Large Animal Dosage

Horses

- Not absorbed orally. Use IV for treatment of chronic recurrent airway obstruction (RAO): 2-5 mcg/kg q6-8h IV, or as needed.

Regulatory Information

Terbutaline has similar properties as clenbuterol and should not be administered to animals intended for food.

RCI Classification: 3

Testosterone

tess-toss'ter-one

Trade and Other Names: Testosterone cypionate ester: Andro-Cyp, Andronate, Depo-Testosterone, and generic brands and testosterone propionate ester: Testex and Malogen (in Canada)

Functional Classification: Hormone

Pharmacology and Mechanism of Action

Testosterone ester for injection is available in two forms: testosterone cypionate and testosterone propionate. It is used to supplement testosterone in deficient animals. It will also produce anabolic effects. Testosterone esters are administered IM to avoid first-pass effects that occur from oral administration. Esters in oil are absorbed more slowly from intramuscular injections. Esters are then hydrolyzed to free testosterone. Other agents with more specific anabolic activity include boldenone, oxymetholone, nandrolone, stanozolol, and methyltestosterone.

Indications and Clinical Uses

Anabolic agents have been used for reversing catabolic conditions, increasing weight gain, increasing muscling in animals, and stimulating erythropoiesis. Testosterone and other anabolic agents have also been abused in people for athletic performance.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are caused by excessive androgenic action of testosterone. Prostatic hyperplasia is possible in male dogs. Masculinization can occur in female dogs. Hepatopathy is more common with oral methylated testosterone formulations than with injected formulations.

Contraindications and Precautions

Use cautiously in patients with hepatic disease. Do not administer to pregnant animals. This drug has potential for abuse in humans for anabolic uses.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Use of testosterone androgens has not been evaluated in clinical studies in veterinary medicine. Use is based primarily on experimental evidence or experiences in people.

Patient Monitoring and Laboratory Tests

Monitor hepatic enzymes in treated patients periodically.

Formulations

Testosterone cypionate ester is available in 100- and 200-mg/mL injections. Testosterone propionate ester is available in 100-mg/mL injections.

Stability and Storage

Testosterone is insoluble in water but soluble in oils and ethanol. Protect from light, heat, and freezing. When mixed with oil, it has been stable for 60 days.

Small Animal Dosage

Dogs and Cats

- Testosterone cypionate ester: 1-2 mg/kg q2-4weeks IM.
- Testosterone propionate ester: 0.5-1 mg/kg 2-3 times/week IM.

Large Animal Dosage

There are no large animal formulations available, except for implants for calves. Do not administer injections to animals intended for food.

Regulatory Information

Testosterone is a Schedule III controlled drug.
RCI Classification: 4

T

Tetracycline, Tetracycline Hydrochloride

tet-rah-sye'kleen

Trade and Other Names: Panmycin, Duramycin powder, and Achromycin V

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Tetracycline antibiotic. Mechanism of action of tetracyclines is to bind to 30S ribosomal subunit and inhibit protein synthesis. The action is time-dependent and

740 Tetracycline, Tetracycline Hydrochloride

against some bacteria is bacteriostatic. Tetracycline, like other tetracyclines, has a broad spectrum of activity including bacteria, some protozoa, *Rickettsiae*, and *Ehrlichiae*. Resistance is common. Tigecycline is a new tetracycline that has improved activity against bacteria that are resistant to other drugs. However, there are no reports of the use of tigecycline in animals.

Indications and Clinical Uses

Tetracyclines are used to treat a variety of infections, including soft tissue infections, pneumonia, and UTIs. Other drugs in this group that are used more frequently in animals for treatment include oxytetracycline, minocycline, and doxycycline. Consult sections containing those drugs for a more complete list of clinical use and indications.

Precautionary Information

Adverse Reactions and Side Effects

Tetracyclines in general may cause renal tubular necrosis at high doses.

Tetracyclines can affect bone and teeth formation in young animals. Tetracyclines have been implicated in drug fever in cats. Hepatotoxicity may occur at high doses in susceptible individuals.

Contraindications and Precautions

Do not use in young animals because it can affect bone and teeth formation.

Drug Interactions

Tetracyclines bind to compounds that contain calcium, which decreases oral absorption. Do not mix with solutions that contain iron, calcium, aluminum, or magnesium.

Instructions for Use

Pharmacokinetic and experimental studies have been conducted in small animals but not in clinical studies. Use of tetracyclines in small animals has primarily been replaced by doxycycline. The most common oral tetracycline in horses is doxycycline or minocycline.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms ≤ 2 mcg/mL for streptococci and ≤ 4 mcg/mL for other organisms. However, on the basis of plasma concentrations achieved, 1 mcg/mL or less should be used for animals. Tetracycline is used as a marker to test susceptibility for other drugs in this class such as doxycycline, minocycline, and oxytetracycline. When using tetracycline to test for susceptibility to oxytetracycline in pathogens from cattle, use a break point of ≤ 2 mcg/mL for susceptible bacteria. When using tetracycline to test for susceptibility to oxytetracycline in pathogens from swine, use a break point of ≤ 0.5 mcg/mL for susceptible bacteria.

Formulations

Tetracycline is available in 250- and 500-mg capsules, 500-mg calf bolus, 100-mg/mL oral suspension, and 25 and 324 g/lb of powder.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Tetracycline has poor aqueous solubility. However, tetracycline hydrochloride is more soluble (100 mg/mL). The pH of tetracycline hydrochloride solution is approximately 2.0. It will decompose if kept at alkaline pH. Tetracycline

hydrochloride is unstable, and compounded preparations are better prepared from tetracycline base as a suspension. Tetracycline will darken with exposure to light. Protect from freezing.

Small Animal Dosage

Dogs and Cats

- 15-20 mg/kg q8h PO.
- 4.4-11 mg/kg q8h IV or IM.
- Rickettsial infection (dogs): 22 mg/kg q8h for 14 days PO.

Large Animal Dosage

Calves and Pigs

For treatment of enteritis and pneumonia: 11 mg/kg q12h administered in the water or as a bolus. When administered in the water, the dose may actually vary among animals, depending on their water intake.

Regulatory Information

Cattle and pig withdrawal times: 5 days meat for oral powder; 18 days meat; 72 hours milk when used as intrauterine bolus in cattle; and 12, 14, and 24 days when oral tablets are used, depending on product (check label).

Thenium Closylate

thee'nee-um kloe'sill-ate

Trade and Other Names: Canopar

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Antiparasitic drug. Thenium is an antiparasitic drug with action specific for hookworms.

Indications and Clinical Uses

Thenium closylate is used to treat adult forms of the species *Ancylostoma caninum* and *Uncinaria stenocephala* (hookworms).

Precautionary Information

Adverse Reactions and Side Effects

Thenium may cause occasional vomiting after oral administration.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Tablet is bitter if coating is broken.

Patient Monitoring and Laboratory Tests

Monitor fecal samples for evidence of parasites.

Formulations

Thenium closylate is available in 500-mg tablets (veterinary preparation).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- Dogs weighing >4.5 kg: 500 mg PO once and repeat in 2-3 weeks.
- Dogs weighing 2.5-4.5 kg: 250 mg (half tablet) twice a day PO for 1 day; repeat in 2-3 weeks.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Theophylline

thee-off'ih-lin

Trade and Other Names: Many generic brands and theophylline sustained release.

Functional Classification: Bronchodilator

Pharmacology and Mechanism of Action

Methylxanthine bronchodilator. Nonselective phosphodiesterase (PDE) inhibitor. Phosphodiesterase is the enzyme that converts cyclic adenosine monophosphate (cyclic AMP) to inactive forms. Therapeutic effects may be caused by cyclic AMP or antagonism of adenosine. There appears to be anti-inflammatory action and bronchodilating action. Sustained-release preparations are used to decrease frequency of administration. Oral theophylline is well-absorbed orally in dogs, cats, and horses with bioavailability exceeding 90%. After absorption, theophylline has a half-life in dogs, cats, and horses of 5-6 hours, 14-18 hours, and 12-15 hours, respectively. Some oral formulations contain aminophylline, and theophylline is the active component of aminophylline.

Indications and Clinical Uses

Theophylline is administered for inflammatory airway disease in cats, dogs, and horses. Use in animals has been primarily derived from empirical use, some experimental models, and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. It has been used to control clinical signs of reversible airway constriction, such as seen with feline asthma. In dogs, the uses include collapsing trachea, bronchitis, and other airway diseases. In horses, it will relieve signs of recurrent airway obstruction (heaves), but the IV dose may cause adverse effects in horses. Other drugs (e.g., clenbuterol, albuterol) are often used for this condition in horses. It has not been effective for respiratory diseases in cattle. In dogs and cats, human-labeled extended-release tablets and capsules may be used twice daily in dogs and once daily in cats to achieve effective blood concentrations.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include nausea, vomiting, and diarrhea. With high doses, tachycardia, excitement, tremors, and seizures are possible. Cardiovascular and CNS adverse effects appear to be less frequent in dogs than people. Overdoses can cause hypokalemia.

Contraindications and Precautions

Administer with caution to patients with cardiovascular disease or patients with seizure disorders.

Drug Interactions

Use cautiously with other phosphodiesterase inhibitors such as pentoxifylline, sildenafil (Viagra), and pimobendan. Many drugs will inhibit the metabolism of theophylline and potentially increase concentrations. Drugs responsible include cimetidine, erythromycin, fluoroquinolones, and propranolol. Some drugs will decrease concentrations by increasing metabolism. Such drugs include phenobarbital and rifampin.

Instructions for Use

Adjust dose to maintain therapeutic blood levels. Older slow-release and extended-release formulations are no longer available. Pharmacokinetic studies have established doses for human-labeled tablets and capsules in dogs and cats. These formulations have produced the most consistent plasma concentrations from oral dosing.

Patient Monitoring and Laboratory Tests

Plasma concentrations of theophylline should be monitored in patients receiving chronic therapy to maintain plasma concentrations between 10 and 20 mcg/mL. Regularly monitor plasma concentrations in patients receiving chronic treatment. Peak-trough concentration measurements are encouraged.

Formulations

Theophylline is available in 100-, 125-, 200-, 250-, and 300-mg tablets; 27-mg/5-mL (5.3-mg/mL) oral solution or elixir; and injection in 5% dextrose. Theophylline extended release is available in 100-, 200- and 300-mg tablets (Theochron). However, availability of various sizes of extended-release formulations may vary. The manufacturers have discontinued other extended-release formulations such as Slo-Bid and Theo-Dur.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Theophylline is slightly soluble in water (8 mg/mL). Theophylline has been mixed with some oral liquids and found to be stable if administered shortly after mixing. When using the slow-release tablets or capsules in dogs and cats, do not disrupt coating on formulation.

Small Animal Dosage

Dogs

- Theophylline: 9 mg/kg q6-8h PO (immediate-release formulations)
- Theophylline sustained-release: 10 mg/kg q12h PO.

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Cats

- 4 mg/kg q8-12h PO (immediate-release formulations).
- Theophylline sustained release: 20 mg/kg for tablets (100 mg per cat) q24h PO or 25 mg/kg for extended-release (125 mg per cat) q24h PO. With long-term use in cats, this interval may be increased to q48h.

Large Animal Dose

- Horses, treatment of recurrent airway obstruction (RAO): 5 mg/kg q12h PO.
- Although theophylline has been administered to horses IV, this administration has caused transient excitement and restlessness. Give IV administration slowly.
- Cattle use as a bronchodilator: 20 mg/kg q12h PO. When treating diseases secondary to virus infections, decrease frequency to once every 24 hours.

Regulatory Information

Withdrawal times are not established. However, for extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

Thiabendazole

thye-ah-ben'dah-zole

Trade and Other Names: Omnizole, Equizole, TBZ, and Thibenzole

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Benzimidazole antiparasitic drug. Like other benzimidazoles, it produces a degeneration of the parasite microtubule and irreversibly blocks glucose uptake in parasites. Inhibition of glucose uptake causes depletion of energy stores in parasite, eventually resulting in death. However, there is no effect on glucose metabolism in mammals.

Indications and Clinical Uses

Availability of commercial forms of thiabendazole has been limited. In horses, thiabendazole has been used for control of large and small strongyles; *Strongyloides*; and pinworms of the genera *Strongylus*, *Cyathostomum*, *Cylicobrachytus* and related genera *Craterostomum*, *Oesophagodontus*, *Poteriostomum*, and *Oxyuris*. In ruminants it has been used for infections of GI roundworms in sheep and goats (*Trichostrongylus* spp., *Haemonchus* spp., *Ostertagia* spp., *Cooperia* spp., *Nematodirus* spp., *Bunostomom* spp., *Strongyloides* spp., *Chabertia* spp., *Oesophagostomum* spp., *Trichostrongylus colubriformis* and *T. axei*, and *Ostertagia* spp.).

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are uncommon.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Thiabendazole is ordinarily administered to horses and cattle. Experience in small animals is limited.

Patient Monitoring and Laboratory Tests

Monitor fecal samples for evidence of intestinal parasites.

Formulations Available

Thiabendazole is available in paste, pellets, and solution for oral administration and premix for feeds. Some formulations are no longer commercially available.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 50 mg/kg q24h for 3 days; repeat in 1 month.
- Treating respiratory parasites: 30-70 mg/kg q12h PO.

Cats

- *Strongyloides* spp: 125 mg/kg q24h for 3 days.

Large Animal Dosage

Horses

- 44 mg/kg PO (single dose).

Sheep and Goats

- 44 mg/kg PO (single dose); up to 67 mg/kg PO for some infections.

Cattle

- 67 mg/kg PO (single dose), up to 111 mg/kg PO for more severe infections.

Pigs (baby pigs)

- 67-90 mg/kg PO.

Regulatory Information

Withdrawal time for milk: 96 hours.

Sheep and goat withdrawal time (meat): 30 days.

Cattle withdrawal time (meat): 3 days.

Pig withdrawal time (meat): 30 days.

Thiacetarsemide Sodium

thye-ass-et-ars'ah-mide soe-dee-um

Trade and Other Names: Caparsolate

Functional Classification: Antiparasitic

Pharmacology and Mechanism of Action

Organic arsenical that produces toxicity in parasites such as adult heartworms.

Indications and Clinical Uses

Thiacetarsemide is used for treatment of adult heartworm infections. Caparsolate is no longer recommended as an adulticide heartworm treatment by the American

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Heartworm Society. Caparsolate is less effective in cats than in dogs, with a higher incidence of adverse reactions. In dogs, melarsomine is considered safer and has replaced thiacetarsamide for routine treatment.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are common, especially anorexia, vomiting, and hepatic injury. Pulmonary thromboembolism may occur as a consequence of heartworm kill.

Contraindications and Precautions

Its use is not recommended in cats unless they can be carefully monitored. Cats are less susceptible to arsenical toxicity than dogs, but they are more prone to pulmonary thromboembolism. If cats are treated, they should be confined under close observation for 3-4 weeks.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Thiacetarsamide is administered via four injections over 2 days; however, if severe adverse effects are observed, discontinue regimen. Extravasation can result in skin slough. It is recommended to substitute melarsomine for thiacetarsamide, if possible, for treating heartworm disease.

Patient Monitoring and Laboratory Tests

Monitor renal and hepatic function.

Formulations

Thiacetarsamide is available in 10-mg/mL injections. There are no longer commercial supplies of thiacetarsamide, and its availability is uncertain.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 2.2 mg/kg IV twice daily for 2 days.

Cats

- Not recommended, unless the cat can be closely supervised. Dose is 2.2 mg/kg twice daily IV for 2 consecutive days.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Thiamine Hydrochloride

thye'ah-min hye-droe-klor'ide

Trade and Other Names: Vitamin B₁, Bewon, and generic brands

Functional Classification: Vitamin

Pharmacology and Mechanism of Action

Vitamin B₁ is used for treatment of vitamin deficiency. Vitamin B complex often contains thiamine (B₁), riboflavin, niacinamide, and cyanocobalamin B₁₂.

Indications and Clinical Uses

Thiamine is used to provide Vitamin B₁ supplementation or to treat vitamin B₁ deficiency.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are rare because water soluble vitamins are easily excreted.

Contraindications and Precautions

Administer solutions of vitamin B₁ very slowly IV, if at all. Rapid intravenous administration has caused anaphylactic reactions.

Drug Interactions

Thiamine hydrochloride may be susceptible in incompatibility when this hydrochloride is mixed with alkalinizing solutions.

Instructions for Use

Vitamin B supplements are administered often in combination with other B vitamins as vitamin B complex solutions.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Thiamine is available in 250-mcg/5-mL elixir, 5- to 500-mg tablets, and 100- and 500-mg/mL injections.

Vitamin B complex aqueous solutions for injection usually contain 12.5 mg/mL of vitamin B₁.

Stability and Storage

Store in a tightly sealed container, at room temperature, protected from light. When mixed with other solutions (e.g., fluid solutions), incompatibility may result.

Small Animal Dosage

Dogs

- 10-100 mg/dog/day PO.
- 12.5-50 mg/dog/day IM or SQ.

Cats

- 5-30 mg/cat/day PO, up to a maximum dose of 50 mg/cat/day.
- 12.5-25 mg/cat/day IM or SQ.

Large Animal Dosage

All doses are listed on a per animal basis.

Lambs

- 12.5-25 mg/day IM.

Sheep and Pigs

- 65-125 mg/day IM.

Calves and Foals

- 37.5-65 mg/day IM.

Cattle and Horses

- 125-250 mg/day IM.

Regulatory Information

Withdrawal time for animals intended for food: 0 days.

Thioguanine

thye-oh-gwah'neen

Trade and Other Names: Generic brands

Functional Classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Antimetabolite of purine analogue type. Thioguanine inhibits DNA synthesis in cancer cells.

Indications and Clinical Uses

Thioguanine is used in some anticancer protocols. It is not commonly used in animals. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects, as with any anticancer drug, are expected. Adverse effects from thioguanine may be similar to those observed from mercaptopurine.

Immunosuppression and leukopenia are common.

Contraindications and Precautions

Do not administer to patients with depressed bone marrow.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Thioguanine may be combined with other agents for treatment of cancer.

Patient Monitoring and Laboratory Tests

Monitor CBC to screen for evidence of bone marrow toxicity.

Formulations

Thioguanine is available in 40-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 40 mg/m² q24h PO.

Cats

- 25 mg/m² q24h PO for 1-5 days, then repeat every 30 days.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Thiopental Sodium

thye-oh-pen'tahl soe'dee-um

Trade and Other Names: Pentothal

Functional Classification: Anesthetic, barbiturate

Pharmacology and Mechanism of Action

Ultrashort-acting barbiturate. Anesthesia is produced by CNS depression without analgesia. Anesthesia is terminated by redistribution in the body.

Indications and Clinical Uses

Thiopental is used primarily for induction of anesthesia or for short duration of anesthesia (10-15-minute procedures). It induces a rapid, smooth, and generally excitement-free induction. It can be administered intravenously, with prior premedication of other anesthetic adjuncts such as tranquilizers and sedatives (e.g., alpha-2 agonists, phenothiazines, and opiates).

Precautionary Information

Adverse Reactions and Side Effects

The most common effect is transient apnea and respiratory depression. Other adverse effects are related to the anesthetic effects of the drug. Thiopental may cause cardiovascular depression with a slight decrease in stroke volume and little change in cardiac output or blood pressure. Premedication will reduce the risk of cardiovascular events. Supplementation with oxygen during induction also will decrease cardiovascular events. Overdoses are caused by rapid or repeated injections. Avoid extravasation outside of the vein.

Contraindications and Precautions

Use carefully in patients with respiratory or cardiac disease. Do not use unless there is an ability to monitor and maintain respiration.

Drug Interactions

Thiopental is compatible with other anesthetics. However, use of other sedatives and anesthetics will lower dose of thiopental. Thiopental has been combined with propofol in a 1:1 mixture without loss of effectiveness. This mixture of 1:1 2.5% thiopental and propofol has been used to induce anesthesia in dogs.

Instructions for Use

Therapeutic index is low. Use only in patients in which it is possible to monitor cardiovascular and respiratory functions. Thiopental is often administered with other anesthetic adjuncts.

Patient Monitoring and Laboratory Tests

Monitor cardiovascular and respiratory function during anesthesia with thiopental.

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Formulations

Thiopental is available in 250-mg to 10-g vials (mix to desired concentration).

Stability and Storage

Thiopental, when prepared properly, is chemically stable and resists bacterial growth for up to 4 weeks when refrigerated. Thiopental has a pH of 10-11 and should not be mixed with acidifying solutions. If mixed with other drugs, the alkalinity may affect their stability. Propofol has been mixed with thiopental sodium in a 1:1 mixture and they are physically and chemically compatible if used promptly.

Small Animal Dosage

Dogs

- 10-25 mg/kg IV (to effect).

Cats

- 5-10 mg/kg IV (to effect).

Large Animal Dosage

Cattle

- Induction: 6-12 mg/kg IV (to effect).

Pigs

- 10-20 mg/kg IV (to effect).

Regulatory Information

Extralabel use: Establish a withdrawal time of at least 1 day for meat and 24 hours for milk.

Pig withdrawal time (meat): 0 days.

Schedule II controlled drug.

RCI Classification: 2

Thiotepa

thye-oh-tep'ah

Trade and Other Names: Thioplex and generic brands

Functional Classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Thiotepa is an alkylating agent of the nitrogen mustard type (similar to cyclophosphamide).

Indications and Clinical Uses

Thiotepa is used for various tumors, especially malignant effusions. The most common mode of administration is in a lesion or locally (e.g., in a bladder). For cancer of the bladder, 30 mg is diluted in 30 mL of distilled water and instilled directly in the bladder once per week.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are similar to other anticancer agents and alkylating drugs (many of which are unavoidable). Bone marrow suppression is the most common effect.

Contraindications and Precautions

Avoid use in animals with depressed bone marrow.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

One should consult specific cancer chemotherapy protocol for guidance on administration. Thiotepea usually is administered directly in body cavities.

Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow suppression.

Formulations

Thiotepea is available in 15-mg injections (usually in a solution of 10 mg/mL).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. When mixing solution, add 1.5 mL of sterile water to each vial. This solution is stable for 5 days if refrigerated. Solutions may be clear to slightly opaque, but if cloudiness or precipitate appears, discard vial.

Small Animal Dosage

Dogs and Cats

- 0.2-0.5 mg/m² weekly or daily for 5-10 days IM, intracavitary, or intratumor.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Thyroid Releasing Hormone

Trade and Other Names: TRH, Protirelin, Thyrel

Functional Classification: Hormone, thyroid

Pharmacology and Mechanism of Action

Thyroid-releasing hormone (TRH) is used to detect hyperthyroidism when T₄ is not elevated, yet hyperthyroidism is suspected. It is a synthetic tripeptide that is believed to be structurally identical to the naturally-occurring thyrotropin-releasing hormone produced by the hypothalamus.

Indications and Clinical Uses

TRH has been used for diagnostic testing. See thyrotropin (TSH) for diagnostic testing for hypothyroidism. There are no specific therapeutic uses.

Precautionary Information

Adverse Reactions and Side Effects

No significant adverse effects have been reported. Allergic reactions are possible.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Used for diagnostic purposes.

Patient Monitoring and Laboratory Tests

Monitor thyroid concentrations. Collect post TRH T4 sample at 4 hours after test dose.

Formulations

Thyrel TRH (Protirelin) is supplied as 1 mL ampuls. Each ampul contains 500 µg protirelin, but is currently difficult to obtain.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- Collect baseline T4, followed by 0.1 mg/kg IV. Collect post-TRH T4 sample at 4 hours.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Thyrotropin

thye-roe-troe'pin

Trade and Other Names: Thytropar, Thyrogen, and TSH

Functional Classification: Hormone, thyroid

Pharmacology and Mechanism of Action

Thyroid-stimulating hormone (TSH) is used for diagnostic testing; it stimulates normal secretion of thyroid hormone. The formulations available include Thyrogen (thyrotropin alpha for injection), which is a purified recombinant form of human TSH produced by recombinant DNA technology. An older form, Thytropar, is difficult to obtain. The amino-acid sequence of thyrotropin alpha is identical to that of human pituitary thyroid-stimulating hormone. TSH activity is not species specific and the human product may be used in animals.

Indications and Clinical Uses

TSH is used to stimulate secretion of thyroid hormone for diagnostic testing. Because of the limited availability of TSH for diagnostic testing and the high cost of the human form, this test is rarely performed.

Precautionary Information

Adverse Reactions and Side Effects

Adverse reactions are rare. In people, allergic reactions have occurred.

Contraindications and Precautions

No contraindications have been reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

To prepare solution, add 2 mL sodium chloride to a 10-unit vial. Consult testing laboratory for specific guidelines for thyroid testing.

Patient Monitoring and Laboratory Tests

After IV injection, collect post TSH sample at 4 or 6 hours. See dosing section for complete information on testing in dogs.

Formulations

Recombinant human TSH, also known as thyrotropin alpha or Thyrogen, is available in a 1.1 mg vial containing thyrotropin alpha. After reconstitution with 1.2 mL of sterile water, the thyrotropin alpha concentration is 0.9 mg/mL (see dose section for specific instructions for preparing canine dose). The pH of the reconstituted solution is approximately 7.0. Other forms (Thytropar) are difficult to obtain. Bovine TSH is no longer available.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Reconstituted solutions retain potency for 2 weeks at 2°C-8°C, for 4 weeks at 4°C, and 8 weeks if frozen.

Small Animal Dosage

Dogs

- 50-100 mcg injection per dog.
- Diagnostic testing for dogs: Reconstitute 1 vial (1.1 mg) with 6 mL sterile water and divide into 12 aliquots. Place 0.5 mL in plastic insulin syringes and store in freezer. For each dose, thaw syringe and administer IV one syringe per dog (approximately 92 mcg per dog). Measure thyroid hormone (T₄) at 4 or 6 hours post-injection. Post-TSH response should be at least 1.87 mcg/dL over baseline, or >3.5 mcg/mL.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Ticarcillin Disodium

tye-kar-sill'in dye-soe-dee-um

Trade and Other Names: Ticar and Ticillin

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Like other beta lactams, ticarcillin binds penicillin-binding proteins (PBP) that weaken or interfere with cell wall formation. After binding to PBP, the cell wall weakens or undergoes lysis. Like other beta lactams, this drug acts in a time-dependent manner, which indicates that it is more effective when drug concentrations are maintained above the minimum inhibitory concentration (MIC)

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values during the dose interval. Ticarcillin has action similar to ampicillin/amoxicillin and a spectrum similar to carbenicillin. Ticarcillin is primarily used for gram-negative infections, especially those caused by *Pseudomonas* species.

Indications and Clinical Uses

Ticarcillin has been used in animals for treatment of various infections, including pneumonia, soft tissue infections, and bone infections. Ticarcillin has similar activity as ampicillin, but it is extended to include many organisms that otherwise are resistant to ampicillin, such as *Pseudomonas aeruginosa* and other gram-negative bacilli. Its activity is enhanced when administered with an aminoglycoside. Use in animals has been primarily derived from empirical use and derived from pharmacokinetic-pharmacodynamic information. It is administered IV in most animals; intramuscular administration can be painful. Ticarcillin also has been infused in the uterus of horses to treat metritis.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are uncommon. However, allergic reactions are possible. High doses can produce seizures and decreased platelet function.

Contraindications and Precautions

Administer cautiously, if at all, to animals with penicillin allergies.

Drug Interactions

Do not combine in same syringe or in vial with aminoglycosides.

Instructions for Use

Ticarcillin may be combined with clavulanic acid (see ticarcillin–clavulanate section for more details). Ticarcillin is synergistic with, and often combined with, aminoglycosides (e.g., amikacin and gentamicin). Lidocaine (1%) may be used for reconstitution to decrease pain from intramuscular injection (see Formulations section).

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is ≤ 64 mcg/mL for *Pseudomonas* and ≤ 16 mcg/mL for gram-negative enteric organisms.

Formulations

Ticarcillin is available in 3-g vials. Mix 3-g vial with 6 mL sterile water, sodium chloride, or 1% lidocaine hydrochloride solution (without epinephrine) to produce a final concentration of 384.6 mg/mL. Ticarcillin–clavulanate is also available (see next section for more information).

Stability and Storage

Store powder for injection in original vial, protected from light, and at room temperature. Use reconstituted solution immediately. If diluted for IV administration with sodium chloride or 5% dextrose, it may be stable for up to 72 hours at room temperature or 14 days if refrigerated. IV solution prepared in lactated Ringer's solution is stable for up to 48 hours at room temperature or 14 days if refrigerated. If diluted IV solutions are frozen, they are stable for up to 30 days but should be used within 24 hours once thawed. Do not refreeze thawed solutions.

Small Animal Dosage

Dogs and Cats

- 33-50 mg/kg q4-6h IV or IM.

Large Animal Dosage

Horses

- 44 mg/kg q6-8h IV or IM.
- Ticarcillin also has been used in horses as an intrauterine infusion at a dose of 12.4 mg/kg diluted in 60-100 mL saline.

Regulatory Information

Withdrawal times are not established. However, excretion is similar to other beta-lactam antibiotics, such as ampicillin. Follow ampicillin guidelines for withdrawal times.

Ticarcillin + Clavulanate Potassium

tye-kar-sill'in + klav'yoo-lan'ate

Trade and Other Names: Timentin

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Action and spectrum are the same as ticarcillin, except clavulanic acid has been added to inhibit bacterial beta-lactamase and increase spectrum of activity. However, clavulanate does not increase activity against *Pseudomonas* compared to ticarcillin alone.

Indications and Clinical Uses

Ticarcillin + clavulanate has been used in animals for treatment of various infections, including pneumonia, soft tissue infections, and bone infections. Ticarcillin has similar activity as ampicillin but is extended to include many organisms that otherwise are resistant to ampicillin, such as *Pseudomonas aeruginosa* and other gram-negative bacilli. When combined with clavulanate, the activity against some strains of gram-negative bacteria and *Staphylococcus* is improved. However, methicillin-resistant staphylococci are resistant to ticarcillin. Its activity against *Pseudomonas aeruginosa* may be enhanced when administered with an aminoglycoside. Use in animals has been primarily derived from empirical use and pharmacokinetic–pharmacodynamic information. It is administered IV in most animals; intramuscular administration can be painful.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are uncommon. However, allergic reactions are possible. High doses can produce seizures and decreased platelet function.

Contraindications and Precautions

Administer cautiously, if at all, to animals with penicillin allergies.

Drug Interactions

Do not combine in same syringe or in vial with aminoglycosides.

Instructions for Use

Ticarcillin is synergistic with, and often combined with, aminoglycosides (e.g., amikacin and gentamicin). Lidocaine (1%) may be used for reconstitution to decrease pain from intramuscular injection.

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is $\leq 64/2$ mcg/mL for *Pseudomonas* and $\leq 16/2$ mcg/mL for gram-negative bacilli. (The “/” distinguishes the ticarcillin from the clavulanate concentrations.)

Formulations Available

Ticarcillin + clavulanate is available in 3-g/vial injections. Each 3-g vial contains ticarcillin (as disodium) and 0.1 g clavulanic acid (as potassium). It also contains 4.75 mEq sodium and 0.15 mEq potassium per gram.

Stability and Storage

Store in original vial and at room temperature. The reconstituted solution is stable for up to 6 hours at room temperature or 72 hours if refrigerated. The IV diluted solution (10 to 100 mg/mL) prepared with lactated Ringer's or sodium chloride is stable for up to 24 hours at room temperature, up to 4 days if refrigerated, or 30 days if frozen. The intravenous solution diluted to 10 to 100 mg/mL with 5% dextrose may be stored for up to 24 hours at room temperature, up to 3 days if refrigerated, or 7 days if frozen. When using frozen solutions, thaw at room temperature or in refrigerator, but do not speed thawing by using immersion in water baths or by microwave. The thawed solution is stable for 24 hours at room temperature or 7 days if refrigerated. Do not refreeze thawed solutions.

Small Animal Dosage

Dogs and Cats

- Dose according to rate for ticarcillin: 33-50 mg/kg q4-6h IV or IM.

Large Animal Dosage

Horses

- 44 mg/kg q6-8h IV or IM (of the ticarcillin component).
- Ticarcillin-clavulanate also has been used in horses as an intrauterine infusion at a dose of 12.4 mg/kg ticarcillin and 0.4 mg/kg clavulanate diluted in 60-100 mL saline.

Regulatory Information

Withdrawal times are not established. However, excretion is similar to other beta-lactam antibiotics, such as ampicillin. Follow ampicillin guidelines for withdrawal times.

Tiletamine + Zolazepam

till-eh'tah-meen + zole-az'eh-pam

Trade and Other Names: Telezol and Zoletil

Functional Classification: Anesthetic

Pharmacology and Mechanism of Action

Anesthetic. It is a combination of tiletamine (dissociative anesthetic agent similar in action to ketamine) and zolazepam (benzodiazepine similar in action as diazepam). Tiletamine + zolazepam produces a short duration (30 minutes) of anesthesia. In cats, the effect of the zolazepam will have a longer duration than tiletamine. In dogs, the tiletamine will have a longer duration than the zolazepam. Therefore, anesthesia appears to be smoother in cats than in dogs.

Indications and Clinical Uses

Tiletamine + zolazepam is used for short-term anesthesia in animals. For longer procedures, other drugs should be used.

Precautionary Information

Adverse Reactions and Side Effects

Tiletamine + zolazepam has a wide margin of safety, which is greater in cats than dogs. Side effects include excessive salivation (may be antagonized with atropine), erratic recovery, and muscle twitching. Drying of the cornea may occur unless ophthalmic ointment is applied to the eyes. Adverse reactions have been observed when administered to ferrets.

Contraindications and Precautions

Low doses do not provide sufficient anesthesia for surgery. Do not use in patients with pancreatic disease.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Administer by deep intramuscular injection.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during anesthesia. Monitor body temperature because of risk of hypothermia.

Formulations

Tiletamine + zolazepam is available in 50 mg of each component per milliliter (100 mg total).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- Initial IM dose is 6.6-10 mg/kg for minor procedures.
- Short-term anesthesia: 10-13 mg/kg IM.

Cats

- 10-12 mg/kg IM for minor procedures and higher doses of 14-16 mg/kg IM for surgery.

Doses are based on combined milligrams of each component.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).
Schedule III controlled drug

Tilmicosin Phosphate

til-mye'koe-sin foss'fate

Trade and Other Names: Micotil and Pulmotil tilmicosin premix

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Macrolide antibiotic. It inhibits bacteria by binding to 50S ribosome and inhibiting protein synthesis. The spectrum of activity is limited primarily to gram-positive aerobic bacteria; *Mycoplasma*; and respiratory pathogens such as *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni* (formerly *Haemophilus somnus*). Tilmicosin administered to calves (15 mg/kg SQ) reduced expression of prostaglandin (PGE₂) stimulated by bacteria. There also may be some anti-inflammatory effects such as reduced leukocyte release of inflammatory mediators in the lungs associated with tilmicosin treatment. There also may be reduced prostaglandin synthesis with tilmicosin administration in alveolar macrophages.

Indications and Clinical Uses

Tilmicosin activity against respiratory pathogens is effective for treating bovine respiratory disease (BRD). In cattle, one injection has duration of at least 72 hours, based on high concentrations achieved in lung. Tilmicosin also has been used as a prophylactic treatment for calves that are entering feedlots. The use of tilmicosin at the time of feedlot arrival has reduced incidence of respiratory disease in cattle. Tilmicosin (Pulmotil) is used in medicated feed for swine for control of swine respiratory disease (SRD).

Precautionary Information

Adverse Reactions and Side Effects

Tilmicosin may be cardiotoxic in some animals. Injections to pigs have been fatal because of cardiotoxicity. The cardiac effects are increased heart rate and decreased contractility. However, administration of tilmicosin premix in feed of pigs has been safe. In dogs, tilmicosin injections have caused cardiac toxicosis and may be caused by calcium-channel blockade; it was reversed by administration of calcium. In goats, injections >10 mg/kg IM or SQ can cause toxicity. In horses, injections of tilmicosin IM or SQ >10 mg/kg can lead to toxicity. Do not administer IV to any species. Treatment of accidental injection in people must be prompt to avoid fatal reactions. Treatment consists of beta-adrenergic agonists (e.g., dobutamine) and supportive care.

Contraindications and Precautions

Tilmicosin reaches high concentrations in milk for up to 42 days. Do not administer to lactating dairy cattle. Do not administer to goats. Do not administer to any animals IV or death can result. People handling tilmicosin

should take precautions to prevent accidental injection. Fatal cardiac reactions caused by injections have been reported in people. Accidental injection in people requires immediate treatment.

Drug Interactions

The cardiac adverse effects are exacerbated by administration of beta blockers such as propranolol. Dobutamine and administration of calcium may offset cardiac effects.

Instructions for Use

Administer SQ. If a person handling the drug is accidentally injected, consult a physician immediately. Severe cardiac toxicity has occurred in some species of animals.

Patient Monitoring and Laboratory Tests

Susceptibility information: CLSI breakpoint for susceptible organisms is less than or equal to 8 mcg/mL for bovine respiratory pathogens, and less than or equal to 16 mcg/mL for swine respiratory disease pathogens. Use of break points for other macrolides may identify organisms sensitive or resistant to tilmicosin.

Formulations

Tilmicosin is available in 300-mg/mL injection (Micotil) and 200 g/kg (90.7 g/lb) of premix (Pulmotil).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

It is not recommended for small animals.

Large Animal Dosage

Cattle

- 10 mg/kg SQ single dose. Avoid intravenous or intramuscular administration.

Sheep

- 10 mg/kg SQ single dose.

Goats

Do not use.

Horses

Do not use. Safety not established.

Pigs

- Pneumonia: 181-383 g/ton of feed. Feed only this ration for 21 days, beginning at the time of disease outbreak.

Regulatory Information

Cattle withdrawal time (meat): 28 days. No withdrawal time established for milk; if injected intrammary to lactating cows, discard milk for a minimum of 82 days.

Pig withdrawal time (meat): 7 days.

Sheep withdrawal time (meat): 28 days.

Tiludronate Disodium

Til-u-droe'na-te dye-soe'dee-um

Trade and Other Names: Tildren (veterinary form), Skelid (human form)

Functional Classification: Antihypercalcemic

Pharmacology and Mechanism of Action

Bisphosphonate drug. Drugs in this class also include pamidronate, etidronate, and pyrophosphate. These drugs are characterized by a germinal bisphosphonate bond. Their clinical use resides in their ability to inhibit bone resorption. These drugs decrease bone turnover by inhibiting osteoclast activity, inducing osteoclast apoptosis, retarding bone resorption, and decreasing the rate of osteoporosis. Inhibition of bone resorption is via inhibition of the mevalonate pathway.

Bisphosphonates are classified as nitrogen-containing and non-nitrogenous based on the structure, with the nitrogen-containing drugs being more potent. Tiludronate is a non-nitrogenase compound. Tiludronate also may have some anti-inflammatory properties. Tiludronate has a plasma half-life in horses of 3-7 hours, but bone levels may be retained for months.

Indications and Clinical Uses

Tiludronate is licensed in countries in Europe but not in the United States. Other bisphosphonate drugs are used in people to treat osteoporosis and treatment of hypercalcemia of malignancy. In horses, tiludronate is used to treat palmar foot pain caused by navicular disease. It also is used to treat distal tarsal osteoarthritis (bone spavin). Like other drugs in this class, it is helpful for managing complications associated with pathologic bone resorption. It also may provide pain relief in patients with pathologic bone disease.

Efficacy studies conducted in horses have shown that at a dose of 0.1 mg/kg for 10 days (1.0 mg total dose), it was effective for treatment of navicular disease and distal tarsal osteoarthritis. Beneficial effects for treating chronic lameness are less certain.

Precautionary Information

Adverse Reactions and Side Effects

Reaction to tiludronate has only been reported for horses. After intravenous infusion, an increase in heart rate and transient hypocalcemia have been observed. Neither effect is considered significant. In people, there is some concern that it may result in excessive mineralization and hardening of the bone, which may result in a greater risk of fractures. However, this effect has not been reported for animals. No adverse effects on bone mineral density have been reported. In people, gastrointestinal problems are a concern with bisphosphonates; therefore, colic is a concern with treatment in horses but has not been reported as a significant problem.

Contraindications and Precautions

No contraindications have been identified in animals.

Drug Interactions

Do not mix with solutions containing calcium (e.g., lactated Ringer's solution).

Precautionary Information

Drug Interactions

If antacids are used concurrently, magnesium hydroxide and calcium carbonate may reduce effectiveness.

Instructions for Use

For intravenous infusion, dilute in solvent and infuse intravenously.

Patient Monitoring and Laboratory Tests

Monitor serum calcium and phosphorus. Monitor urea nitrogen, creatinine, urine-specific gravity, and food intake in treated animals.

Formulations

Tiludronate is available in 50-mg vials for injection to be reconstituted with 10 mL of solvent.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- No doses have been established for dogs or cats.

Large Animal Dosage

Horses

- 1 mg/kg administered as 0.1 mg/kg per day for 10 days intravenously. In Europe, it is administered as single 1 mg/kg infusion for one dose.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Tinidazole

tih-nih'dah-zole

Trade and Other Names: Tindamax

Functional Classification: Antiprotozoal

T

Pharmacology and Mechanism of Action

Antiprotozoal with action similar to metronidazole. It is a second-generation nitroimidazole in which the activity involves generation of free nitroradicals via metabolism that occurs within protozoa. It has action against *Trichomonas*, *Giardia*, and intestinal protozoal parasites. It also has in vitro activity against anaerobic bacteria and *Helicobacter*. Half-life is approximately 5.5 hours in horses, 8.5 hours in cats, and 4.5 hours in dogs. Oral absorption in dogs, cats, and horses is approximately 100%.

Indications and Clinical Uses

Tinidazole is indicated to treat diarrhea and other intestinal problems caused by intestinal protozoa such as *Giardia*, *Trichomonas*, and *Entamoeba*. Tinidazole also is active against many anaerobic bacteria and may be used as a substitute for

metronidazole in small animals and horses for treatment of a variety of anaerobic infections.

Precautionary Information

Adverse Reactions and Side Effects

Tinidazole has similar action as metronidazole. With high doses it can cause neurological problems, including ataxia, tremors, nystagmus, and seizures. The CNS signs are related to inhibition of action of GABA and are responsive to benzodiazepines (diazepam). Like other nitroimidazoles, it has the potential to produce mutagenic changes in cells, but this has not been demonstrated in vivo. Like other nitroimidazoles, it has a bitter taste and can cause vomiting and anorexia. However, the bitter taste is not as bad as that of metronidazole.

Contraindications and Precautions

Do not administer to animals that may be prone to seizures. Do not administer to animals already known to be sensitive to metronidazole. Do not administer to pregnant animals.

Drug Interactions

Like other nitroimidazoles, it can potentiate the effects of warfarin and cyclosporine via inhibition of drug metabolism.

Instructions for Use

Give oral dose with food to minimize the unpleasant taste and decrease nausea.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. Most anaerobic bacteria have minimum inhibitory concentration (MIC) values below 2 mcg/mL.

Formulations

Tinidazole is available in 250- and 500-mg tablets.

Stability and Storage

Tablets have been crushed and mixed with flavorings to improve palatability. These suspensions are stable for 7 days.

Small Animal Dosage

Dogs

- 15 mg/kg q12h PO.

Cats

- 15 mg/kg q24h PO. Duration of therapy will depend on whether one is treating *Giardia* (5 days) or other anaerobic infections (longer than 5 days).

Large Animal Dosage

Horses

- 10-15 mg/kg q12h PO.

Regulatory Information

Do not administer to animals that produce food. Administration of nitroimidazoles to animals intended for food is prohibited.

Tobramycin Sulfate

toe-brah-mye'sin sul'fate

Trade and Other Names: Nebcin

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Aminoglycoside antibacterial drug. Like other aminoglycosides, tobramycin is bactericidal. It binds to the 30S ribosomal subunit in bacteria to inhibit protein synthesis and lead to cell death. It is concentration dependent in its antibacterial action. It has a similar spectrum to amikacin and gentamicin, although it is more active than gentamicin against gram-negative bacteria. Generally, if an organism is sensitive to tobramycin it will also be sensitive to amikacin. Tobramycin pharmacokinetics in animals indicates that it has similar clearance and distribution as other aminoglycosides.

Indications and Clinical Uses

Tobramycin, like other aminoglycosides, is used to treat serious systemic infections caused by gram-negative bacteria. It is often administered simultaneously with beta-lactam antibiotics to produce a synergistic effect. The infections treated include pneumonia, soft tissue infections, and sepsis. Like many off-label antibiotics in animals, the use in animals has been primarily derived from empirical use and from pharmacokinetic–pharmacodynamic information. Tobramycin has also been used topically. Tobramycin has been used in nebulizing solutions for respiratory infections.

Precautionary Information

Adverse Reactions and Side Effects

Nephrotoxicity is the most dose-limiting toxicity. Ensure that patients have adequate fluid and electrolyte balance during therapy. Ototoxicity and vestibulotoxicity also are possible.

Contraindications and Precautions

When used with anesthetic agents, neuromuscular blockade is possible. Do not mix in a vial or syringe with other antibiotics.

Drug Interactions

Avoid mixing in vials with other drugs. It is incompatible with other antibiotics and inactivation occurs rapidly.

Instructions for Use

Inject IV or IM. Synergistic effects with beta-lactam antibiotics have been demonstrated in vitro, but it is not known if this translates to a clinical effect. For nebulization treatment of respiratory infections, administer 160 mg of tobramycin (total dose) twice daily for 28 days. The solution used for nebulization (in individual packets with no preservatives) is called TOBI, but it is more expensive than injectable formulations. Tobramycin injectable has been used instead, but it contains preservatives that could induce bronchospasm. Use diluted tobramycin with 3 mL of saline and administer albuterol before nebulization to decrease bronchospasm.

Patient Monitoring and Laboratory Tests

Susceptibility testing: The CLSI minimum inhibitory concentration (MIC) value break point for susceptibility is ≤ 4 mcg/mL. Monitor BUN, creatinine, and urine for evidence of renal toxicity. Blood levels can be monitored to detect problems with systemic clearance. When monitoring trough levels in a patient dosed once daily, the trough levels should be below the limit of detection. Alternatively measure half-life from samples taken at 1 hour and 2 to 4 hours post-dosing. Clearance should be above 1.0 mL/kg/min and half-life should be less than 2 hours.

Formulations

Tobramycin is available in 40-mg/mL injections.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Store powder at room temperature. Reconstituted solutions are stable for 24 hours at room temperature and 96 hours refrigerated. Do not use discolored solutions. Tobramycin sulfate diluted in fluids can be frozen and stable for 30 days. Ophthalmic solutions have been compounded and shown to be stable for 90 days. Do not mix in a vial or syringe with other antibiotics, especially beta-lactam agents (penicillins and cephalosporins) because inactivation may occur.

Small Animal Dosage**Dogs**

- 9-14 mg/kg q24h SQ, IM, or IV.

Cats

- 5-8 mg/kg q24h SQ, IM, or IV.

Nebulization therapy is sometimes used in small animals. (See Instructions for Use section for details on nebulization therapy.)

Large Animal Dosage**Horses**

- 6.6 mg/kg q24h IV or IM.

Regulatory Information

Do not administer to animals intended for food or animals that produce food. Other drugs in this class require extralabel withdrawal times of 18 months.

Tocainide Hydrochloride

toe-kay'nide hye-droe-klor'ide

Trade and Other Names: Tonocard

Functional Classification: Antiarrhythmic

Pharmacology and Mechanism of Action

Antiarrhythmic drug. Tocainide is a Class Ib antiarrhythmic. Like other Class I drugs, such as lidocaine, it blocks sodium channels in cardiac tissues and inhibits Phase 0 depolarization to suppress spontaneous depolarization.

Indications and Clinical Uses

Tocainide is an oral substitute used for treatment and control of ventricular arrhythmias. The use in veterinary medicine has been uncommon. Use in animals has been primarily derived from empirical use and experience in humans.

There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

In dogs, anorexia and GI toxicity have been reported. Arrhythmias, vomiting, and ataxia also are possible. (In one study, 35% of dogs showed GI effects.)

Contraindications and Precautions

Use cautiously in animals that are also receiving beta blockers. Do not use in patients with heart block.

Drug Interactions

No drug interactions have been reported for animals.

Instructions for Use

Tocainide has limited experience in animals. However, clinical studies demonstrate efficacy.

Patient Monitoring and Laboratory Tests

Therapeutic concentrations are 6-10 mcg/mL.

Formulations

Tocainide is available in 400- and 600-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 15-20 mg/kg q8h PO.

Cats

No dose has been established.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Toceranib phosphate

toe-cer-a-nib

Trade and Other Names: Palladia

Functional Classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. For treatment of Grade II or III cutaneous mast cell tumors in dogs. Toceranib (Palladia) is a receptor tyrosine kinase (RTK) inhibitor that kills tumor cells and decreases the blood supply to the tumor. The antiangiogenic properties occur via inhibition of RTK activity (otherwise known as vascular

766 Toceranib phosphate

endothelial growth factor [VEGF]). The effect of toceranib is to produce antiangiogenic and antiproliferative properties that limit growth of the tumor. After administration toceranib is widely distributed ($VD >20$ L/kg) and has a half-life of approximately 16-17 hours. It has good oral absorption (77%) and high protein binding (91%-93%). Feeding does not affect oral absorption. High concentrations appear in the bile, liver, and feces and indicate that it is primarily eliminated by metabolism and there is little drug excreted in the urine (renal clearance is approximately 7%). A similar drug that has been used for the same indication in dogs in Europe is masitinib (Masivet) at a dose of 12.5 mg/kg once daily orally.

Indications and Clinical Uses

Toceranib is an approved anticancer agent for dogs. The use has been established in clinical studies for Grade II or III cutaneous mast cell tumors. Many dogs are also treated with corticosteroids (prednisolone). Although it is approved for mast cell tumors in dogs, some clinicians have used it to treat adenocarcinoma, melanoma, and carcinoma; however, efficacy for these indications has not yet been established. There are no reports available to document efficacy or safety in cats.

Precautionary Information

Adverse Reactions and Side Effects

Dogs with mast cell tumors often have gastrointestinal problems associated with the tumor and treatment. Therefore, many dogs are treated simultaneously with antihistamines and drugs to suppress stomach acid (e.g., H_2 blockers or proton pump inhibitors). The most common adverse effects are diarrhea, loss of appetite, lameness, weight loss, and blood in the feces. It should not be administered during pregnancy.

Contraindications and Precautions

Daily dosing should not be administered because of frequency of adverse events. People handling the drug, especially pregnant women, should receive proper instructions about the drug's adverse effects.

Drug Interactions

No drug interactions have been reported for animals. Metabolism is primarily via flavin mono-oxygenase (FMO), which is not typically involved in drug-drug interactions. It is not known if toceranib may be responsible for drug-drug interactions that involve the cytochrome P450 system.

Instructions for Use

Toceranib is approved for cutaneous mast cell tumor in dogs. There is clinical use for other tumors, but efficacy has not yet been established for other uses.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. If assays are available, the targeted plasma drug concentration is 40 ng/mL or greater for 48 hours.

Formulations

Toceranib is available in 10-, 15-, and 50-mg tablets, which are film coated and should not be split.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Toceranib is only soluble at low pH values ($pH <3$). If mixed in solutions, it will precipitate at higher pH values.

Small Animal Dosage

Dogs

- 3.25 mg/kg, PO, every other day. Some clinicians lower the dose to 2.5 mg/kg on a schedule of 3 days per week (M,W,F). The minimum effective dose is 2.2 mg/kg every other day. If adverse reactions occur, discontinue the drug (for up to 2 weeks) and reinstate treatment at a lower dose.

Cats

No dose established.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to food-producing animals.

Toltrazuril

tole-traz'yoo'ril

Trade and Other Names: Baycox

Functional Classification: Antiprotozoal

Pharmacology and Mechanism of Action

Antiprotozoal drug. Coccidiostat. Toltrazuril is a triazinone effective for *Isospora* and coccidiosis, *Toxoplasma gondii*, and *Eimeria* spp. Toltrazuril is a derivative of another drug, ponazuril, that is also used for the same conditions. Toltrazuril sulfone (ponazuril) is found in serum and cerebral spinal fluid (CSF) of treated horses. See section on ponazuril for more details.

Indications and Clinical Uses

Toltrazuril has been used as a treatment of equine protozoal myeloencephalitis (EPM) caused by *Sarcocystis neurona*. However, it is recommended to use an approved drug, ponazuril (Marquis), for treatment of horses.

Precautionary Information

Adverse Reactions and Side Effects

Administration of 50 mg/kg to horses (5 and 10 times the recommended dose) produced minor adverse effects, according to the manufacturer. There were minimal changes in the serum analysis.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Although toltrazuril has been used in horses, the approved drug ponazuril is preferred for use.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Toltrazuril is not currently available in commercial formulations in the US for horses. It is available in suspension for poultry and livestock in other countries and has been imported to the US after permission from the FDA.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

None have been reported for small animals.

Large Animal Dosage

Horses

- EPM caused by *S. neurona*: 5-10 mg/kg (7.5 mg/kg for most horses) q24h PO for a minimum of 30 days.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Tramadol Hydrochloride

tram'ah-dole

Trade and Other Names: Ultram, and generic brands. Outside the US, Tramadon and Altadol

Functional Classification: Analgesic

Pharmacology and Mechanism of Action

Analgesic. Tramadol is a racemic mixture (R & S) that has a complicated mechanism of action. It has some mu-opioid receptor action, but this effect is 10 times lower than codeine and 6000 times lower than morphine. Tramadol also inhibits the reuptake of norepinephrine (NE) and serotonin (5 HT) and produces secondary effects on alpha-2 adrenergic receptors in pain pathways. One isomer has greater effect on 5 HT reuptake and greater affinity for mu-opiate receptors. The other isomer is more potent for NE reuptake and less active for inhibiting 5 HT reuptake. Taken together, the effects of tramadol may be explained through inhibition of 5 HT reuptake, action on alpha₂ receptors, and mild activity on opiate mu-receptors. Tramadol has as many as 11 metabolites. One metabolite (o-desmethyl tramadol, also called M1) may have greater opiate effects than the parent drug (for example, 200-300 times greater opiate effect than tramadol) but still lower than morphine. In animals that produce this metabolite in sufficient amounts, some analgesic action may be attributed to opiate-mediated effects from the active metabolite. The other metabolites have not been shown to have active analgesic activity. The pharmacokinetics of tramadol and metabolites have been studied extensively in dogs, horses, and cats. The pharmacokinetics are inconsistent with variation in clearance, oral absorption, and metabolism to the active metabolite varying among studies within and between species. Some studies have shown that the active metabolite (M1) in dogs is a minor metabolite (10%-16% of tramadol concentrations), but in other studies the levels of this metabolite were either too low to quantify or

nonexistent and may not contribute significantly to the analgesic effects. Tramadol half-life in dogs is approximately 1.0-2.7 hours with variable oral absorption, but oral absorption may be as high as 65%. In cats the half-life is 3-4 hours and they produce higher and more sustained concentrations of the active metabolite (M1) than other animals—presumably because of differences in enzyme activity. Active metabolite concentration in cats parallels the concentrations of tramadol. Horses produce only low or undetectable levels of the active metabolite. In horses the oral absorption has been extremely variable, ranging from 3% to 64%, but in most studies it has been low. In most studies the half-life in horses is approximately 1.5-2.5 hours. A drug with similar structure and activity as tramadol is tapentadol (Nucynta). Tapentadol is used for moderate pain in people (50-200 mg q4-6h), but its use has not been reported in animals.

Indications and Clinical Uses

Tramadol has been used as an analgesic in people, dogs, cats, horses, and minor species (e.g., rabbits, goats). It is an alternative to pure opiate analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs) in patients that require treatment for mild to moderate pain. In people it is regarded as a mild analgesic, but the pharmacokinetics of tramadol is different in people compared to animals. Clinical effects in humans cannot necessarily be extrapolated to animals. In animals studies—both clinical and experimental—the results have been inconsistent to demonstrate its effectiveness as an analgesic. However, studies have varied in the dose, route, and pain stimulus evaluated. There has been some evidence of analgesia after administration for treating pain associated with elective surgery, but there is a lack of evidence when experimental models of pain have been used. Some studies that have demonstrated efficacy have used injectable formulations (at 2-4 mg/kg), rather than oral forms. It may be more effective when used with an NSAID, or other analgesics such as ketamine or alpha-2 agonists. Tramadol has also been administered by the epidural route (diluted in saline) in horses, dogs, and cats (1-2 mg/kg). Although some analgesic was documented in these studies, the effects and pharmacokinetics were similar to other parenteral routes of administration, and it is assumed that tramadol is rapidly distributed systemically after epidural administration.

Precautionary Information

Adverse Reactions and Side Effects

In cats, some vomiting, behavior changes, excitement, and mydriasis may be observed, which is dose related. Both euphoria and dysphoria have been observed in cats. In horses, there may be short-term (approximately 20-40 minutes) agitation, head nodding, decreased gut sounds, trembling, muscle fasciculations, tachycardia, sweating, and ataxia. The effects in horses are most prominent after a rapid IV injection and minimized if the injection is administered slowly over 10 minutes. In dogs, adverse effects have been rare. Some sedation has been observed, which is dose related. There have been minimal cardiovascular or gastrointestinal problems in dogs. At very high doses in dogs, seizures may occur. If adverse effects occur, they are only partially antagonized by naloxone.

Contraindications and Precautions

Use cautiously with other drugs that have CNS-depressing effects, such as opiates, alpha₂-agonists, or serotonin uptake inhibitors (e.g., antidepressants and behavior-modifying drugs). Tramadol may potentiate their actions. Metabolites

may be eliminated via the urine. Use with caution in animals with renal disease or seizure disorders.

Drug Interactions

No drug interactions have been reported in animals. However, because of multiple effects from tramadol (serotonin reuptake inhibition, adrenergic effects, and opiate effects), interactions are possible with other drugs that act via similar mechanisms. Serotonin syndrome is theoretically possible when used with other serotonin reuptake inhibitors, but such interactions have not been reported in animals. It has been used safely with NSAIDs. It has been administered with inhalant anesthetics without any signs of adverse drug interaction.

Instructions for Use

Dosing information is based on experimental studies in dogs, cats, and horses and some clinical studies. In most animals the oral immediate-release tablets are administered, either whole or crushed and mixed with a vehicle. In some countries an injectable formulation is available that has been injected IV, IM, SQ, and epidurally. Tramadol extended-release (ER) tablets have been used in people, but in dogs these tablets show delayed absorption and plasma levels five times less than people at equivalent (mg/kg) doses. Therefore, ER tablets for people may be inequitable in dogs and cats.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. Tramadol is not routinely measured, but effective concentrations have been reported to be in the range of 200-400 ng/mL for tramadol and 20-40 ng/mL for the active metabolite(M1).

Formulations

Tramadol immediate-release tablets are available in 50-mg tablets. Tramadol extended-release (ER) is available in 100-, 200-, or 300-mg tablets. In the US, injectable formulations are not available. However, in Europe and other countries, an injectable formulation is available as a 50-mg/mL injection that can be diluted further in 0.9% saline solution for intravenous administration. Compounded formulations of tramadol have been prepared in sterile water at a concentration of 10 mg/mL. This solution is stable up to 1 year if stored in the refrigerator protected from light.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Tramadol is water soluble. When mixed with aqueous vehicles, it has maintained potency and been stable for weeks. However, stability of compounded formulations that may contain flavorings and other excipients has not been evaluated.

Small Animal Dosage

Dogs

- 5 mg/kg q6h to q8h PO. If an injectable form is available, 4 mg/kg IV, q6-8h.

Cats

- Starting at 2 mg/kg and increasing up to 4 mg/kg q8-12h PO. When injectable forms have been available, it also has been injected at a dose of 2 mg/kg IV and 2-4 mg/kg SQ, q8h.

Large Animal Dosage

Horses

- 2 mg/kg IV (slowly) and 4-5 mg/kg PO. In horses the optimum dosing interval is not known, but because of the short half-life, every 6 hours may be appropriate. Do not exceed 2 mg/kg IV or 5 mg/kg oral in horses.

Regulatory Information

No regulatory information is available. The half-life in most animals is short, and extended withdrawal times may not be necessary in food-producing animals. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Trandolapril

tran-doe'lah-pril

Trade and Other Names: Mavik

Functional Classification: Vasodilator, angiotensin-converting enzyme (ACE) inhibitor

Pharmacology and Mechanism of Action

Like other ACE inhibitors, it inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and will stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. The ability of aldosterone to cause sodium and water retention contributes to congestion. Trandolapril, like other ACE inhibitors, will cause vasodilation and decrease aldosterone-induced congestion, but ACE inhibitors also contribute to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins. Trandolapril is converted to active trandolaprilat after administration.

Indications and Clinical Uses

Trandolapril, like other ACE inhibitors, is used for treatment of hypertension and for management of CHF. Compared to other ACE inhibitors, such as enalapril, it is not used commonly in veterinary medicine and the use has been derived from anecdotal experiences.

Precautionary Information

Adverse Reactions and Side Effects

Trandolapril may cause azotemia in some patients; carefully monitor patients receiving high doses of diuretics.

Contraindications and Precautions

Use cautiously with other hypotensive drugs and diuretics. Nonsteroidal anti-inflammatory drugs (NSAIDs) may decrease vasodilating effects. Discontinue ACE inhibitors in pregnant animals; they cross the placenta and have caused fetal malformations and death of the fetus.

Drug Interactions

Use cautiously with other hypotensive drugs and diuretics. NSAIDs may decrease vasodilating effects.

Instructions for Use

It has not been used extensively in veterinary patients. Most of the experience has been extrapolated from uses in people.

Patient Monitoring and Laboratory Tests

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

Formulations Available

Trandolapril is available in 1-, 2-, and 4-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

The dose has not been established for dogs. The dose in people is 1 mg/person/day to start, then increase to 2-4 mg/day.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Trazodone Hydrochloride

Traz'-oh-done

Trade and Other Names: Desyrel and generic

Functional Classification: Antianxiety agent, behavioral modification

Pharmacology and Mechanism of Action

Trazodone is an antianxiety agent. It is a triazolopyridine derivative and belongs to the phenylperazine group of centrally acting drugs. It acts both as a serotonin 2A (5-HT_{2A}) receptor antagonist and a serotonin reuptake inhibitor (SSRI), with little effect on dopamine. It also has nonspecific sedating properties and is used as a sedative and hypnotic. It has an active metabolite that also may have effects on the serotonin-1 receptor. The action as an antidepressant and antianxiety agent appears to be distinct from tricyclic antidepressants and SSRIs. It is highly metabolized in people, but the metabolism and pharmacokinetics are not well understood in animals. The half-life is 6-9 hours in people, but it has not been established for dogs.

Indications and Clinical Uses

Trazodone has been used in dogs for events that trigger anxiety such as visits to the veterinarian, thunderstorms, noise phobias, travel in a car, and other phobias and generalized anxiety events. Although trazodone has been helpful to relieve anxiety in these situations, it has a delayed onset of activity, and can be unpredictable. To optimize the effects, it should be administered approximately 1 hour prior to an anticipated anxiety-inducing event.

Precautionary Information

Adverse Reactions and Side Effects

Although use has been limited, trazodone has been used in dogs without reports of serious adverse effects. It may have fewer anticholinergic effects than tricyclic antidepressants. It has not produced adverse cardiac effects or seizure activity.

Contraindications and Precautions

Because of the effect of trazodone on serotonin metabolism, reuptake, and receptors, its use with other drugs that affect serotonin should be done with caution. Serotonin-syndrome effects have not been observed in dogs, but it should be used cautiously with drugs such as SSRIs (fluoxetine, paroxetine), tricyclic antidepressants (clomipramine), tramadol, and monoamine oxidase inhibitors (selegiline).

Drug Interactions

Trazodone is highly metabolized by cytochrome P450 enzymes. Such enzymes can be inhibited or induced by coadministration with other drugs. Although specific drug interactions have not been reported for dogs, there should be caution when administering to animals receiving other drugs known to affect cytochrome P450 enzymes.

Instructions for Use

Start with a low dose (approximately 2 mg/kg) and work up gradually to higher doses, as needed. Compared to other behavior-modifying drugs such as SSRIs and tricyclic antidepressants, trazodone has a more rapid onset of effect. It may be administered 1 hour prior to an anticipated event that elicits anxiety in an animal such as thunderstorms, loud noises, car ride, or visit to the veterinarian. It may be administered with benzodiazepine drugs.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

It is available as 50-, 100-, 150-, and 300-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- Dogs: 2-5 mg/kg, PO, as needed, but generally every 8 to 24 hours; or administer a single dose 1 hour prior to an anticipated event that may trigger anxiety.

Large Animal Dosage

No dose is established for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Triamcinolone Acetonide, Triamcinolone Hexacetonide, Triamcinolone Diacetate

trye-am-sin'oh-lone

Trade and Other Names: Vetalog, Triamtabs, Aristocort, and generic brands

Functional Classification: Corticosteroid

Pharmacology and Mechanism of Action

Glucocorticoid anti-inflammatory drug. Anti-inflammatory effects are complex, but they are primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. There is disagreement on the potency of triamcinolone. Most human references indicate that triamcinolone has potency that is approximately equal to methylprednisolone (about five times cortisol and 1.25 times prednisolone). However, many veterinary dermatologists suggest that potency is higher—6 to 10 times more potent than prednisolone or approximately equal to dexamethasone. Triamcinolone acetonide is often used for local treatment or to produce a sustained concentration. It is an injectable suspension that is slowly absorbed from intramuscular or intralesional injection site.

Indications and Clinical Uses

Triamcinolone, like other corticosteroids, is used to treat inflammatory and immune-mediated diseases in animals. It is used for similar purposes as prednisolone. The long-acting injectable formulation (triamcinolone acetonide) is used for intralesional therapy of tumors and similar purposes as methylprednisolone acetate. Large animal uses include treatment of inflammatory conditions and of recurrent airway obstruction (RAO), formerly called chronic obstructive pulmonary disease (COPD), in horses. Triamcinolone acetonide is also given intra-articularly to horses for treatment of arthritis.

Precautionary Information

Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic-pituitary adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, impaired wound healing, and immunosuppression. When triamcinolone acetonide is used for ocular injections, there is some concern that granulomas may occur at the injection site. In horses, adverse effects include increased risk of laminitis in horses, although evidence for this effect has been controversial.

Contraindications and Precautions

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously in animals with diabetes or renal failure or in pregnant animals.

Drug Interactions

Use cautiously, if at all, with nonsteroidal anti-inflammatory drugs (NSAIDs) because it may potentiate the GI toxicity.

Instructions for Use

Triamcinolone, like other corticosteroids such as prednisolone, is administered in a variety of doses, depending on the severity of the condition being treated. Note that cats may require higher doses than dogs (sometimes twice as high).

Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an adrenocorticotropic hormone (ACTH) stimulation test to monitor adrenal function.

Formulations

Vetalog (veterinary preparation) is available in 0.5- and 1.5-mg tablets. Human preparation of triamcinolone is available in 1-, 2-, 4-, 8-, and 16-mg tablets and a 10-mg/mL injection.

Triamcinolone acetonide is available in 2- and 6-mg/mL suspension injections.

Triamcinolone hexacetonide is available in a 20-mg/mL suspension.

Triamcinolone diacetate is available in a 25-mg/mL suspension.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

- Anti-inflammatory: 0.5-1 mg/kg q12-24h PO, then taper dose to 0.5-1 mg/kg q48h PO. (However, the manufacturer recommends doses of 0.11 to 0.22 mg/kg/day.)
- Dermatologists have used triamcinolone tablets at doses of 0.2-0.6 mg/kg/day for treatment of immune-mediated diseases, with maintenance doses of 0.1-0.2 mg/kg q48h, PO.
- Triamcinolone acetonide: 0.1-0.2 mg/kg IM or SQ; repeat in 7-10 days.
- Intralesional: 1.2-1.8 mg or 1 mg for every centimeter diameter of tumor q2wks.

Large Animal Dosage

Horses

- 0.5-1 mg/kg q12-24h PO.
- Triamcinolone acetonide suspension: 0.022-0.044 mg/kg as a single dose IM.
- RAO: 0.09 mg/kg IM as a single dose.
- Intra-articular: 6-18 mg as a total dose (usually 9-12 mg). Repeat in 4-13 days if necessary.

Cattle

- Induction of parturition: 0.016 mg/kg IM, 1 week before induction of parturition with dexamethasone.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Triamterene

trye-am'ter-een

Trade and Other Names: Dyrenium

Functional Classification: Diuretic

Pharmacology and Mechanism of Action

Potassium-sparing diuretic. Triamterene has similar action to spironolactone, except that spironolactone has a competitive inhibiting effect on aldosterone; triamterene does not.

Indications and Clinical Uses

Triamterene has been used infrequently in veterinary medicine.

For treating congestive diseases, spironolactone is used more frequently. Use of triamterene in animals is derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

Precautionary Information

Adverse Reactions and Side Effects

Triamterene can produce hyperkalemia in some patients.

Contraindications and Precautions

Do not use in dehydrated patients. Nonsteroidal anti-inflammatory drugs (NSAIDs) may interfere with action. Avoid supplements that are high in potassium.

Drug Interactions

No specific drug interactions are reported for animals. However, use cautiously with other drugs that may contain potassium or cause potassium retention. Such drugs include trimethoprim.

Instructions for Use

There is little clinical experience available for triamterene. There is no convincing evidence that triamterene is more effective than spironolactone.

Patient Monitoring and Laboratory Tests

Monitor hydration status, serum potassium levels, and renal function.

Formulations

Triamterene is available in 50- and 100-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

- 1-2 mg/kg q12h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).
 RCI Classification: 4

Trientine Hydrochloride

trye-en'teen hye-droe-klor'ide

Trade and Other Names: Syprine

Functional Classification: Antidote

Pharmacology and Mechanism of Action

Chelating agent. Trientine chelates copper to enhance its clearance in the urine. It may be more potent than penicillamine.

Indications and Clinical Uses

Trientine is used to chelate copper when penicillamine cannot be tolerated in a patient. Use in animals has been primarily derived from empirical use and experience in humans. It may produce fewer gastrointestinal problems compared to penicillamine.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals.

Contraindications and Precautions

Do not administer to pregnant animals; it may be teratogenic.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Trientine is used only in patients that cannot tolerate penicillamine.

Patient Monitoring and Laboratory Tests

Monitor copper levels in treated patients.

Formulations

Trientine is available in 250-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 10-15 mg/kg q12h PO, 1-2 hours before feeding.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Trifluoperazine Hydrochloride

trye-floo-oh-pare'ah-zeen hye-droe-klor'ide

Trade and Other Names: Stelazine

Functional Classification: Antiemetic, phenothiazine

Pharmacology and Mechanism of Action

Phenothiazine. Like other phenothiazines, it is a central-acting dopamine (D₂) antagonist and suppresses dopamine activity in the CNS to produce sedation and prevent vomiting. Other phenothiazines include acepromazine, chlorpromazine, perphenazine, prochlorperazine, promazine, propi-promazine, and triflupromazine.

Indications and Clinical Uses

Trifluoperazine is used for treatment of anxiety, to produce sedation, and as an antiemetic. It is a weaker sedative than some of the other phenothiazines. In people it is used to treat psychotic disorders. Use in animals has been primarily derived from empirical use and experience in humans.

Precautionary Information**Adverse Reactions and Side Effects**

Adverse effects have not been reported in animals but are expected to be similar to other phenothiazines. Phenothiazines can lower the seizure threshold in susceptible animals, although this is controversial for acepromazine. They can also cause sedation as a common side effect and extrapyramidal side effects (involuntary muscle movements) in some individuals.

Contraindications and Precautions

Use cautiously in patients that are hypotensive.

Drug Interactions

No drug interactions have been reported in animals. However, these drugs may be subject to cytochrome P450 drug interactions.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Trifluoperazine is available in a 10-mg/mL oral solution; 1-, 2-, 5-, and 10-mg tablets; and 2-mg/mL injections.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Trifluoperazine is soluble in water and slightly soluble in ethanol. It is oxidized rapidly if exposed to air or light.

Small Animal Dosage

Dogs and Cats

- 0.03 mg/kg q12h IM.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Triflupromazine Hydrochloride

trye-floo-proe'mah-zeen hye-droe-klor'ide

Trade and Other Names: Vesprin and Fluopromazine (former name)

Functional Classification: Antiemetic, phenothiazine

Pharmacology and Mechanism of Action

Phenothiazine. Central-acting dopamine (D₂) antagonist. Triflupromazine suppresses dopamine activity in the CNS to produce sedation and prevent vomiting. Compared to other phenothiazines, triflupromazine may have stronger antimuscarinic activity. Other phenothiazines include acepromazine, chlorpromazine, perphenazine, prochlorperazine, promazine, propiopromazine, and trifluoperazine.

Indications and Clinical Uses

Triflupromazine is used to produce sedation and as an antiemetic. In people it is used to treat psychotic disorders. Use in animals has been primarily derived from empirical use and experience in humans. Little information on animal use is available.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals but are expected to be similar to other phenothiazines. Phenothiazines can lower the seizure threshold in susceptible animals. They can also cause sedation as a common side effect and extrapyramidal side effects (involuntary muscle movements) in some individuals.

Contraindications and Precautions

Use cautiously in patients that are hypotensive.

Drug Interactions

No drug interactions have been reported in animals. However, these drugs may be subject to cytochrome P450 drug interactions.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Triflupromazine is available in 10- and 20-mg/mL injections.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage**Dogs and Cats**

- 0.1-0.3 mg/kg q8-12h IM or PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

Trilostane

trye'loe-stane

Trade and Other Names: Modrenal and Vetoryl

Functional Classification: Adrenal suppressant

Pharmacology and Mechanism of Action

Trilostane inhibits synthesis of cortisol in dogs. It is a competitive inhibitor of 3-beta-hydroxysteroid dehydrogenase, which will interfere with the steps that lead to cortisol secretion from the adrenal cortex. This enzyme is also involved with synthesis of aldosterone, corticosterone, and androstenedione. It also affects conversion of pregnenolone to progesterone. Therefore, these hormones also may be decreased from treatment with trilostane. It is used for pituitary-dependent hyperadrenocorticism (PDH) in dogs. Compared to mitotane, which destroys adrenocortical cells, trilostane produces a transient decrease in cortisol.

Indications and Clinical Uses

Trilostane is used to treat hypercortisolemia (hyperadrenocorticism) in dogs (Cushing's disease). Cortisol concentrations will decrease as early as 7-10 days after initiating treatment with trilostane. It is reported to improve polyuria, polydipsia, and polyphagia in 70%-80% of dogs with PDH. Treatment with mitotane has been compared with trilostane and it has been shown that each drug, although acting through different mechanisms, produces similar survival times in dogs with PDH. Other drugs used to treat canine Cushing's disease include mitotane (Lysodren), selegiline (Anipryl), and ketoconazole—all drugs acting through different mechanisms. Treatment of Alopecia-X in dogs (Pomeranians and poodles) has been effective in most animals (9-12 mg/kg/day PO). Trilostane also has been effective in cats, with no reported adverse effects. In horses, it has been used to treat pituitary pars intermedia dysfunction (equine Cushing's disease), and there is preliminary evidence of some benefit from trilostane at a dose of 1 mg/kg per day, PO.

Precautionary Information

Adverse Reactions and Side Effects

In some dogs, transient lethargy, anorexia, or vomiting is observed. Trilostane decreases aldosterone; therefore electrolyte concentrations should be monitored. Hyponatremia and hyperkalemia are possible and may be observed in some dogs sensitive to the mineralocorticoid inhibition.

Contraindications and Precautions

Trilostane will decrease synthesis of adrenocortical hormones. Use cautiously in animals with low potassium concentrations. Do not use with aldosterone antagonists, such as spironolactone.

Instructions for Use

Adjust dose as needed by monitoring cortisol concentrations. Trilostane is a short-acting drug with a duration of 8-10 hours. Most dogs can be controlled with once-daily treatment, but consider administration twice daily in patients that are not adequately controlled.

Patient Monitoring and Laboratory Tests

Monitor cortisol concentrations in treated animals starting at approximately 10-14 days after starting treatment, then approximately every 3 months. The baseline serum cortisol can be used to monitor effectiveness of trilostane therapy. The ideal target range is 1.27-2.9 mcg/dL (35-80 nmol/L). If further evaluation is needed, use the adrenocorticotrophic hormone (ACTH) stimulation test. Perform testing at peak trilostane concentrations (4-6 hours after trilostane administration). Cortisol concentrations of 1.45-5.4 mcg/dL (40-150 nmol/L) have been considered adequate after ACTH stimulation. If cortisol is too low, consider lowering the dose; if cortisol is too high, consider increasing the dose. Monitor sodium and potassium concentrations in treated dogs. If necessary, supplement with potassium because of aldosterone inhibition.

Formulations

Veterinary formulations approved in the US include capsules of 10, 30, and 60 mg. In Europe capsules of 10, 30, 60, and 120 mg have been available.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 3-6 mg/kg/day PO. Adjust dose based on cortisol measurements.
- Dogs 4.5-10 kg: 30 mg q24h PO.
- Dogs 10-20 kg: 60 mg q24h PO.
- Dogs 20-40 kg: 120 mg, q24h PO.
- Dogs 40-60 kg: 180 mg, q24h PO.
- Dose interval: Twice-daily treatment has been considered in some dogs using a dose of 1.5-3 mg/kg q12h PO.
- Treatment of Alopecia-X: 9-12 mg/kg/day PO.

Cats

- 6 mg/kg q24h PO, and gradually increase (as needed) to 10 mg/kg q24h.

Large Animal Dosage

Horses

- 0.4-1 mg/kg/day PO (added to feed).

Regulatory Information

Trilostane should not be used in animals that produce food.

Trimeprazine Tartrate and Trimeprazine-Prednisolone

trye-mep'rah-zeen tar'trate

Trade and Other Names: Temaril, Panectyl (in Canada), Alimemazine, and Temaril-P (with prednisolone)

Functional Classification: Antiemetic, phenothiazine

Pharmacology and Mechanism of Action

Phenothiazine with antihistamine activity. It has actions similar to other antihistamines, but it also produces sedation similar to other phenothiazines.

Indications and Clinical Uses

Trimeprazine is used alone, or in combination with corticosteroids, for inflammatory and allergic problems. The most common use is for pruritus in dogs in combination with prednisolone (Temaril-P). It also has been used for treating motion sickness and is approved in combination with prednisolone as an antitussive in dogs. The combination Temaril-P with prednisolone also is approved to treat pruritus in animals. Therapeutic effect is attributed to the combined antihistamine and sedative effect of trimeprazine and the anti-inflammatory effect of prednisolone. This combination may be more effective for pruritus than prednisolone alone.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are attributed to the antihistamine and phenothiazine effects. The most common is sedation, but ataxia and behavior changes also can occur.

Contraindications and Precautions

Phenothiazines can potentially lower seizure threshold in sensitive animals, although this has not been shown for acepromazine in animals and has not been reported for trimeprazine.

Drug Interactions

No drug interactions have been reported for animals.

Instructions for Use

There is evidence that trimeprazine is more effective when combined with prednisolone for treatment of pruritus. Combination product is Temaril-P, which contains trimeprazine and prednisolone.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Trimeprazine is available in 2.5-mg/5-mL syrup and 2.5-mg tablets.

Temaril-P is available in tablets that contain 5 mg trimeprazine + 2 mg prednisolone.

Capsules are available with 3.75 mg trimeprazine + 1 mg prednisolone and 7.5 mg trimeprazine + 2 mg prednisolone.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.5 mg/kg q12h PO.
- Prednisolone–trimeprazine: Start with 0.5 mg/kg prednisolone + 1.25 mg/kg trimeprazine per day. Taper dose to 0.3 mg/kg prednisolone + 0.75 mg/kg trimeprazine once daily or once every other day, PO.
- Tablet equivalents: Half tablet for dogs <4.5 kg; one tablet for dogs 5-9 kg; two tablets for dogs 10-18 kg; and three tablets for dogs >20 kg. All doses started with twice daily and eventually tapered to once daily and once every other day.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

Trimethobenzamide

trye-meth-oh-ben'zah-mide

Trade and Other Names: Tigan

Functional Classification: Antiemetic

Pharmacology and Mechanism of Action

Antiemetic. Trimethobenzamide inhibits vomiting at the chemoreceptor trigger zone (CRTZ).

Indications and Clinical Uses

Trimethobenzamide is used for antiemetic treatment, especially when vomiting is induced from the CRTZ (e.g., from chemotherapeutic drugs). Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Other antiemetics (e.g., maropitant) are more often used in dogs and cats.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects not reported in animals.

Contraindications and Precautions

Not recommended for use in cats.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Efficacy as antiemetic not reported in animals.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Trimethobenzamide is available in 100-mg/mL injections and 100- and 250-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

• 3 mg/kg q8h IM or PO.

Cats

Not recommended.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Trimethoprim + Sulfadiazine

trye-meth'oh-prim + sul-fah-dye'ah-zeen

Trade and Other Names: Tribriessen, Uniprim, Tucoprim, and Di-Trim

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Trimethoprim-sulfonamides combine the antibacterial drug action of trimethoprim and a sulfonamide. The activity is attributed to their synergistic effect in inhibiting folic acid metabolism in bacteria. Sulfonamides are competitive inhibitors of dihydrofolate synthesis. Trimethoprim inhibits the enzyme dihydrofolate reductase. When used in combination, it has a broad spectrum of activity against susceptible bacterial infections (gram-negative and gram-positive). Trimethoprim + sulfadiazine is only available as a veterinary preparation; trimethoprim + sulfamethoxazole is a human preparation. There are no published reports of differences in efficacy between trimethoprim + sulfadiazine versus trimethoprim + sulfamethoxazole. The primary difference between sulfamethoxazole and sulfadiazine is that sulfamethoxazole is metabolized more extensively and sulfadiazine may attain higher active urine concentrations in some patients. The pharmacokinetics varies among species and routes of administration. In most animals the trimethoprim is eliminated faster than the sulfonamide component. The combination is administered as a 1:5 ratio (trimethoprim:sulfonamide), but the ratio after administration varies considerably to 1:20 or lower. A ratio of 1:20 has been suggested as optimum for antibacterial effects, but this ratio has not been confirmed in clinical studies in animals.

Indications and Clinical Uses

Trimethoprim + sulfadiazine is used to treat a variety of infections in dogs, cats, horses, and some exotic animals. The combination has efficacy for susceptible bacterial infections (gram-negative and gram-positive), including respiratory infections, soft tissue and skin infections, wounds, abscesses, and urogenital infections. In horses, they have been used for respiratory infections, joint infections, abdominal infections, prostate infections, soft tissue and soft tissue infections, and infections of the CNS. The combination also is used occasionally for infections caused by protozoa (e.g., coccidial and *Toxoplasma* infections). The combination has not been successful for treating infections in abscesses or infections caused by anaerobic bacteria, possibly because of interactions with material in necrotic tissues.

Precautionary Information

Adverse Reactions and Side Effects

In horses oral administration of trimethoprim–sulfonamides may be associated with diarrhea. Other effects observed in horses include idiosyncratic neurological reactions consisting of behavior changes, gait abnormalities, and hyperesthesia. These effects improved soon after discontinuing medication. Adverse effects associated with sulfonamides in dogs include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites; therefore more toxic metabolite may accumulate in some animals. More descriptions of adverse reactions from sulfonamides are listed for individual drugs. Trimethoprim–sulfonamides may decrease thyroid hormone after treatment in dogs. Effects on thyroid function are most apparent after 2 weeks of treatment, but they are reversible.

Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed. If diarrhea develops in horses, discontinue treatment.

Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde, which may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for intravenous forms of trimethoprim-sulfonamides.

Instructions for Use

Dose listed is of the combined components; 30 mg/kg = 5 mg/kg trimethoprim and 25 mg sulfonamide. There is evidence that 30 mg/kg/day is efficacious for pyoderma; for other infections, 30 mg/kg twice daily has been recommended. Oral trimethoprim is not absorbed in ruminants.

Patient Monitoring and Laboratory Tests

Culture and sensitivity testing: CLSI break point for sensitive organisms is less than or equal to 2/38 mcg/mL. For streptococci, this break point is less than or equal to

786 Trimethoprim + Sulfamethoxazole

2/38 mcg/mL. Values listed are the concentration of trimethoprim/sulfonamide ratio. Trimethoprim-sulfonamides may affect the monitoring of thyroid hormones. In dogs, trimethoprim + sulfadiazine may cause a functional hypothyroidism and lower total T-4 concentrations. Trimethoprim + sulfamethoxazole decreased thyroid function at 30 mg/kg q12h and also at 15 mg/kg q12h. Trimethoprim + sulfadiazine at 15 mg/kg q12h for 4 weeks did not affect thyroid function in one study. Effects of trimethoprim-sulfonamides on thyroid function in dogs are reversible. In horses, trimethoprim + sulfadiazine did not affect assays of thyroid function.

Formulations

Trimethoprim + sulfadiazine is available in 30-, 120-, 240-, 480-, and 960-mg tablets. (All formulations have a ratio of 5:1, sulfadiazine to trimethoprim.) Recently, tablets have become less available. It is also available as an oral paste for horses. As a powder for horses, each gram contains 67 mg trimethoprim and 333 mg of sulfadiazine. It has also been available as a 48% injectable suspension for horses, but availability of injectable formulations has diminished.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs and Cats

(Doses are listed as the combined sulfonamide + trimethoprim.)

- 15 mg/kg q12h PO or 30 mg/kg q12-24h PO.
- *Toxoplasma*: 30 mg/kg q12h PO.

Large Animal Dosage

Horses

- 30 mg/kg (25 mg sulfonamide + 5 mg trimethoprim) q12h PO for acute treatment. For some infections, treatment once a day at 30 mg/kg may be sufficient.

Cattle

No dose has been established. Trimethoprim is not absorbed orally in ruminants, but it is absorbed in calves. Trimethoprim + sulfadoxine has been used in cattle (16 mg/kg combined drug every 24 hours IV or IM), but this drug is not available in the US.

Regulatory Information

Withdrawal times are not available. Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle. Do not use in horses intended for food.

Trimethoprim + Sulfamethoxazole

trye-meth'oh-prim + sul-fah-meth-oks'ah-zole

Trade and Other Names: Bactrim, Septra, and generic brands

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Trimethoprim-sulfonamides combine the antibacterial drug action of trimethoprim and a sulfonamide. The activity is attributed to their synergistic effect in inhibiting

folic acid metabolism in bacteria. Sulfonamides are competitive inhibitors of dihydrofolate synthesis. Trimethoprim inhibits the enzyme dihydrofolate reductase. When used in combination, it has a broad spectrum of activity against susceptible bacterial infections (gram-negative and gram-positive). Trimethoprim has been combined with both sulfadiazine and sulfamethoxazole. Trimethoprim + sulfadiazine is only available as a veterinary preparation; trimethoprim + sulfamethoxazole is a human preparation. There are no published reports of differences in efficacy between trimethoprim + sulfadiazine versus trimethoprim + sulfamethoxazole. The primary difference between sulfamethoxazole and sulfadiazine is that sulfamethoxazole is metabolized more extensively. Sulfadiazine may attain higher active urine concentrations in some patients. The combination is administered as a 1:5 ratio (trimethoprim-to-sulfonamide), but the ratio after administration varies considerably to 1:20 or lower. A ratio of 1:20 has been suggested as optimum for antibacterial effects, but this ratio has not been confirmed in clinical studies in animals.

Indications and Clinical Uses

Trimethoprim + sulfamethoxazole is used to treat a variety of infections in dogs, cats, horses, and some exotic animals. Trimethoprim + sulfamethoxazole is used for treatment of UTIs, skin and soft-tissue infections, prostate infections, pneumonia, and CNS infections. In horses, they have been used for respiratory infections, joint infections, abdominal infections, soft tissue infections, and infections of the CNS. The combination has not been successful for treating infections in abscesses or infections caused by anaerobic bacteria. The combination also is used occasionally for infections caused by protozoa (e.g., coccidial and *Toxoplasma* infections).

Precautionary Information

Adverse Reactions and Side Effects

In horses oral administration of trimethoprim–sulfonamides may be associated with diarrhea. Other effects observed in horses include idiosyncratic neurological reactions consisting of behavior changes, gait abnormalities, and hyperesthesia. These effects improved soon after discontinuing medication. Adverse effects associated with sulfonamides administered to dogs include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites and higher levels of more toxic metabolites. More descriptions of adverse reactions from sulfonamides are listed for individual drugs. Trimethoprim–sulfonamides may decrease thyroid hormone after treatment in dogs. Effects on thyroid function are most apparent after 2 weeks of treatment, but they are reversible.

Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed. The injectable preparation contains benzyl alcohol, which may cause reactions in small patients. The injectable preparation should be diluted and injected slowly IV.

Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by

methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde, which may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for intravenous forms of trimethoprim–sulfonamides.

Instructions for Use

The dose listed is of the combined components: 30 mg/kg = 5 mg/kg trimethoprim and 25 mg sulfonamide. There is evidence that 30 mg/kg/day is efficacious for pyoderma; for other infections, 30 mg/kg twice daily has been recommended. When using the injectable formulation, each 5-mL vial should be diluted in 75–125 mL of 5% dextrose. The diluted formulation should then be administered by intravenous infusion over 60 minutes.

Patient Monitoring and Laboratory Tests

Culture and sensitivity testing: CLSI break point for sensitive organisms is $\leq 2/38$ mcg/mL. For streptococci, this break point is $\leq 2/38$ mcg/mL.

Values listed are the concentration of trimethoprim–sulfonamide ratio.

In dogs, trimethoprim + sulfadiazine may cause a functional hypothyroidism and lower total T4 concentrations. Trimethoprim + sulfamethoxazole decreased thyroid function at 30 mg/kg q12h and at 15 mg/kg q12h. Trimethoprim + sulfadiazine at 15 mg/kg q12h for 4 weeks did not affect thyroid function in one study. Effects of trimethoprim–sulfonamides on thyroid function in dogs are reversible. In horses, trimethoprim + sulfadiazine did not affect assays of thyroid function.

Formulations

Trimethoprim + sulfamethoxazole is available in 480- and 960-mg tablets and a 240-mg/5-mL oral suspension (all formulations have ratio of 5:1 sulfamethoxazole to trimethoprim).

As an injection, it is available as 80 mg sulfamethoxazole and 16 mg trimethoprim per milliliter in 5-mL vials.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Injectable formulations should be stored at room temperature and not refrigerated. Injectable formulation contains 0.3% sodium hydroxide.

Small Animal Dosage

Dogs and Cats

(Doses are listed as the combined sulfonamide + trimethoprim.)

- 15 mg/kg q12h PO or 30 mg/kg q12-24h PO.
- 30 mg/kg q12h IV (see Instructions for Dosing section for preparation of intravenous formulation).

Large Animal Dosage

Horses

- 30 mg/kg (25 mg sulfonamide + 5 mg trimethoprim) q12h PO for acute treatment. For some infections, treatment once a day at 30 mg/kg may be sufficient.

Cattle

No dose is established. Trimethoprim is not absorbed orally in ruminants, but it is absorbed in calves. Trimethoprim + sulfadoxine has been used in cattle (16 mg/kg combined drug every 24 hours IV or IM), but this drug is not available in the US.

Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle. However, trimethoprim + sulfadoxine has a withdrawal time in Canada for cattle of 10 days (meat) and 96 hours (milk).

Tripeleannamine Citrate and Tripeleannamine Hydrochloride

tri-peh-len'eh-meen sih'trate

Trade and Other Names: Pelamine, Histanin, and PBZ

Functional Classification: Antihistamine

Pharmacology and Mechanism of Action

Antihistamine (H_1 blocker). Similar to other antihistamines, tripeleannamine acts by blocking the histamine Type 1 receptor (H_1) and suppresses inflammatory reactions caused by histamine. The H_1 blockers have been used to control pruritus and skin inflammation in dogs and cats; however, success rates in dogs have not been high. More commonly used antihistamines include clemastine, chlorpheniramine, diphenhydramine, cetirizine, and hydroxyzine.

Indications and Clinical Uses

Tripeleannamine is used to prevent allergic reactions and for pruritus therapy in dogs and cats. In large animals tripeleannamine hydrochloride is used to treat laminitis, allergy, insect bites, pulmonary edema, and urticaria in horses. In cattle it is used to treat urticaria and allergic reactions. Use in animals has been primarily derived from empirical use and experience in humans. Success rates for treatment of pruritus are low. In addition to the antihistamine effect for treating allergies, these drugs block the effect of histamine in the vomiting center, vestibular center, and other centers that control vomiting in animals.

Precautionary Information**Adverse Reactions and Side Effects**

Sedation is the most common side effect. Antimuscarinic effects (atropine-like effects) also are common. Members of this class (ethanolamines) have greater antimuscarinic effects than other antihistamines. GI adverse effects may occur, such as ileus and decreased stomach emptying.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions are reported for animals.

790 Tulathromycin

Instructions for Use

There are no clinical reports of use in veterinary medicine, and no evidence that it is more efficacious than other drugs in this class.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Tripeleennamine is available in 25- and 50-mg tablets, 20-mg/mL injections (generic), and 5-mg/mL elixir oral liquid. Tripeleennamine hydrochloride (Histatin) is available as a 25-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- The dose is not clearly established. It has been listed as 1 mg/kg q12h PO. In humans, the dose is 1.25 mg/kg q4-6h PO. Tripeleennamine hydrochloride injection: 0.25 mL per 5 kg body weight.

Large Animal Dosage

Pigs, Cattle, Horses: 1 mg/kg IM. Equivalent to 10 mL per 250 kg, or 1 mL per 25 kg body weight.

Regulatory Information

Withdrawal time: Pigs and cattle: 48 hours (meat); 48 hours (milk).

RCI Classification: 3

Tulathromycin

too-lath-roe-mye'sin

Trade and Other Names: Draxxin and Macrolide

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Antibacterial related to the macrolide class of drugs. It is considered a triamylide macrolide, which is derived from azalide macrolides, such as azithromycin. Like other macrolides it inhibits bacterial protein synthesis by binding to the ribosomal 50S subunit. It is considered bacteriostatic, but it may have bactericidal properties in vitro. Because of a positively charged molecule, it may penetrate gram-negative bacteria more easily than other macrolide antibiotics. Tulathromycin has a spectrum of activity that is limited to gram-positive bacteria and some gram-negative bacteria that cause respiratory diseases in cattle and pigs (e.g., *Mannheimia haemolytica*, *Mycoplasma*, and *Pasteurella multocida*). The half-life is long (e.g., 92-hour plasma half-life and 8-day tissue half-life in cattle), which prolongs the drug concentration at the site of infection. Other anti-inflammatory effects attributed to macrolide antibiotics may explain the clinical effects for respiratory infections, such as reduced inflammatory effects and cytokine expression in leukocytes.

Indications and Clinical Uses

In cattle, tulathromycin is used for treatment of bovine respiratory disease (BRD) caused by *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni* (formerly *Haemophilus somnus*). It is also effective for treating infections caused by *Mycoplasma*. It also has been used to prevent infections caused by these pathogens when used prophylactically. A single dose has been effective for bovine infectious keratoconjunctivitis (*Moraxella bovis*). In pigs, it has been used for treatment of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae*, *P. multocida*, *Bordetella bronchiseptica*, and *H. parasuis*. In foals, tulathromycin has been used for treatment of pulmonary abscesses.

Precautionary Information

Adverse Reactions and Side Effects

Serious adverse reactions have not been observed. Injection-site reactions are possible in some animals with swelling or irritation at the injection site. High doses (five times the dose) produced myocardial lesions in some animals. However, most animals have tolerated up to 10 times the labeled dose without toxicity.

Contraindications and Precautions

No specific contraindications have been reported.

Drug Interactions

No drug interactions have been reported.

Instructions for Use

In cattle, administer as a single subcutaneous injection in the neck. In pigs, administer as a single intramuscular injection in the neck. In treated foals (IM injection once per week) self-limiting diarrhea and injection-site reactions (IM injection) developed in approximately one third of the foals.

Patient Monitoring and Laboratory Tests

CLSI break point for susceptibility is ≤ 16.0 mcg/mL. For susceptibility testing, also use erythromycin as a guide.

Formulations

Tulathromycin is available in a 100-mg/mL solution for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

No small animal doses have been established.

Large Animal Dosage

Cattle

- 2.5 mg/kg SQ (neck) as a single injection.

Pigs

- 2.5 mg/kg IM (neck) as a single injection.

Foals

- 2.5 mg/kg IM, once per week.

Regulatory Information

No milk withdrawal times are established.

Do not use in female dairy cattle 20 months of age or older. Do not use in veal calves.

Cattle withdrawal time (meat): 18 days.

Pig withdrawal time (meat): 5 days.

Tylosin

tye'loe-sin

Trade and Other Names: Tylocine, Tylan, and Tylosin tartrate

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Macrolide antibiotic formulated as tylosin tartrate or tylosin phosphate. Like other macrolide antibiotics, tylosin inhibits bacteria by binding to 50S ribosome and inhibiting protein synthesis. Spectrum of activity limited primarily to gram-positive aerobic bacteria. *Clostridium* and *Campylobacter* are usually sensitive. *Escherichia coli* and *Salmonella* are resistant. In pigs, *Lawsonia intracellularis* is sensitive.

Indications and Clinical Uses

In cattle, tylosin is used for treatment of bovine respiratory disease (BRD) caused by *Mannheimia*, *Pasteurella multocida*, and *Histophilus somni* (formerly *Haemophilus somnus*). It is used for interdigital necrobacillosis (foot rot) in cattle caused by *Fusobacterium necrophorum* or *Bacteroides melaninogenicus*. In pigs it is used for treatment of swine arthritis caused by *Mycoplasma hyosynoviae*, swine pneumonia caused by *Pasteurella* spp., swine erysipelas caused by *Erysipelothrix rhusiopathiae*, swine dysentery associated with *Serpulina (Treponema) hyodysenteriae*, and proliferative enteropathy caused by *Lawsonia intracellularis*. For treatment in pigs it is also added to feed (Type A–medicated feed article) or drinking water. In small animals, it is used for gram-positive soft tissue and skin infections. However, the most common use in dogs is for treatment of diarrhea, referred to as “antibiotic-responsive diarrhea,” that has not responded to other antibiotics. The etiology of the diarrhea is not known but may be caused by *Clostridium* or *Campylobacter*. For this use, the powdered formulation (swine formulation) is most often added to food daily for maintenance.

Precautionary Information

Adverse Reactions and Side Effects

Tylosin may cause diarrhea in some animals. However, oral treatment for colitis in dogs has been administered for several months with safety. Skin reactions have been observed in pigs. Administration to horses has been fatal.

Contraindications and Precautions

Do not administer orally to rodents or rabbits. Do not administer to horses. Avoid intravenous administration. Do not inject more than 10 mL in one intramuscular site.

Drug Interactions

Although other macrolides have been associated with inhibition of cytochrome P450 enzymes, no drug interactions have been reported for animals.

Instructions for Use

Tylosin is used in pigs for managing respiratory tract infections. It is rarely used in small animals for uses other than intestinal disease. Powdered formulation (tylosin tartrate) has been administered on food for control of signs of colitis in dogs. Tablets are approved for treatment of colitis in Canada.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Tylosin is available in a soluble powder 100 g per pound, or approximately 3 grams per teaspoon (Tylosin-100 Type A medicated premix). Tylosin tartrate is equal to 800 micrograms per gram of tylosin base. It also is available as a 50- and 200-mg/mL injection (with propylene glycol).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 7-15 mg/kg q12-24h PO.
- 8-11 mg/kg q12h IM.
- Colitis: 12-20 mg/kg q8h with food, then if there is a response, increase the interval to q12h and eventually to q24h. (20 mg/kg is approximately 1/8 teaspoon of tylosin phosphate, or Tylan for a 20-kg dog.)

Cats

- 7-15 mg/kg q12-24h PO.
- 8-11 mg/kg q12h IM.

Large Animal Dosage

Swine

- Treatment of arthritis, erysipelas, and swine dysentery: 8.8 mg/kg q12h IM.

Cattle

- Pododermatitis and pneumonia: 17.6 mg/kg q24h IM.
- Swine: Medicated feed dose is administered at a dose of 22-220 g/kg (of the premix), with dose depending on the specific product. Consult package information.

Regulatory Information

Pig withdrawal time (meat): 14 days.

Cattle withdrawal time (meat): 21 days.

Not to be used in lactating cattle.

Urofollitropin

yoo-roe-fah'lih-troe-pin

Trade and Other Names: Metrodin, FSH, and Fertinex

Functional Classification: Hormone

Pharmacology and Mechanism of Action

Urofollitropin contains follicle-stimulating hormone (FSH) and stimulates ovulation. In people it is used in combination with human chorionic gonadotropin (hCG) to stimulate ovulation.

Indications and Clinical Uses

Although urofollitropin is used in people in combination with hCG to stimulate ovulation, the use in animals is not common.

Precautionary Information

Adverse Reactions and Side Effects

Side effects have not been reported in animals. In people, thromboembolism or severe ovarian hyperstimulation syndrome has been reported. In humans, ovarian enlargement and ovarian cysts have been reported.

Contraindications and Precautions

Do not use in pregnant animals.

Drug Interactions

No drug interactions are reported for animals.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals is extrapolated from the experience in people. Use in humans is followed by administration of hCG.

Patient Monitoring and Laboratory Tests

Monitor estrogen and/or progesterone with treatment.

Formulations

Urofollitropin is available in 75 units per vial for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Doses not established. However, the usual human dose is 75 units/day IM for 7 days. This may be increased to 150 units/day IM for an additional 7 days.

Large Animal Dosage

Doses not established. However, the usual human dose is 75 units/day IM for 7 days. This may be increased to 150 units/day IM for an additional 7 days.

Regulatory Information

It is expected to pose little risk from residues in animals intended for food, and no withdrawal times are recommended.

Ursodiol, Ursodeoxycholic Acid

er-soe-dye'ole, er-soe-dee-oks-ih-koe-lik ass'id

Trade and Other Names: Actigall, Ursodeoxycholic acid, Urso

Functional Classification: Laxative, choleric

Pharmacology and Mechanism of Action

Hydrophilic bile acid. Anticholelithic and choleric. Ursodiol is the short name for ursodeoxycholic acid. This is a naturally occurring, water-soluble bile acid. Ursodiol, like other bile acids, can act as a choleric and increase bile flow. In dogs, it may alter pool of circulating bile acids, displacing the more hydrophobic bile acids or enhancing their secretion in liver and bile. By modulating the composition of biliary bile salts in favor of more hydrophilic bile salts, injury to the biliary epithelium, such as the cytotoxic potential of endogenous bile acids, is less likely than with hydrophobic bile salts.

Indications and Clinical Uses

Ursodiol is used for treatment of liver diseases. It is used to treat primary biliary cirrhosis, cholestatic liver disorders, and chronic liver disease. Although experimental evidence exists for its benefit in dogs, there are no well-controlled clinical trials that demonstrate efficacy. In people it has been used as a laxative and to prevent or treat gallstones.

Precautionary Information

Adverse Reactions and Side Effects

Loose feces and pruritus are the most common problems in people. In animals ursodiol may cause diarrhea. Adverse effects can be decreased by gradually increasing the dose over 1-2 weeks.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions have been identified for animals. In people it interferes with some cholesterol-lowering drugs.

Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. The optimum dose in people is 13-15 mg/kg per day PO. Once or twice daily is as effective as 3-4 times per day. Administer with meals.

Patient Monitoring and Laboratory Tests

Monitor bile acids and hepatic enzymes during treatment to monitor effects.

Formulations

Ursodiol is available in 300-mg capsules and 250- or 500-mg tablets.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Suspensions have been prepared in vehicles for oral use and found to be stable for 35-60 days.

Small Animal Dosage

Dogs and Cats

- 10-15 mg/kg q24h PO; animals with liver disease should receive 15 mg/kg.

Large Animal Dosage

No large animal doses are available.

Regulatory Information

It is expected to pose little risk from residues in animals intended for food, and no withdrawal times are recommended.

Valproic Acid, Valproate Sodium

val-proe'ik ass'id, val'proe-ate soe'dee-um

Trade and Other Names: Depakene (Valproic acid), Depakote (Divalproex), and Epival (in Canada)

Functional Classification: Anticonvulsant

Pharmacology and Mechanism of Action

Anticonvulsant. Action is not known, but valproate may increase GABA concentrations in the CNS. Both valproic acid and valproate sodium are used. Divalproex is composed of both valproic acid and sodium valproate. Equivalent oral doses of divalproex sodium and valproic acid deliver equivalent quantities of valproate ion.

Indications and Clinical Uses

Valproate is used, usually in combination with phenobarbital, to treat refractory epilepsy in animals. Most use has been in dogs, but limited efficacy studies have been reported. The use of valproate in animals has declined because other anticonvulsants for treating refractory epilepsy have been identified such as gabapentin, pregabalin, zonisamide, and levetiracetam.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals, but hepatic failure has been reported in people. Sedation may be seen in some animals.

Contraindications and Precautions

Do not use in pregnant animals. Birth defects have been reported in people.

Drug Interactions

Valproate may cause bleeding if used with drugs that inhibit platelets.

Instructions for Use

This drug is usually used as an add-on with phenobarbital. Controlled-release forms designed for people do not show the same oral absorption profile in dogs as in people.

Patient Monitoring and Laboratory Tests

Therapeutic drug monitoring can be performed; however, therapeutic concentrations have not been established for dogs and cats, and ranges cited for people, 50-100 mcg/mL (desired trough concentration), should be used. Concentrations greater than 100 mcg/mL are associated with adverse effects.

Formulations

Valproic acid immediate release formulations are available in 250-mg capsules and 50-mg/mL syrup. Delayed-release formulations of valproic acid and divalproex are available in 125, 250, and 500 mg tablets or capsules. Divalproex is also available in 125 mg capsules and 250, and 500 mg extended release tablets. Valproate sodium (Depacon) is available in 100-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Valproic acid is slightly soluble in water, but valproate sodium is soluble in water.

798 Vancomycin

Extemporaneous emulsions have been prepared and were comparable to absorption of syrup.

Small Animal Dosage

Dogs

- 50-250 mg per dog, (depending on size) q8h PO.
- Delayed-release formulations: Start with 250 mg per dog q12h PO, and increase to 500 mg per dog q12h, as needed.

Higher doses should be used if dogs are also receiving phenobarbital.

Cats

Dose not established.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Vancomycin

van-koe-mye'sin

Trade and Other Names: Vancocin and Vancoled

Functional Classification: Antibacterial

Pharmacology and Mechanism of Action

Antibacterial drug. Vancomycin is bactericidal for most organisms and bacteriostatic for enterococci. It inhibits the cell wall by binding to the D-alanyl-D-allanine portion of cell wall precursors and interfering with the bacterial cell wall. The bactericidal action occurs by activating bacterial cell wall autolysins. Spectrum includes *Streptococcus*, *Enterococcus*, and *Staphylococcus*. Strains of *Staphylococcus* treated often are called methicillin-resistant *Staphylococcus* (e.g., methicillin-resistant *Staphylococcus aureus* [MRSA] or *Staphylococcus pseudintermedius* [MRSP]).

Indications and Clinical Uses

Vancomycin is used for resistant strains of *Staphylococcus* or *Enterococcus* in animals. It is the most common injectable drug to treat methicillin-resistant *Staphylococcus species* and drug-resistant *Enterococcus* spp. It is not effective against gram-negative bacteria. Vancomycin use is not common in animals because it is inconvenient to administer. However, it can be valuable for treatment of enterococci or staphylococci that are resistant to other antibiotics. It also has been administered orally to people for diarrhea caused by *Clostridium* spp. Occasionally it has been used in horses for local infiltration, such as with regional limb perfusion. It is not allowed in food animals.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported in animals, but the use has been limited to a small number of animals and a full range of possible adverse effects have not been recognized. Adverse effects in people include neutropenia, renal injury (more common with older products that contained impurities), and histamine

release. Reactions, especially those associated with histamine release, are more likely with a rapid injection.

Contraindications and Precautions

Do not administer rapidly IV. It will cause pain if injected by other routes (IM, SQ). Administer by slow infusion to avoid acute adverse reactions.

Drug Interactions

Do not mix with other drugs in infusion solution; there are incompatibilities identified for many drugs. It is incompatible with alkaline solutions.

Instructions for Use

Vancomycin must be administered via IV infusion, although in rare instances intraperitoneal administration has been used in people. (Oral administration is limited to intestinal infections.) Vancomycin systemic use in horses is rare. Local administration in horses via regional limb perfusion has been used for localized joint or bone infections.

Doses are derived from pharmacokinetic studies in each species. In dogs, to maintain the plasma concentration between a suggested window of 10 to 30 $\mu\text{g}/\text{mL}$, the dose rate of 15 mg/kg q8h, IV, is recommended. (This dose actually produces peaks and troughs of approximately 40 and 5 $\mu\text{g}/\text{mL}$, respectively, but it is the most convenient dose that can be used because of the short half-life in dogs.) This dose should be infused slowly over 30 to 60 minutes, or at a rate of approximately 10 mg/min. The total dose to be administered can be diluted in 0.9% saline or 5% dextrose solution but not alkalinizing solutions. Vancomycin is available in vials of 500 mg to 5 g (Vancocin, other brands, and generic).

Patient Monitoring and Laboratory Tests

Monitoring of trough plasma concentrations is recommended to ensure proper dose. Maintain trough concentration above 10 mcg/mL. CLSI guidelines for susceptibility testing list a breakpoint of ≤ 4 mcg/mL for *Enterococcus*, ≤ 1 mcg/mL for *Streptococcus*, and ≤ 4 mcg/mL for *Staphylococcus*.

Formulations

Vancomycin is available in 500-mg and 1-, 5-, and 10-g vials for injection.

Stability and Storage

Stability may be compromised if mixed with other drugs in infusion solutions. Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water and ethanol. After reconstitution with sterile water, it may be further diluted in 5% dextrose or saline. Solutions may have a dark color. After reconstitution it is stable for 14 days either at room temperature or in the refrigerator. Some ophthalmic compounded formulations are not stable and have a low pH that can be irritating to the eyes.

Small Animal Dosage

Dogs

- 15 mg/kg q6-8h IV infusion.
- Constant rate infusion (CRI): Loading dose of 3.5 mg/kg, followed by CRI of 1.5 mg/kg/hr mixed in 5% dextrose in water.

Cats

- 12-15 mg/kg q8h IV infusion

Large Animal Dosage

Horses

- 4.3-7.5 mg/kg q8h IV given as an infusion over 1 hour.
- Regional limb perfusion: Infuse 300 mg diluted in a 0.5% solution.

Regulatory Information

Do not administer to animals intended for food. The Food and Drug Administration has prohibited the extralabel use of glycopeptides in food-producing animals because of risk of producing glycopeptide-resistant bacteria.

Vasopressin

vay-zoe-press'in

Trade and Other Names: Arginine Vasopressin (AVP), Antidiuretic hormone (ADH), Pitressin

Functional Classification: Hormone

Pharmacology and Mechanism of Action

Antidiuretic hormone. Vasopressin mimics the effect of antidiuretic hormone (ADH) on the tubule of the renal tubule. ADH permits reabsorption of water in the renal tubule. Without ADH, more diluted urine is excreted. (See Desmopressin manuscript for additional formulations and use.) Vasopressin also has potent vasopressive activity via activation of the V_1 vascular receptor. The V_1 vascular receptors are in high density on vascular smooth muscle. V_2 receptors occur on the renal-collecting duct, and stimulation increases water reabsorption. Because of the vasopressive action, it has been used to treat vasodilatory shock. During infusion it rapidly increases mean arterial pressure. A related drug, terlipressin, is more specific for the vascular V_1 receptor.

Indications and Clinical Uses

Vasopressin is used for treatment of polyuria caused by central diabetes insipidus. It is not effective for polyuria caused by renal disease. Desmopressin is the preferred formulation used more frequently in animals for treating diabetes insipidus. Vasopressin is used to treat vasodilatory shock via constant rate infusion (CRI) in addition to fluid therapy.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported. Allergic reactions and increase in blood pressure have been reported in people.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

For IV use, dilute in 0.9% saline and titrate dose to effect. For antidiuretic use, doses are adjusted on the basis of monitoring of water intake and urine output.

Patient Monitoring and Laboratory Tests

Monitor blood pressure during infusion to maintain systolic blood pressure of 100-120 mm Hg and urine output of 0.5-1.5 mL/kg/hr. Titrate infusion rate to achieve desired pressure response. When used for antidiuretic effects, monitor water intake, urine output, and urine-specific gravity.

Formulations

Vasopressin is available in 20-units/mL (aqueous) solution.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- Antidiuretic: 10 units IV or IM.
- Vasopressor (shock): 0.01-0.04 units/min. Do not exceed 0.04 Units/min.
- CPR: 0.2-0.8 Units/kg IV.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Verapamil Hydrochloride

ver-ah-mill hye-droe-klor'ide

Trade and Other Names: Calan and Isoptin

Functional Classification: Calcium antagonist

Pharmacology and Mechanism of Action

Calcium-channel blocking drug of the nondihydropyridine group. Verapamil blocks calcium entry into cells via blockade of voltage-dependent slow channel. Verapamil produces vasodilation, negative chronotropic, and negative inotropic effects.

Indications and Clinical Uses

Verapamil has been used to control supraventricular arrhythmias. The use of verapamil has diminished because of adverse effects; it has practically become an outdated drug. The preferred drug from this class to use in animals is usually diltiazem.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects include hypotension, cardiac depression, bradycardia, and AV block. It may cause anorexia in some patients. Verapamil has caused sudden cardiac arrest in some patients with intravenous administration.

Contraindications and Precautions

Do not use in patients with decompensated CHF or advanced heart block. It is not well tolerated in cats.

Drug Interactions

Verapamil, like other calcium-channel-blocking drugs, is subject to interaction with drugs that interfere with the multidrug resistance (MDR) membrane pump (p-glycoprotein) and the cytochrome P450 enzymes. (See Appendix for list of drugs that may cause interference.)

Instructions for Use

Diltiazem is preferred over verapamil in patients with heart failure because of less myocardial depression. Oral formulation not absorbed sufficiently (of the active stereoisomer) for adequate effects.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during treatment.

Formulations

Verapamil is available in 40-, 80-, and 120-mg tablets and a 2.5-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Verapamil is soluble in water. Aqueous solutions are stable for 3 months. Maximum stability is at pH 3-6. It can be mixed with infusion solutions and is compatible. Suspensions have been prepared for oral administration and found to be stable for 60 days.

Small Animal Dosage

Dogs

- 0.05 mg/kg q10-30min IV (maximum cumulative dose is 0.15 mg/kg).
Oral dose is not established.

Cats

Not recommended.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 4

Vinblastine Sulfate

vin-blast'een sul'fate

Trade and Other Names: Velban

Functional Classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Vinblastine, like vincristine, belongs to the vinca alkaloid group of anticancer agents. They have been called "spindle poisons" because they have an affinity for tubulin in cells. Tubulin is the protein that forms the microtubules responsible for chromosome migration during mitosis. Vinca alkaloids block

polymerization of the cellular microtubules and therefore arrest mitosis in metaphase (m-phase specific).

Indications and Clinical Uses

Vinblastine is used in cancer chemotherapy protocols for various tumors. One of the most common uses is for canine mast cell tumors (MCT). Although its structure is similar to vincristine, it has been active against other tumor types and there does not appear to be cross-resistance from vincristine to vinblastine. Vinblastine has been used for lymphoreticular neoplasia. Do not use vinblastine to increase platelet numbers as is done occasionally with vincristine. (Vinblastine may actually cause thrombocytopenia.)

Precautionary Information

Adverse Reactions and Side Effects

The most dose-limiting effect is bone marrow suppression, with the nadir of neutropenia occurring at 1 week after administration and recovery occurring at 2 weeks. Gastrointestinal toxicity is the second most important effect, but it is milder. Vinblastine does not produce neuropathy as vincristine does. It causes tissue necrosis if injected outside the vein.

Contraindications and Precautions

If perivascular injection occurs, immediate flushing of area with fluids is recommended.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Vinblastine may be used with other anticancer drugs or combined with prednisolone for mast cell tumors. The most common dose has been 2 mg/m² every 7 to 14 days by slow IV infusion or rapid IV bolus. But to increase the response rate for mast cell tumors, evidence suggests that dose intensity should be increased to a dose of 3.5 mg/m², IV, every 2 weeks. This dose produced more toxicity but higher efficacy.

Patient Monitoring and Laboratory Tests

Monitor CBC during treatment.

Formulations

Vinblastine is available in 1-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 2 mg/m² IV (slow infusion) once/week. (See Instructions for Use regarding higher doses.)

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Vincristine Sulfate

vin-kris'steen sul'fate

Trade and Other Names: Oncovin, Vincasar, and generic brands

Functional Classification: Anticancer agent

Pharmacology and Mechanism of Action

Anticancer agent. Vincristine, like vinblastine, belongs to the vinca alkaloid group of anticancer agents. They have been called “spindle poisons” because they have an affinity for tubulin in cells. Tubulin is the protein that forms the microtubules responsible for chromosome migration during mitosis. Vinca alkaloids block polymerization of the cellular microtubules and therefore arrest mitosis in metaphase (m-phase specific). Vincristine has an affinity for the tubulin of platelets. For thrombocytopenia, vincristine increases thrombopoiesis, increases fragmentation of megakaryocytes, and decreases platelet destruction. It may also decrease destruction of platelets by macrophages.

Indications and Clinical Uses

Vincristine is used in combination chemotherapy protocols. It is included in several anticancer chemotherapy protocols, usually with corticosteroids, alkylating agents, and other drugs. It has been used in veterinary medicine for lymphoreticular tumors, transmissible venereal tumors (TVT), mammary neoplasia in cats, and other solid tumors. It is a component of several combination protocols and may also be useful as a single agent for some tumors.

Precautionary Information

Adverse Reactions and Side Effects

Vincristine is generally well-tolerated. It is less myelosuppressive than other anticancer drugs. Peripheral neuropathy has been reported, but it is rare. Constipation can occur. Vincristine is irritating to tissues; avoid extravasation outside vein during administration. If accidental injection is made outside the vein, prompt action is needed to avoid severe tissue injury.

Contraindications and Precautions

If perivascular injection occurs, immediate flushing of the area with fluids is recommended to decrease tissue injury. When handling vincristine, pharmacy and hospital staff should take appropriate precautions to prevent exposure to people. Dogs with ABCB-1 mutation (p-glycoprotein deficient) may have increased risk of toxicity.

Drug Interactions

There are no significant drug interactions.

Instructions for Use

Vincristine is used in cancer chemotherapy protocols for various tumors. For example, in the COAP protocol (an acronym for cyclophosphamide, Oncovin, asparaginase, and Prednisolone) the Oncovin component is vincristine. Vincristine also increases numbers of functional circulating platelets and is used for thrombocytopenia. When used to treat immune-mediated thrombocytopenia, it may be administered with a corticosteroid (e.g., prednisone at

2 mg/kg) to produce a rapid increase in functional platelets. This regimen (compared to prednisone alone) has shortened the duration of hospitalization for dogs with immune-mediated thrombocytopenia.

Patient Monitoring and Laboratory Tests

Monitor platelets during therapy if used to increase platelet numbers.

Formulations

Vincristine is available in 1-mg/mL injection.

Stability and Storage

Maintain in the injectable vial. Do not mix with other drugs in vial.

Small Animal Dosage

Dogs and Cats

- Antitumor: 0.5-0.75 mg/m² IV (or 0.025-0.05 mg/kg) once/week.
- Thrombocytopenia: 0.02 mg/kg IV once/week (with prednisolone).

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

Vitamin A

Trade and Other Names: Retinol, Aquasol-A, Vitamin AD, and Vitamins A and D

Functional Classification: Vitamin

Pharmacology and Mechanism of Action

Vitamin A supplement. See also Isotretinoin (Accutane) for analogues used for other conditions.

Indications and Clinical Uses

Vitamin A is used as a supplement for animals with deficiency.

Precautionary Information

Adverse Reactions and Side Effects

Excessive doses can cause bone or joint pain and dermatitis. Other signs of hypervitaminosis A can be excessive bleeding, confusion, diarrhea, and peeling of skin.

Contraindications and Precautions

Hypervitaminosis can occur from high doses of vitamin A administered chronically. Doses needed to cause toxicity can be as high as 10,000 units/kg/day.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

Dosing of vitamin A may be expressed as units or retinol equivalents (RE) or mcg of retinol. One RE equals 1 mcg of retinol. One RE of vitamin A is equal to 3.33 units of retinol.

Patient Monitoring and Laboratory Tests

Monitor for signs of toxicity if high doses are used.

Formulations

Vitamin A is available in 5000 units (1500 RE) per 0.1 mL oral solution and in 10,000-, 25,000-, and 50,000-unit tablets. These tablets are listed as 3000, 7500, and 15,000 REs, respectively. Injectable formulations used in veterinary medicine usually are included with vitamin D. These combinations contain 100,000 units/mL, 200,000 units/mL, or 500,000 units/mL.

Stability and Storage

Store protected from light at room temperature. Vitamin A, like other fat-soluble vitamins, is insoluble in water but soluble in oils. It is subject to oxidation and should be kept in a tightly sealed container.

Small Animal Dosage

Dogs and Cats

- 625-800 units/kg q24h PO.

Large Animal Dosage

All doses are listed as per animal and may be repeated in 2-3 months.

Calves

- 500,000-1 million units IM.

Sheep and Swine

- 500,000-1 million units IM.

Cattle

- 1-2 million units IM.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Vitamin E

Trade and Other Names: Tocopherol, Alpha-tocopherol, Aquasol E, and generic brands

Functional Classification: Vitamin

Pharmacology and Mechanism of Action

Vitamin E also is known as alpha-tocopherol. It is a fat-soluble vitamin that is considered an antioxidant. Vitamin E also is found in solutions as d-alpha-tocopherol (natural source of vitamin E). It is often a component of omega fatty-acid formulations used in oral dietary supplements.

Indications and Clinical Uses

Vitamin E is used as supplement and as treatment of some immune-mediated dermatoses and hepatobiliary disorders. Vitamin E has been used as an oral treatment for discoid lupus in dogs; however, efficacy for many skin diseases has been questioned.

Precautionary Information

Adverse Reactions and Side Effects

Vitamin E at high doses can cause coagulopathies. Doses known to cause coagulopathy are 1000 units/day (15 units/kg/day) in humans. Coagulopathies are caused by a decrease in vitamin K-dependent coagulation factors.

Contraindications and Precautions

Use carefully in animals with coagulopathies.

Drug Interactions

Vitamin E may interact with anticoagulants. Vitamin E may exacerbate the anticoagulant effect of warfarin.

Instructions for Use

Vitamin E has been proposed as treatment for a wide range of human illnesses, but evidence for efficacy in animals is lacking. In animals it is used as adjunctive antioxidant therapy for a variety of diseases.

Patient Monitoring and Laboratory Tests

Monitor for bleeding in animals treated with high doses.

Formulations

Vitamin E is available in capsules, tablets, and an oral solution (e.g., 1000 units/capsule). Injectable formulations for veterinary medicine may also contain vitamins A and D. Usually injectable combinations contain 300 units/mL. Vitamin E also is found in solutions as d-alpha-tocopherol (natural source of vitamin E). It is also often a component of omega fatty-acid formulations.

Stability and Storage

Vitamin E, like other fat-soluble vitamins, is insoluble in water but soluble in oils. Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 100-400 units q12h PO (as alpha-tocopherol).
- Immune-mediated skin disease: 400-600 units q12h PO.
- Discoid lupus erythematosus (dogs): 200-400 units q12h PO.
- Liver disease: 10-15 Units/kg/day, PO.

Large Animal Dosage

All doses are listed as per animal and may be repeated in 2-3 months.

Calves

- 1200-1800 units IM.

Cattle

- 2400-3000 units IM.

Sheep and Swine

- 1200-1800 units IM.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Vitamin K

Trade and Other Names: AquaMEPHYTON (injection), Mephyton (tablets), Veta-K1 (capsules), Veda-K1 (oral and injectable), Vitamin K, Phylloquinone, and Phytomenadione

Functional Classification: Vitamin

Pharmacology and Mechanism of Action

See also Phytonadione for additional information. Vitamin K is a cofactor used to synthesize coagulation factors in the liver (factors II, VII, IX, and X). Vitamin K-1 also is known as phytonadione and phylloquinone (Phytomenadione is the British spelling of Phytonadione). Vitamin K-2 is also known as menaquinone. Vitamin K-3 is known as menadione. Vitamin K-3 is a synthetic analogue and is not equivalent to Vitamin K-1. Vitamin K-3 is not recommended for clinical use. Vitamin K-1 is absorbed better with meals that contain fat.

Indications and Clinical Uses

Vitamin K-1 is a fat-soluble vitamin used to treat coagulopathies caused by anticoagulant toxicosis (warfarin or other rodenticides). Anticoagulants deplete vitamin K in the body, which is essential for synthesis of clotting factors. In large animals, it is used to treat sweet clover poisoning.

Precautionary Information

Adverse Reactions and Side Effects

In people a rare hypersensitivity-like reaction has been observed after rapid intravenous injection. This reaction may be caused by histamine release from a reaction from the drug vehicle Polysorbate 80. Signs resemble anaphylactic shock. These signs also have been observed in animals. To avoid anaphylactic reactions, do not administer IV. Reactions from intramuscular injection, such as hematoma, may occur in animals with coagulopathies.

Contraindications and Precautions

Accurate diagnosis to rule out other causes of bleeding is suggested. Other forms of vitamin K may not be as rapidly acting as vitamin K-1; therefore, consider using a specific preparation. To avoid anaphylactic reactions, do not administer IV.

Drug Interactions

Some drugs, such as cephalosporins, may decrease vitamin K-dependent clotting factors.

Instructions for Use

Consult poison control center for specific protocol if specific rodenticide is identified. Use vitamin K-1 for acute therapy because it is more highly bioavailable.

Administer with food to enhance absorption. Phytonadione and Phytomenadione are synthetic lipid-soluble forms of vitamin K-1. Menadiol is vitamin K-4, which is a water-soluble derivative converted in the body to vitamin K-3 (menadiione).

Injection can be diluted in 5% dextrose or 0.9% saline but not other solutions. Although Vitamin K-1 veterinary labels have listed the intravenous route for administration, these labels have not been approved by the FDA. Therefore, avoid intravenous administration of vitamin K-1. The preferred route is subcutaneous, but intramuscular also can be used. When treating for poisoning by second-generation rodenticides, which have long half-lives, 6 weeks of therapy may be necessary.

Patient Monitoring and Laboratory Tests

Monitoring bleeding times in patients is essential for accurate dosing of vitamin K-1 preparations. When treating long-acting rodenticide poisoning, periodic monitoring of the bleeding times is suggested.

Formulations

Vitamin K is available in 2- or 10-mg/mL injection. Mephyton is a 5-mg tablet. Veta-K1 is a 25-mg capsule. Phytonadione (AquaMEPHYTON) is a 2- or 10-mg/mL injection.

Stability and Storage

Vitamin K, like other fat-soluble vitamins, is insoluble in water but soluble in oils. Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- Short-acting rodenticides: 1 mg/kg/day IM, SQ, or PO for 10-14 days.
- Long-acting rodenticides: 2.5-5 mg/kg/day IM, SQ, or PO for 3-4 weeks, and up to 6 weeks.

Birds

- 2.5-5 mg/kg q24h.

Large Animal Dosage

Cattle, Calves, Horses, Sheep, and Goats

- 0.5-2.5 mg/kg SQ or IM.

Regulatory Information

No meat or milk withdrawal time is necessary.

Voriconazole

vor-ih-kahn'ah-zole

Trade and Other Names: Vfend

Functional Classification: Antifungal

V

Pharmacology and Mechanism of Action

Azole (triazole) antifungal drug. Voriconazole is a second-generation triazole antifungal drug. Similar to the other currently available azole and triazole antifungals, voriconazole inhibits the fungal cytochrome P450-dependent 14 alpha-sterol demethylase, which is essential for formation of ergosterol in the fungal

810 Voriconazole

cell wall. Voriconazole is similar in structure to fluconazole; however, it is more active and potent. Voriconazole is active against dermatophytes and systemic fungi, such as *Blastomyces*, *Histoplasma*, and *Coccidioides*. It also has activity against yeast, such as *Candida* and *Malassezia*. Voriconazole has greater activity against *Aspergillus* and *Fusarium* than other drugs of this class and is indicated for systemic treatment. Voriconazole is more lipophilic than fluconazole and more water soluble than itraconazole or ketoconazole, with intermediate protein binding. These properties provide good oral bioavailability and tissue distribution. Pharmacokinetics may be dose-dependent and variable among animals. Experimental studies in dogs have shown rapid and complete absorption of the drug following oral administration. Oral absorption is higher than in most other drugs in this class. In horses, voriconazole was absorbed 92% and had a half-life of 13 hours.

Indications and Clinical Uses

Voriconazole has been used to treat dermatophytes and systemic fungi, such as *Blastomyces*, *Histoplasma*, and *Coccidioides*. It has been used to treat infections caused by *Aspergillus* and *Fusarium*. The efficacy in humans for treating *Aspergillus* is better than with other oral antifungal drugs and comparable to amphotericin B. Penetration into the CNS and eye is high enough to treat infections in these areas. Most of the use in veterinary medicine has been empirical or extrapolated from the use in humans. Clinical experience in horses has used a dose of 2 mg/kg once-daily PO. But research studies have showed that a dose of 4 mg/kg once daily, PO, or a dose of 3 mg/kg q12h, PO, produces adequate in plasma and tissue concentrations (ocular tear film, CSF, urine, epithelial lining fluid of the lung, and synovial fluid) for susceptible fungi, including *Aspergillus*. It has also been administered topically in horses for ocular fungal infections (using the IV 1% solution every 4 hours). Voriconazole also has been used in birds to control infections caused by *Aspergillus*.

Precautionary Information

Adverse Reactions and Side Effects

Voriconazole has been associated with neurotoxicity in cats at doses of 10 mg/kg via an unknown mechanism. Some cats administered therapeutic doses exhibited CNS signs that resolved after discontinuation of the drug. These reactions have not been reported in other animals (dogs, horses, birds) treated with voriconazole. Although it is generally better tolerated than ketoconazole in most species, vomiting and hepatotoxicity are possible, especially at high doses. In people, transient ocular problems (blurred vision, photophobia) also have been reported.

Contraindications and Precautions

A safe dose has not been identified for cats. Use cautiously in any animal with signs of liver disease. Use cautiously in pregnant animals. At high doses in laboratory animals, drugs in this class have caused fetal abnormalities. Use the oral formulation rather than the IV form in animals with renal disease.

Drug Interactions

Voriconazole is a cytochrome P450 enzyme inhibitor. It may cause drug interactions because of inhibition of P450 enzymes. However, this inhibition is not expected to be as prominent as with ketoconazole.

Instructions for Use

Doses are based on experimental studies in animals with voriconazole. Some uses in animals are based on empiricism or extrapolation from human literature. When used IV, 10-mg/mL solution should be further diluted with fluids to a concentration <5 mg/mL and infused slowly. IV solutions should be used immediately or stored in the refrigerator not longer than 24 hours. It is compatible with lactated Ringer's solution, 5% dextrose, or sodium chloride 0.9%. Do not mix IV solution with blood products or concentrated electrolytes.

Patient Monitoring and Laboratory Tests

Monitor liver enzyme concentrations. MIC values for susceptible fungi are usually <0.5 mcg/mL.

Formulations

Voriconazole is available in 50- and 200-mg tablets and 200-mg (10 mg/mL) injection. The IV solution requires reconstitution to 10 mg/mL, then dilution to 5 mg/mL or less for CRI (3 mg/kg/hr for 1-2 hours). A variety of compounded forms have been prepared for animals: A drug suspension for animals has been prepared by mixing crushed tablets (200 mg) with 20 mL water and 60 mL Ora-Plus to make a suspension of 2.5 mg/mL. After mixing this suspension was stable for 17 days. A compounded mixture also has been prepared by mixing two 200-mg tablets crushed to a powder and mixed with 10 mL of a suspending agent and flavoring agent (Ora Plus/Ora Sweet, in a ratio of 1:1). Final formulation was 40 mg/mL and was stable for 30 days at room temperature or in the refrigerator. For horses, crushed tablets have been mixed with 30 mL of corn syrup and administered orally via syringe.

Stability and Storage

Store in a tightly sealed container, protected from light, at room temperature. Compounded formulations may be stable and potent if used immediately after mixing. See section on Formulations for stability information on compounded preparations. Use intravenous formulation immediately after mixing or store in the refrigerator for not longer than 24 hours. Do not mix IV solutions with concentrated electrolytes or blood products.

Small Animal Dosage

Dogs

- 4-5 mg/kg q12h PO.

Cats

Safe doses have not been identified.

Birds

- 10 mg/kg q12h, oral, administered as powder or crushed tablets mixed with water in a liquid suspension (0.5 mg/mL).

Large Animal Dosage

Horses

- 2-4 mg/kg q24h, or 3 mg/kg q12h, PO.
- 1.5 mg/kg q24h IV.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Warfarin Sodium

war'far-in soe'dee-um

Trade and Other Names: Coumadin and generic brands

Functional Classification: Anticoagulant

Pharmacology and Mechanism of Action

Anticoagulant. Warfarin sodium depletes vitamin K, which is responsible for generation of clotting factors. Half-life of warfarin in animals is 36-42 hours (20-30 hours in cats).

Indications and Clinical Uses

In small animals, it has been used to treat hypercoagulation disease and prevent thromboembolism. In horses, warfarin has been used to treat navicular disease, although it is not popular for this use.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are attributable to decreased blood clotting. Spontaneous bleeding can result in blood loss, hemoperitoneum, hemothrosis, gastrointestinal bleeding, epistaxis, and excessive bleeding from trauma or surgery.

Contraindications and Precautions

Do not administer to animals that may be prone to bleeding. Administer carefully with other drugs that are known to interfere with coagulation.

Drug Interactions

Multiple drugs and some foods may affect warfarin's action. Some of these that may potentiate warfarin's action include aspirin, chloramphenicol, phenylbutazone, ketoconazole, and cimetidine. Drug interactions are possible with administration with other highly protein-bound drugs, but such reactions are poorly documented in animals. Drug interactions are also possible with trimethoprim sulfonamides and metronidazole. Do not administer with some cephalosporin drugs (particularly those with N-methylthiotetrazole [NMTT]) because cephalosporins may induce bleeding through anti-vitamin-K-dependent mechanisms.

Instructions for Use

Warfarin response can be highly variable among animals. Pharmacokinetic studies have attempted to correlate plasma pharmacokinetics with clinical response (prothrombin time [PT]). However, such a correlation has been difficult to demonstrate. A particular dose and plasma concentration that produces an effective prolongation of prothrombin time in one patient may not be effective in another individual. Because of the variation in response, adjust doses by monitoring bleeding times in treated animals. For a rapid effect, consider a loading dose of 6 mg/kg once daily for two treatments in dogs. Initial doses in cats have ranged from 0.06 to 0.09 mg/kg (0.25-0.5 mg/cat/day). When dividing tablets for treatment, it is best to crush up a whole tablet into a powder and divide the doses equally from the powder. When tablets are cut into halves or quarters, there is uneven distribution of warfarin within the tablet. Some fractions of the tablet may contain a higher amount than others.

Patient Monitoring and Laboratory Tests

Adjust dose by monitoring clotting time. Optimum dose is highly individualistic. The best method to monitor warfarin therapy is with the one-stage PT. Prothrombin times are reported in seconds and recorded as a ratio of the prothrombin time of the patient to the mean normal prothrombin time of the laboratory and as the international normalized ratio (INR). The INR is the most reliable way to monitor the prothrombin time. In animals the dose is adjusted to maintain PT at 1.5 to 2 times normal (or INR of 2-3).

Formulations

Warfarin sodium is available in 1-, 2-, 2.5-, 4-, 5-, 7.5-, and 10-mg tablets.

Stability and Storage

Warfarin sodium is soluble in water. It is light sensitive and should be packaged in tight containers. Solutions should have a pH >8 to maintain solubility. Some tablets do not have the drug distributed evenly; therefore, uneven doses can result from splitting tablets.

Small Animal Dosage

Dogs

- 0.1-0.2 mg/kg q24h PO. Start with this dose q12h for the first 2-4 days because of a lag time before maximum effect is observed.

Cats

- Start with 0.25 or 0.5 mg/cat/day and adjust dose based on bleeding time assessment.

Large Animal Dosage

Horses

- 0.02 mg/kg q24h PO (9 mg per 450 kg of body weight [1000 pounds]). Increase this dose gradually (by increments of 20%) until a 2- to 4-second increase in PT bleeding time is achieved. Allow 7 days between changes in dose.

Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 5

Xylazine Hydrochloride

zye'lah-zeen hye-droe-klor'ide

Trade and Other Names: Rompun and generic brands

Functional Classification: Alpha₂-adrenergic agonist, analgesic, sedative

Pharmacology and Mechanism of Action

Alpha₂-adrenergic agonist. Alpha₂-agonists decrease release of neurotransmitters from the neuron. They decrease transmission via binding to presynaptic alpha₂-receptors (negative feedback receptors). The result is decreased sympathetic outflow, analgesia, sedation, and anesthesia. Other drugs in this class include medetomidine, dexmedetomidine, romifidine, detomidine, and clonidine. Xylazine is not as specific as other drugs in this group. Receptor binding studies indicate that alpha₂/alpha₁-adrenergic receptor selectivity was 1620 for medetomidine and 160 for xylazine.

Indications and Clinical Uses

Xylazine is used for short-term sedation, anesthesia, and analgesia in horses, dogs, cats, cattle, and exotic animals. Like other alpha₂-agonists, it is used as an anesthetic adjunct and analgesic. The duration of effect is approximately 30 minutes. Compared to xylazine, dexmedetomidine and medetomidine produce better sedation and analgesia than xylazine in dogs. Romifidine produces the longest duration of sedative effects, followed by detomidine, medetomidine, and xylazine.

Precautionary Information

Adverse Reactions and Side Effects

In small animals, vomiting is the most common acute effect, which is more prominent in cats. Xylazine produces sedation and ataxia. Xylazine, like other alpha₂-agonists, decreases sympathetic output. Cardiovascular depression may occur. Cardiac effects can include sinoatrial block, first- and second-degree AV block, bradycardia, and sinus arrhythmia. In ruminants, use of xylazine may decrease GI motility and cause bloating, salivation, and regurgitation. Note that cattle, sheep, and goats are much more sensitive to xylazine than other animals, which requires lowering the dose. Like other alpha₂-agonists, xylazine produces transient hyperglycemia, which may increase urine flow.

Contraindications and Precautions

Ruminants are much more sensitive to xylazine than other species, and lower doses must be used compared with other animals. Use cautiously in animals that are pregnant. Xylazine impairs blood flow to the uterus during gestation in cows and may decrease oxygen delivery to fetus, especially in late gestation. Use caution when using xylazine to sedate pregnant cows. It also may induce labor. Use cautiously, if at all, in patients with cardiac disease. Because of cardiac depression, it should not ordinarily be used with tranquilizers such as phenothiazines. Reverse effects of xylazine with an alpha₂-antagonist (e.g., yohimbine or atipamezole) if there are dangerous adverse effects.

Drug Interactions

Use with opioid analgesic drugs will greatly enhance the CNS depression. Consider lowering doses if administered with opioids. Do not administer with other drugs that cause significant cardiac depression.

Instructions for Use

Xylazine is often used in combination with other drugs (e.g., ketamine or butorphanol). It is not necessary to premedicate animals with atropine. For large animals, if sedation is needed without recumbency, use the lower end of the dose range.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during anesthesia with xylazine. It may cause increased plasma glucose in animals.

Formulations Available

Xylazine is available in 20- and 100-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs

- 1.1 mg/kg IV.
- 2.2 mg/kg IM.
- Short-term treatment of pain: 0.1-0.5 mg/kg IM, IV, or SQ.

Cats

- 1.1 mg/kg IM.
- Emetic dose: 0.4-0.5 mg/kg IV.
- Short-term treatment of pain: 0.1-0.5 mg/kg IM, IV, or SQ.

Large Animal Dosage

Horses

- 1-2 mg/kg IM.
- 0.5-1.1 mg/kg IV.
- For colic pain: 0.3-0.5 mg/kg IV (150-250 mg IV for average-size horse).

Pigs

- 0.5-3 mg/kg IM. (Use in combination with other drugs in swine (e.g., 2 mg/kg xylazine + 10 mg/kg ketamine, administered IM). It is unreliable alone.)

Cattle

- 0.1-0.2 mg/kg IM.
- 0.03-0.1 mg/kg IV.

Sheep

- 0.1-0.3 mg/kg IM.
- 0.05-0.1 mg/kg IV.

Goats

- 0.05-0.5 mg/kg IM.
- 0.01-0.5 mg/kg IV.

Regulatory Information

Withdrawal time for cattle: At doses of 0.016-0.1 mg/kg, 5 days meat and 72 hours milk. At doses of 0.05-0.3 mg/kg, 10 days meat and 120 hours milk. In Canada it is listed as 3 days for meat and 48 hours for milk, whereas in the UK it is listed as 14 days for meat and 48 hours for milk. (If yohimbine is used as reversal, use withdrawal time of 7 days meat and 72 hours milk.)

RCI Classification: 3

Yohimbine

yoe-him' been

Trade and Other Names: Yobine

Functional Classification: Alpha₂-receptor antagonist

Pharmacology and Mechanism of Action

Alpha₂-adrenergic antagonist. It antagonizes the action of other drugs that stimulate the alpha₂-receptor.

Indications and Clinical Uses

Yohimbine is used primarily to reverse actions of xylazine or detomidine.

Atipamezole is another alpha₂-antagonist that is more specific and is preferred to use in small animals to reverse dexmedetomidine or medetomidine.

Precautionary Information

Adverse Reactions and Side Effects

High doses can cause tremors and seizures.

Contraindications and Precautions

When administering to reverse an alpha₂-agonist, monitor heart rate and rhythm carefully during treatment.

Drug Interactions

No drug interactions are reported, except the antagonism of alpha₂-agonists.

Instructions for Use

Reverses signs of sedation and anesthesia caused by alpha₂-agonists.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during use of yohimbine.

Formulations

Yohimbine is available in a 2-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

- 0.11 mg/kg IV.
- 0.25-0.5 mg/kg SQ or IM.

Large Animal Dosage

Cattle and Sheep

- To reverse xylazine or medetomidine: 0.125-0.2 mg/kg IV.

Regulatory Information

Food animal withdrawal time: At least 7 days for meat and 72 hours for milk.

RCI Classification: 2

Zidovudine

zye-doe'vyoo-deen

Trade and Other Names: Retrovir

Functional Classification: Antiviral

Pharmacology and Mechanism of Action

Antiviral drug. Zidovudine (AZT) acts to inhibit the viral enzyme reverse transcriptase that prevents conversion of viral RNA into DNA. Other drugs in this class include lamivudine, didanosine, and zalcitabine.

Indications and Clinical Uses

In people, AZT is used to treat HIV (AIDS). In animals, it has been experimentally used for treatment of feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) infection in cats. In cats, doses of 25 mg/kg q12h IV or PO produced drug concentrations in the effective range. However, efficacy in cats has been controversial and disappointing (less effective than expected).

Precautionary Information

Adverse Reactions and Side Effects

Anemia and leucopenia have been observed in treated animals. It has not been used often in animals; therefore, a full range of potential adverse effects has not been reported.

Contraindications and Precautions

No contraindications are reported for animals.

Drug Interactions

No drug interactions have been reported in animals.

Instructions for Use

At this time, experience with using AZT for treating viral disease in animals is largely experimental or anecdotal. This drug may help some cats with FIV and may prevent persistent FeLV, but documentation of efficacy is lacking.

Patient Monitoring and Laboratory Tests

Monitor the packed-cell volume (PCV) in treated cats and perform a CBC periodically.

Formulations

AZT is available in a 10-mg/mL syrup and a 10-mg/mL injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Cats

- 15 mg/kg q12h PO, up to 20 mg/kg q8h PO.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.

Zilpaterol Hydrochloride

Zil-pat'-e-role

Trade and Other Names: Zilmax

Functional Classification: Beta-adrenergic agonist

Pharmacology and Mechanism of Action

Zilpaterol is a synthetic beta (β)-receptor adrenergic agonist. It resembles other β -agonists in some actions to produce effects similar to norepinephrine. Zilpaterol is administered to cattle, in feed, as a growth promotant, and to improve feed efficiency. Zilpaterol, like other β -adrenergic agonists, stimulate β_2 -adrenergic receptors in muscle and promote muscle gain with less fat. Subsequently, if fed to cattle at approved levels, zilpaterol increases feed efficiency and improves muscle weight gain. In clinical studies, it substantially increased skeletal muscle mass and cross-sectional area of individual muscles.

Indications and Clinical Uses

Zilpaterol is fed to cattle (Type A medicated feed) to improve weight gain and muscle mass. It has been approved in other countries for several years and recently has been approved for use in the US.

Precautionary Information

Adverse Reactions and Side Effects

Like other β -adrenergic agonists, zilpaterol can produce cardiovascular problems associated with increased stimulation of receptors at high doses.

Contraindications and Precautions

Severe adverse effects such as tachycardia, tremors, and muscle fasciculations have been observed in horses. Zilpaterol should not be administered to horses, and precautions should be taken to ensure that horses are not accidentally exposed to zilpaterol-treated cattle feed.

Because β -adrenergic agonists such as clenbuterol are abused in humans for the purpose of promoting muscle gain and fat loss, there is a possibility that zilpaterol also could be abused in the same manner.

Labeling should include the following information: (a) Do not allow horses or other equines access to feed containing zilpaterol. (b) Not for use in animals intended for breeding. (b) Do not use in veal calves.

Drug Interactions

Use caution when administering to animals receiving other adrenergic medications.

Instructions for Use

Zilpaterol is used to increase rate of weight gain, improve feed efficiency, and increase carcass leanness in cattle fed in confinement for slaughter during the last 20 to 40 days on feed. It should be fed continuously as the sole ration during the last 20 to 40 days on feed.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

Type A medicated articles containing 21.77 g zilpaterol hydrochloride per pound.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

- No small animal dose is established. No established uses for small animals.

Large Animal Dosage

Do not administer to horses.

Cattle dose: 6.8 g/ton of feed to provide 60 to 90 mg zilpaterol hydrochloride per head per day.

Regulatory Information

Cattle withdrawal time for slaughter: 3 days.

Zinc

Trade and Other Names: Zinc

Functional Classification: Nutritional supplement

Pharmacology and Mechanism of Action

Zinc is an essential element important in more than 200 metalloenzymes. It also is important for nucleic acid, cell membrane, and protein synthesis. It is also important for growth, tissue repair, and cell division. Zinc acts as a chelating agent, and it competes with iron to inhibit fibrosis and collagen formation. The benefits have been seen in experimental animals and in humans with liver disease. One of the uses has been to manage hepatic cirrhosis. Zinc also may act as an antioxidant and prevent membrane damage. Zinc also induces the production of metallothionein in intestinal mucosal cells, which binds copper from the diet and prevents uptake to the liver.

Indications and Clinical Uses

It has been used to treat zinc-deficient diseases such as those that cause dermatologic problems. It is also used as an antifibrotic agent in liver disease. One of the other uses of zinc is as a chelating agent in animals. Most commonly, zinc has been used as a cupruritic to decrease copper concentrations in animals with liver disease, often in combination with other drugs (e.g., penicillamine). When used to treat copper liver disease, it is slow acting and may take as long as 3 months for the full effect.

Precautionary Information

Adverse Reactions and Side Effects

The most common effect is GI problems, including nausea and vomiting. Hemolysis and anemia can be observed with high doses.

Contraindications and Precautions

If intravenous forms are used (e.g., zinc sulfate), adverse effects may be more likely because ordinarily the oral absorption is more limited.

Drug Interactions

Oral absorption is impaired from tetracyclines, iron, copper, phytates (found in bran and grains), and penicillamine.

Instructions for Use

Administer without food to improve oral absorption, but a small meal will often prevent some of the nausea associated with treatment. When considering various forms, the gluconate form may be better tolerated than the sulfate or acetate form.

Patient Monitoring and Laboratory Tests

Monitor blood zinc concentrations at least monthly to prevent high levels, which cause hemolysis. Blood zinc concentrations should ideally be 200 to 500 mcg/dL. A concentration above 800 mcg/dL is considered toxic, but levels above 200 mcg/dL are needed to treat copper liver disease.

Formulations

Zinc is available in several forms, including zinc sulfate (23% zinc), zinc gluconate (14% zinc), and zinc acetate (35% zinc). Zinc gluconate is available in tablets ranging from 1.4 to 52 mg (10 mg zinc gluconate = 1.4 mg of elemental zinc). Zinc sulfate is available in capsules 25- and 50-mg elemental zinc (110 mg zinc sulfate = 25 mg elemental zinc). Zinc sulfate is available in tablets: 15, 25, 45, and 50 mg (elemental zinc, 66 mg zinc sulfate = 15 mg elemental zinc). Injectable zinc sulfate is 50-mg/mL (20.2 mg elemental zinc per mL) solution for IV use.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage

Dogs and Cats

Adjust dose based on measuring plasma zinc concentrations.

- Hepatic disease in dogs: 100 mg elemental zinc per dog, q12h, PO, or 3 mg zinc gluconate/kg per day, or 2 mg zinc sulfate/kg per day, PO. (Consider including vitamin E with treatment.)
- Zinc supplement: 1 mg/kg elemental zinc of gluconate or sulfate three times/day PO, or 1.5 to 3 mg (of elemental zinc) zinc acetate daily per animal PO.
- Dermatologic use: 10 mg/kg daily (zinc sulfate or zinc gluconate).
- Intravenous zinc treatment: 50 mcg elemental zinc/kg infused IV slowly per day.

Large Animal Dosage

No specific doses have been reported. Extrapolate dose needed from small animal use (approximately 1 mg/kg elemental zinc three times per day PO) and adjust dose by monitoring zinc concentrations.

Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Zoledronate

Zoe'-le-droe-nate

Trade and Other Names: Zometa, Zoledronic acid

Functional Classification: Antihypercalcemic

Pharmacology and Mechanism of Action

Bisphosphonate drug. Zoledronate is zoledronic acid (Zometa). Drugs in this class include pamidronate, etidronate, tiludronate, and alendronate. These drugs are a group of drugs characterized by a germinal aminobisphosphonate bond. They slow the formation and dissolution of hydroxyapatite crystals. Their clinical use resides in their ability to inhibit bone resorption. These drugs decrease bone turnover by inhibiting osteoclast activity, inducing osteoclast apoptosis, retarding bone resorption, and decreasing the rate of osteoporosis. Inhibition of bone resorption is via inhibition of the mevalonate pathway. In dogs, after infusion the half-life was approximately 2.2 hours, with a volume of distribution of 0.28 L/kg.

Indications and Clinical Uses

Zoledronate, like other bisphosphonate drugs, is used to treat refractory hypercalcemia, osteoporosis, and treatment of hypercalcemia of malignancy. In animals, bisphosphonates are helpful for managing neoplastic complications and pain associated with pathologic bone resorption. They also may provide pain relief in patients with pathologic bone disease. It has been used in similar protocols as for pamidronate but has the advantage of a 15-minute infusion IV rather than 2-4 hours for pamidronate.

Precautionary Information

Adverse Reactions and Side Effects

Zoledronate may be safer than pamidronate. Fever, joint pain, and myalgias have been observed in people, but otherwise no serious adverse effects have been identified. The use in animals has not been common enough to identify a wider range of adverse effects. In people, there is some concern that the use of bisphosphonates produces excessive mineralization and hardening of the bone, which may result in a greater risk of fractures. However, this effect has not been reported for animals.

Contraindications and Precautions

Do not administer during pregnancy.

Drug Interactions

Do not mix with calcium or other divalent cation-containing infusion solutions, such as lactated Ringer's solution. It should be administered as a single intravenous solution in a line separate from other drugs.

Instructions for Use

Zoledronate is intended for IV infusion. Dilute vial in 0.9% saline or 5% dextrose solution for IV use. If not used immediately after dilution, the solution should be refrigerated, and the refrigerated solution then should be equilibrated to room temperature prior to administration. The total time between dilution, storage in the refrigerator, and end of administration must not exceed 24 hours.

822 Zonisamide

Patient Monitoring and Laboratory Tests

Monitor serum calcium and phosphorus. Monitor urea nitrogen, creatinine, urine-specific gravity, and food intake in treated animals.

Formulations

Zoledronate is available in a 4 mg per 5 mL vial for infusion.

Stability and Storage

Store in a vial at room temperature. Vials may be diluted in fluid solutions. Storage and stability information is listed in the Instructions for Use section.

Small Animal Dosage

Dogs

- 0.2-0.25 mg/kg IV infused over 15 minutes, diluted in 100 mL 0.9% saline (large dogs) or 50 mL 0.9% saline (small dogs).

Cats

- 0.2 mg/kg IV over 15 minutes diluted in a volume of 25 mL every 21-28 days.

Large Animal Dosage

No doses have been reported for large animals.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Zonisamide

zoe-nis'a-mide

Trade and Other Names: Zonorgan

Functional Classification: Anticonvulsant

Pharmacology and Mechanism of Action

Anticonvulsant. Mechanism of action is uncertain, but it may potentiate the action of GABA, an inhibitory neurotransmitter, or it may stabilize membranes and suppress propagation of seizures from an epileptic foci via changes in sodium and calcium conductance. Half-life in dogs has been reported to be approximately 15 hours in one study and 16 hours (plasma) to 57 hours (red blood cells [RBCs]) in another study. In cats, the half-life is longer than in dogs (33 hours).

Indications and Clinical Uses

Zonisamide is used to treat refractory seizures in dogs when other drugs have not been effective. It has been effective in experimentally induced seizures in dogs and in approximately 50% of dogs with refractory epilepsy. It has been used as an add-on with other anticonvulsant drugs such as phenobarbital and potassium bromide.

Precautionary Information

Adverse Reactions and Side Effects

At the suggested clinical doses, adverse effects have not been reported for dogs. Adverse reactions can include lethargy, ataxia, and vomiting. Like other

anticonvulsants, ataxia, sedation, and CNS changes are possible. In safety studies, beagles received 75 mg/kg/day for 1 year with minimal side effects. In cats, adverse effects include mild gastrointestinal problems, sedation, and ataxia.

Contraindications and Precautions

Because zonisamide resembles sulfonamides in structure, use cautiously in animals that are sensitive to these drugs. (See sulfonamide manuscripts for full details on sulfonamide adverse effects.)

Drug Interactions

When administered concurrently with phenobarbital, the half-life of elimination is more rapid for zonisamide, which may necessitate higher doses. It is expected to potentiate other CNS depressants and anticonvulsants.

Instructions for Use

Most experience with zonisamide in animals has been preliminary work in dogs with refractory epilepsy. Although low doses may produce plasma concentrations within the therapeutic range reported for people, when administered with phenobarbital, drug concentrations may be lower because drug metabolism is increased. Zonisamide half-life was shorter in dogs receiving phenobarbital concurrently. These observations indicate that higher doses may be needed for combination therapy with phenobarbital compared to monotherapy. With chronic treatment some tolerance that reduces efficacy after 2-3 months may develop.

Patient Monitoring and Laboratory Tests

Effective plasma concentrations in animals have been suggested to be 10-40 mcg/mL.

Formulations

Zonisamide is available in 25-, 50-, and 100-mg capsules.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

Small Animal Dosage

Dogs

- 10 mg/kg q12h PO.

Cats

- Dose regimens have not been defined in cats, but 10 mg/kg have been used in experimental cats.

Large Animal Dosage

No dose has been reported for large animals.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

APPENDIX A

Calculation of Drug Doses

How to Calculate Milliliters (mL) Needed

Dose (mg/kg) × kilograms body weight = total dose needed (mg)

Strength of solution (mg/mL) = (% strength) × 10

$$\frac{\text{Total dose needed}}{\text{Strength of solution (mg/mL)}} = \text{mL needed}$$

Example

20 kg dog needs 15 mg/kg of a 20% solution

20 kg × 15 mg/kg = 300 mg total dose needed

Strength of solution = 20% × 10 = 200 mg/mL

mL needed = 300 mg / 200 mg/mL = 1.5 mL

How to Calculate Tablets Needed

Dose (mg/kg) × kilograms body weight = total dose needed (mg)

$$\frac{\text{Total dose needed}}{\text{Strength of tablet}} = \text{Number of tablets needed}$$

Example

20 kg dog needs 12 mg/kg

Tablet size is 100 mg

20 kg × 12 mg/kg = 240 mg total dose needed

240 mg / 100-mg tablets = 2.4 tablets

(In most instances, you would round up to 2½ tablets if the medication has sufficient safety.)

How to Calculate Infusion Rates

Dose (mg/kg/min) × kilograms body weight = total dose needed (mg) per minute

If dose is listed in micrograms/kg/min, multiply by 1000 for mg/kg/min.

Strength of solution (mg/mL) = (% strength) × 10

$$\frac{\text{Total dose needed per minute}}{\text{Strength of solution (mg/mL)}} = \text{mL needed per minute}$$

mL needed per minute × 60 = mL needed per hour

Administer the total mL to fluid administered in each hour interval. If fluid is to be administered over 24 hours: mL needed per hour × 24 = mL needed per day.

Example:

- 20 kg dog needs 0.15 mg/kg/min (150 mcg/kg/min) of a 10% solution
- Fluid rate (lactated Ringer's solution) is 60 mL/kg/day
- 20 kg × 0.15 mg/kg/min = 3.0 mg needed per minute
- Strength of solution = 10% × 10 = 100 mg/mL

- mL needed per min = $(3.0 \text{ mg per min})/100 \text{ mg/mL} = 0.03 \text{ mL per min}$
- $0.03 \text{ mL per minute} \times 60 \text{ min/hr} = 1.8 \text{ mL added to each hour of fluids}$
- Fluid rate is $60 \text{ mL/kg/day} = 2.5 \text{ mL/kg/hr} = 50 \text{ mL/hr}$ for a 20-kg dog.

To each 50 mL/hr fluid volume to be infused, add 1.8 mL of medication. If drug is stable in solution for 24 hours, total amount can be added to a 24-hour volume of fluid:

Total fluid needed per 24 hours = $60 \text{ mL/kg/day} \times 20 \text{ kg} = 1200 \text{ mL}$

$1.8 \text{ mL per hour} \times 24 \text{ hr} = 43.2 \text{ mL per day added to } 1200 \text{ mL total fluid requirement.}$

APPENDIX B

Controlled Substance Charts: United States and Canada

Drug Examples	United States*
Heroin, LSD, peyote, marijuana, mescaline	Schedule I <ul style="list-style-type: none">• High abuse potential• No currently accepted medical use• No veterinary uses identified
Morphine and morphine derivatives and synthetic opioids. Drugs used in veterinary medicine include morphine, meperidine, etorphine, hydrocodone, hydromorphone, oxymorphone, codeine (in some forms), and pentobarbital.	Schedule II <ul style="list-style-type: none">• High abuse potential; potentially severe psychologic or physical dependence• Currently accepted medical use but may be severely restricted• Telephone orders to a pharmacy are allowed only in emergencies if written Rx follows promptly• No refills allowed
Drugs used in veterinary medicine include anabolic steroids (stanozolol, oxymetholone, testosterone, methyltestosterone, boldenone, trenbolone), barbiturates (thiamylal, thiopental), opioids (burpenorphine and codeine in some forms), and ketamine and derivatives (ketamine and tiletamine + zolazepam).	Schedule III <ul style="list-style-type: none">• Abuse potential less than the drugs/substances in Schedules I and II; potentially moderate or low physical dependence or high psychologic dependence• Currently accepted medical use• Telephone orders to pharmacy permitted• Veterinarian may authorize limited refills
Drugs used in veterinary medicine include opioids (butorphanol and pentazocine), benzodiazepines (diazepam, oxazepam, midazolam, clonazepam, clorazepate, and alprazolam), and phenobarbital	Schedule IV <ul style="list-style-type: none">• Abuse potential relative to drugs/substances in Schedule III; potentially limited to physical or psychologic dependence• Currently accepted medical use• Telephone orders to pharmacy permitted• Veterinarian may authorize limited refills
Codeine preparations used as antitussives and some opioids used as antidiarrheals (e.g., diphenoxylate)	Schedule V <ul style="list-style-type: none">• Lowest abuse potential; potentially very limited physical or psychologic dependence• Currently accepted medical use• Veterinarian can determine refills• Some products containing limited amounts of Schedule V substances (e.g., cough suppressants) available OTC

*Complete list for the United States can be located at www.justice.gov/dea/pubs/scheduling.html.

Drug Examples	Canada
Sedatives such as barbiturates and derivatives (secobarbital), thiobarbiturates (pentothal sodium); anabolic steroids	<p><i>Part G of the Food and Drug Regulation (FDR)</i></p> <ul style="list-style-type: none"> • Controlled drugs • Misuse potential • Verbal and written prescriptions under certain conditions • Only prescribed if required for medical condition • Specified number of refills (conditions apply) • Records must be kept • May be administered under emergency situations (conditions apply)
Amphetamines	<p><i>Part G of the FDR</i></p> <ul style="list-style-type: none"> • Designated controlled drug • May be used for designated medical conditions outlined in FDR
Benzodiazepine tranquilizers, such as diazepam and lorazepam	<p><i>Benzodiazepines and Other Targeted Substances Regulations</i></p> <ul style="list-style-type: none"> • Misuse potential • Verbal and written prescriptions under certain conditions • Only prescribed if required for medical condition • Specified number of refills (conditions apply) • Records must be kept • May be administered under emergency situations (conditions apply)
Opiates: heroin, morphine, codeine (in some forms) and analgesics such as pentazocine and fentanyl	<p><i>Narcotic Control Regulation</i></p> <ul style="list-style-type: none"> • High misuse potential • Written prescriptions for specific medical conditions† • Records of opiate prescription file must be kept • No refills (limited amounts in a prescription) • Heroin and methadone are subject to specific controls
LSD, mescaline (peyote), harmaline, psilocin, and psilocybin (magic mushrooms)	<p><i>Part J of the FDR</i></p> <ul style="list-style-type: none"> • Considered “restricted drugs” • High misuse potential • No recognized medical use • Marijuana exemption from FDR, if produced for medical reasons

†Verbal prescriptions are permitted for certain opioid preparations (such as Tylenol No. 2 and No. 3) but not for opiate alone or opiates with one other active nonopioid ingredient.

APPENDIX C

Drugs for Infections Commonly Seen in Small Animals

Infection Site	First-Choice Drugs	Alternate-Choice Drugs
Skin: pyoderma or other skin infection	Amoxicillin-clavulanate Cephalosporin†	Trimethoprim-sulfonamides‡ Fluoroquinolone* Clindamycin Lincomycin
Urinary tract	Cephalosporin† Amoxicillin/ampicillin Amoxicillin-clavulanate	Trimethoprim-sulfonamides‡ Fluoroquinolone* Tetracycline
Respiratory tract	Amoxicillin-clavulanate Fluoroquinolone* Cephalosporin†	Macrolide (erythromycin, azithromycin) Aminoglycosides (amikacin, gentamicin) Doxycycline Clindamycin
Septicemia¶	Amoxicillin-clavulanate Cephalosporin*	Trimethoprim-sulfonamides‡ Chloramphenicol Extended-spectrum cephalosporin§
Bone and joint	Fluoroquinolone* Cephalosporin† Amoxicillin-clavulanate	Aminoglycoside Extended-spectrum cephalosporin§ Trimethoprim-sulfonamides‡ Clindamycin
Intracellular pathogens	Doxycycline Fluoroquinolone*	Extended-spectrum cephalosporin§ Fluoroquinolone* Azithromycin Clindamycin

*Fluoroquinolone = enrofloxacin, difloxacin, marbofloxacin, or orbifloxacin (difloxacin not registered for cats).

†Cephalosporin = cephalexin, cefpodoxime proxetil, cefadroxil or cefovecin.

‡Trimethoprim-sulfonamides = trimethoprim-sulfadiazine, trimethoprim-sulfamethoxazole or ormetoprim-sulfadimethoxine.

§Extended-spectrum cephalosporin = second-generation or third-generation drugs (e.g., cefotetan, ceftazidime, ceftaxitin, cefotaxime).

¶Combinations of drugs are often used in acute febrile septicemia. Such combinations may include a beta-lactam plus an aminoglycoside or a fluoroquinolone plus amoxicillin-clavulanate.

APPENDIX D

Antibiotic Drug Selection for Equine Bacterial Pathogens

Pathogen	Drug Choice	Alternate Choice
Gram-Positive		
<i>Rhodococcus equi</i>	Erythromycin ± Rifampin; Azithromycin	Clarithromycin
<i>Streptococcus</i> spp.	Penicillin G, Ampicillin, Ceftiofur	Trimethoprim-Sulfonamides, Erythromycin, Chloramphenicol
<i>Staphylococcus aureus</i>	Trimethoprim/ Sulfonamide	Enrofloxacin, Orbifloxacin, Chloramphenicol, Gentamicin
Gram-Negative		
<i>Escherichia coli</i>	Gentamicin, Amikacin	Ceftiofur, Enrofloxacin, Orbifloxacin, Marbofloxacin, Trimethoprim/Sulfonamide
<i>Klebsiella pneumoniae</i>	Gentamicin, Amikacin	Ceftiofur, Enrofloxacin, Orbifloxacin, Marbofloxacin, Trimethoprim/Sulfonamide
<i>Enterobacter</i> spp.	Gentamicin, Amikacin	Ceftiofur, Enrofloxacin, Trimethoprim/Sulfonamide
<i>Pseudomonas aeruginosa</i>	Gentamicin, Amikacin, Ticarcillin	Enrofloxacin, Cefepime, Ceftazidime
<i>Pasteurella</i> spp.	Ampicillin, Ceftiofur, Trimethoprim/ Sulfonamide	Enrofloxacin, Orbifloxacin, Marbofloxacin, Chloramphenicol, Tetracycline
<i>Actinobacillus</i> spp.	Ampicillin, Penicillin, Trimethoprim/ Sulfonamides	Enrofloxacin, Amikacin, Gentamicin, Ceftiofur
Anaerobes		
<i>Clostridium</i> , <i>Fusobacterium</i> , <i>Peptostreptococcus</i> , <i>Bacteroides</i> spp.	Metronidazole, Penicillin G	Chloramphenicol, Cefotetan (injectable) or Cefoxitin (injectable)
Other		
<i>Lawsonia intracellularis</i>	Oxytetracycline, Doxycycline (oral only)	Chloramphenicol, Erythromycin, Clarithromycin, Azithromycin
<i>Ehrlichia</i>	Oxytetracycline, Doxycycline (oral only)	Chloramphenicol
<i>Neorickettsia risticii</i> (Potomac horse fever)	Oxytetracycline, Doxycycline (oral only)	

APPENDIX E

Drugs That May Induce Cytochrome P-450 Enzymes

- Alcohol
- Chlorinated hydrocarbons
- Diazepam (Valium)
- Diphenhydramine
- Estrogens
- Griseofulvin
- Hyperthyroidism
- Pentobarbital
- Phenobarbital
- Phenylbutazone
- Phenytoin (Dilantin)
- Progestogens
- Rifampin
- St. John's wort

APPENDIX F

Drugs That May Inhibit Cytochrome P-450 Enzymes

- Amiodarone
- Chloramphenicol
- Cimetidine
- Cisapride
- Clarithromycin
- Cyclophosphamide
- Diltiazem
- Erythromycin
- Felbamate
- Fluoroquinolones
- Interferon (vaccines)
- Itraconazole
- Ketoconazole
- Omeprazole
- Organophosphates
- Phenylbutazone
- Quinidine
- Tetracycline
- Verapamil
- Voriconazole

APPENDIX G

Drugs That May Inhibit the P-Glycoprotein Membrane Transporter Coded by *ABCB1* (also known as *MDR1*)

- Bromocriptine
- Carvedilol
- Chlorpromazine
- Cyclosporine
- Erythromycin
- Fluoxetine
- Grapefruit juice
- Itraconazole
- Ketoconazole
- Methadone
- Paroxetine
- Pentazocine
- Quinidine
- St. John's wort
- Tamoxifen
- Verapamil

APPENDIX H

Drugs That Are Substrates for the P-Glycoprotein Membrane Transporter Coded by *ABCB1* (also known as *MDR1*)

- Aldosterone
- Amitriptyline
- Cortisol
- Cyclosporine
- Dexamethasone
- Digoxin
- Diltiazem
- Doxorubicin
- Doxycycline
- Erythromycin
- Itraconazole
- Ivermectin
- Ketoconazole
- Levofloxacin
- Loperamide
- Methylprednisolone
- Morphine
- Ondansetron
- Phenothiazines
- Tacrolimus
- Terfenadine
- Tetracycline
- Verapamil
- Vinblastine
- Vincristine

APPENDIX I

Fluid Solutions for Intravenous Use

Solution Type	Na ⁺ (mEq/L)	K ⁺ (mEq/L)	Cl ⁻ (mEq/L)	Ca ⁺⁺ (mEq/L)	Mg ⁺⁺ (mEq/L)	Buffer (mEq/L)	Osmolality (mOsm/L)	pH
Ringer's solution	147	4	156	4	0	0	310	5-7.5
Lactated Ringer's solution	130	4	109	3	0	28 (lactate)	275	6-7.5
0.9 % NaCl	154	0	154	0	0	0	308	4.5
5% dextrose	0	0	0	0	0	0	252	4-6.5
2.5% dextrose/0.45% NaCl	77	0	77	0	0	0	280	4.5
Plasma-Lyte	140	5	98	0	3	27 (acetate)	294	4-6.5
Dextran 6% and 0.9% NaCl	154	0	154	0	0	23 (gluconate)	310	3.0-7.0
Hetastarch	154	0	154	0	0	0	309	5.5
Pentastarch	154	0	154	0	0	0	326	5.0
Hemoglobin glutamer (Oxyglobin)							300	7.8
Normosol-R	140	5	98	0	3	27 (acetate) 23 (gluconate)	294	6.6

APPENDIX J

Compounded Formulations: What to Look for to Detect Incompatibility or Instability

Liquid-Dose Forms

- Color change (pink or amber)
- Signs of microbial growth
- Cloudiness, haze, flocculent or film formation
- Separation of phases (e.g., oil and water, emulsion)
- Precipitation, clumping, crystal formation
- Droplets or fog forming on inside of container
- Gas or odor release
- Swelling of container

Solid-Dose Forms

- Odor (sulfur or vinegar odor)
- Excessive powder or crumbling
- Cracks or chips in tablets
- Swelling of tablets or capsules

“Rules”

- Do not mix drugs that require reconstitution in a vial with other drugs, and do not add other drugs to the vial.
- Do not mix drugs that are not in an aqueous vehicle (e.g., propylene glycol) with IV fluids.
- Do not mix hydrochloride salts (HCl) or drugs with buffers (citrates, bicarbonates, phosphates).
- Beyond-use-date for compounded drugs (the date after which a compounded preparation is not to be used) is 14 days for water-containing formulations (refrigerated); 6 months for nonaqueous liquids and solid formulations; and 60 days for other formulations. These times may be exceeded if there is valid scientific stability information.

APPENDIX K

Prescription Writing Reference ... Do's and Don'ts

Veterinarian Information

Always Include

Prescribing veterinarian's name
Practice address
Practice telephone number
DEA # (if written for a controlled substance)
Current date
Rx

- **Drug Name:** (Print FULL brand name or generic name ... NEVER abbreviate)
- **Dosage Form:** (Specify tablet, capsule, suspension, other)
- **Strength:** (mg, g, µg, etc.) or concentration (mg/ml) ... Use metric units and use mcg for µg whenever possible
- **Total Quantity:** (# 10 [for 10 tablets]; 60 mL)
- **Sig:** *Include the following:* Dose (individual), route, frequency; duration, indication or use
- **Number of Refills:** Define the number legally permitted
- **Designate:** Whether or not generic substitution is permissible
- **Signature**

Owner Information

Always Include

- Patient's name (in "quotes")
- Patient's age or date of birth
- Owner's name (or that of an owner representative)
- Owner's address
- Owner's phone number

Common Prescription Writing Errors to Avoid

- Always use metric units: e.g., g (gram) for solids; ml or mL (milliliter) for liquids.
- Use per instead of a slash (/), which can be interpreted as the number 1.
- Use units instead of the abbreviation u, which can be interpreted as 0 or 4 or m.
- Use once daily instead of sid, which has been interpreted as 5/d or 5 per day. (NOTE: "sid" is not a conventional prescription abbreviation.)
- Use three times daily instead of tid, and use four times daily instead of qid.
- Use every other day instead of qod.
- AVOID CONFUSING ABBREVIATIONS—abbreviations like qd, qid, and qod are easily confused with each other
- **When writing numbers:**
 - Use a leading zero with decimals (e.g., use 0.5 mL rather than .5 mL).
 - Avoid using a trailing zero (e.g., use 3 rather than 3.0).
 - ALWAYS—When in doubt, spell it out.

APPENDIX L

How to Report an Adverse Drug Reaction

1. Phone the drug sponsor to report an Adverse Drug Experience (ADE) if it is an FDA-approved animal drug. Obtain drug sponsor phone numbers from the product label or from the company's Web site. When phoning the pharmaceutical company, inform them that you wish to speak with a veterinarian on their staff to report an adverse drug experience.

Contact the FDA and complete Form 1932a. This form may be completed regardless of whether the drug is an animal-approved drug or human-approved drug. The FDA can be contacted from their Web site at www.fda.gov/AnimalVeterinary/SafetyHealth.

The FDA also may be contacted at this address:

ADE Reporting System
Center for Veterinary Medicine
U.S. Food & Drug Administration
7500 Standish Place
Rockville, MD 20855-2773
Telephone: 1-888-FDA-VETS (888-332-8387)

When completing Form 1932a, supply as much history and clinical data as possible, including concurrent medications administered to the animal.

2. **Animal Biologics: Vaccines, Bacterins:**

Contact the U.S. Department of Agriculture (USDA) Center for Veterinary Biologics (CVB):

Fax to (515) 337-6120 or telephone (800) 752-6255, or visit their Web site at www.aphis.usda.gov/animal_health/vet_biologics/vb_adverse_event.shtml.

3. **Pesticides: Topically Applied External Parasiticides**

Contact the U.S. Environmental Protection Agency (EPA)
(800) 858-PEST (800-858-7378)

www.epa.gov/pesticides/

or

<http://pi.ace.orst.edu/vetrep/>

APPENDIX M

Drugs Prohibited from Use in Food-Producing Animals

Because they present a risk to public health, the following drugs are prohibited in food-producing animals:

Chloramphenicol

Clenbuterol

Diethylstilbestrol (DES)

Dimetridazole

Furazolidone

Nitrofurazone (and other nitrofurans)

Fluoroquinolones (extralabel use)

Glycopeptide antibiotics (e.g., vancomycin)

Ipronidazole (and other nitroimidazoles)

Phenylbutazone in female dairy cattle > 20 months of age

Sulfonamide drugs in lactating dairy cattle*

Adamantane and neuraminidase inhibitor classes of drugs approved for treating or preventing influenza A are prohibited therapy in chickens, turkeys, and ducks.

*With the exception of sulfadimethoxine, sulfabromomethazine, and sulfaethoxypradazine, approved for use in some feeds.

APPENDIX N

Performance Horse Drug Regulations and Restrictions *Association of Racing Commissioners International, Inc., Uniform Classification Guidelines for Foreign Substances (Revised January 2010)*

The following definitions, regulations, and restrictions are adapted from the Racing Commissioners International web site: www.arci.com, and FEI Clean Sport Prohibited Substances List: <http://www.feicleansport.org/>.

RCI Drug Classification Scheme is based on (1) pharmacology, (2) drug use patterns, and (3) the appropriateness of a drug for use in the racing horse.

Classification Definitions

Class 1

Stimulant and depressant drugs that have the highest potential to affect performance and that have no generally accepted medical use in the racing horse. Many of these agents are Drug Enforcement Agency (DEA) schedule II substances. These include the following drugs and their metabolites: opiates, opium derivatives, synthetic opioids and psychoactive drugs, amphetamines and amphetamine-like drugs, as well as related drugs, including but not limited to apomorphine, nikethamide, mazindol, pemoline, and pentylenetetrazol. Though not used as therapeutic agents, all DEA Schedule I agents are included in Class 1 because they are potent stimulant or depressant substances with psychotropic and often habituating actions.

Class 2

Drugs that have a high potential to affect performance, but less of a potential than drugs in Class 1. These drugs are 1) not generally accepted as therapeutic agents in racing horses, or 2) they are therapeutic agents that have a high potential for abuse. Drugs in this class include: psychotropic drugs, certain nervous system and cardiovascular system stimulants, depressants, and neuromuscular blocking agents. Injectable local anesthetics are included in this class because of their high potential for abuse as nerve-blocking agents.

Class 3

Drugs that may or may not have generally accepted medical use in the racing horse, but the pharmacology of which suggests less potential to affect performance than drugs in Class 2. Drugs in this class include bronchodilators, anabolic steroids, and other drugs with primary effects on the autonomic nervous system, procaine, antihistamines with sedative properties and the high-ceiling diuretics.

Class 4

This class includes therapeutic medications that would be expected to have less potential to affect performance than those in Class 3. Drugs in this class includes less potent diuretics; corticosteroids; antihistamines and skeletal muscle relaxants without prominent central nervous system (CNS) effects; expectorants and mucolytics; hemostatics; cardiac glycosides and anti-arrhythmics; topical anesthetics; antidiarrheals; and mild analgesics. This class also includes the nonsteroidal anti-inflammatory drugs (NSAIDs), at concentrations greater than established limits.

Class 5

This class includes those therapeutic medications for which concentration limits have been established by the racing jurisdictions, as well as certain miscellaneous agents such as dimethylsulfoxide (DMSO) and other medications as determined by the regulatory bodies. Included specifically are agents that have very localized actions only, such as anti-ulcer drugs, and certain anti-allergic drugs. The anticoagulant drugs are also included.

Prohibited substances in racing horses

- A) The possession and/or use of a drug, substance or medication, specified below, on the premises of a facility under the jurisdiction of the regulatory body for which a recognized analytical method has not been developed to detect and confirm the administration of such substance; or the use of which may endanger the health and welfare of the horse or endanger the safety of the rider or driver; or the use of which may adversely affect the integrity of racing:
 - 1) Erythropoietin
 - 2) Darbepoetin
 - 3) Oxyglobin
 - 4) Hemopure
- B) The possession and/or use of a drug, substance, or medication on the premises of a facility under the jurisdiction of the regulatory body that has not been approved by the U.S. Food and Drug Administration (FDA) for use in the United States.
- C) The practice, administration, or application of a treatment, procedure, therapy, or method identified below, which is performed on the premises of a facility under jurisdiction of a regulatory body and which may endanger the health and welfare of the horse or endanger the safety of the rider or driver, or the use of which may adversely affect the integrity of racing:

Equine prohibited drugs: FEI Clean Sport Prohibited Substances Database (Revised January 2010).

FEI (Fédération Equestre Internationale) has published guidelines to assist veterinarians to make a distinction between the use of routine, legitimate medication and deliberate and calculated doping to affect a horse's performance. The prohibited substance searchable database is available at:

<http://prohibitedsubstancesdatabase.feicleansport.org/>

FEI Clean Sport Prohibited Substances List (updated January 2010)

http://www.feicleansport.org/ProhibitedSubstancesList_Jan2010.pdf

APPENDIX O

Important Internet Sites for Drug Information

Drug Compounding: FDA Policy (2003 revision)

www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074656.htm

Drug Interactions

<http://medicine.iupui.edu/clinpharm/ddis/>

www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionsLabeling/ucm080499.htm

FDA Home Page

www.fda.gov/cvm/

FDA Adverse Drug Reports: Cumulative Summary

www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm055369.htm

FDA Adverse Drug Reaction Reporting Site

www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm055305.htm

FDA Approved Animal Drug Products: Animal Drugs @ FDA

www.accessdata.fda.gov/scripts/animaldrugsatfda/

FDA Approved Human Drug Products: Drugs @ FDA

www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

AAVPT USP Veterinary Drug Information

www.aavpt.org/USPmonographs.shtml

Extralabel (off label) Drug Use Information

www.avma.org/reference/amduca/amduca1.asp

U.S. Drug Enforcement Administration (DEA) Controlled Substances Drug Schedules

www.justice.gov/dea/pubs/scheduling.html

Euthanasia Formulations and References (updated June 2007):

www.avma.org/issues/animal_welfare/euthanasia.pdf

APPENDIX P

Important Contact Information for Veterinary Drugs

Animal Blood Banks

Animal Blood Bank Hotline: 800-243-5759

A 24-hour hotline that focuses on transfusion medicine (particularly blood component therapy), recommending dosages and infusion rates.

Veterinarian's Blood Bank: (812) 358-8500

Commercial blood bank.

Animal Blood Resources International: (517) 851-8244

A 24-hour commercial blood bank.

Eastern Veterinary Blood Bank: 800-949-EVBB (800-949-3822)

A 24-hour commercial blood bank that focuses on transfusion medicine.

HEMOPET: (714) 891-2022

A national, full-service, nonprofit blood bank and educational network for animals; accessible 24 hours.

Poison Control Centers

ASPCA National Animal Poison Control Center: 888-4ANI-HELP
(888-426-4435)

Fee \$50 per case; no extra charge for follow-up calls.

PET POISON HELPLINE: (800) 213-6680

Nationwide, 24-hour service offered by the Pet Poison Center. Available to pet owners and veterinary professionals. A fee of \$35 per case is charged, with no extra charge for follow-up calls.

National Pesticide Information Center: (800) 858-7378; email: npic@ace.orst.edu

Drug Enforcement Agency (DEA)

Office of Diversion Control, Registration Section: 800-882-9539

Food and Drug Administration Center for Veterinary Medicine (FDA/CVM):
888-FDA-VETS (888-332-8387)

Food Animal Residue Avoidance Databank (FARAD): 888-USFARAD
(888-873-2723); Web site: www.farad.org. To send comments or question to FARAD, please do so by sending an e-mail to USFarad@gmail.com. Please do not send any extra-label drug use questions to this e-mail address.

FARAD is sponsored by the USDA to prevent residues of drugs and other chemicals in food animals.

APPENDIX Q Solution Compatibility Chart

Intravenous Medication	D2	1/2W	D5W	D10W	D5/1/4NS	D5/1/2NS	D5NS	NS	1/2NS	R	LR	D5R	D5LR	Dextran 6%/D5W/NS	Fruc 10%/W/NS	Invert sug 10%/W/NS	Na lactate 1/6 M
Acetazolamide	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Acyclovir	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C		
Aminophylline	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C		
Ammonium chloride																	
Amikacin			C					C									
Amphotericin B			C					C									
Ampicillin			C					C									
Ascorbic acid	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Calcium chloride			C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Calcium gluconate			C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Cefazolin Na			C	C	C	C	C	C	C	C	C	C	C	C	C	W	C
Cefazolin Na			C	C	C	C	C	C	C	C	C	C	C	C	C	W	C
Cefotaxime Na			C	C	C	C	C	C	C	C	C	C	C	C	C		
Cefotetan			C	C	C	C	C	C	C	C	C	C	C	C	C		
Cefoxitin Na			C	C	C	C	C	C	C	C	C	C	C	C	C		
Ceftazidime			C	C	C	C	C	C	C	C	C	C	C	C	C	W	C
Cimetidine			C	C	C	C	C	C	C	C	C	C	C	C	C	W	C
Ciprofloxacin			C	C	C	C	C	C	C	C	C	C	C	C	C		
Clindamycin			C	C	C	C	C	C	C	C	C	C	C	C	C		
Cyclosporine			C	C	C	C	C	C	C	C	C	C	C	C	C		

Continued

Intravenous Medication	D2 1/2W		D5W	D10W	D5/1/4NS	D5/1/2NS	D5NS	NS	1/2NS	R	LR	D5R	D5LR	Dextran 6%/D5W/NS	Fruc 10%/W/NS	Invert sug 10%/W/NS	Na lactate 1/6 M
	D2	1/2W	D5W	D10W	D5/1/4NS	D5/1/2NS	D5NS	NS	1/2NS	R	LR	D5R	D5LR	Dextran 6%/D5W/NS	Fruc 10%/W/NS	Invert sug 10%/W/NS	Na lactate 1/6 M
Dexamethasone	C		C	C				C									C
Dobutamine HCl	C		C	C				C			C						C
Dopamine HCl	C		C	C				C			C						C
Doxycycline	C		C	C				C		C						W	C
Epinephrine	C		C	C				C		C							C
Famotidine	C		C	C				C		C							C
Fentanyl	C		C	C				C									C
Furosemide	C		C	C				C									C
Gentamicin	C		C	C				C		C							C
Heparin Na	C		C	C				C		C							C
Hydrocortisone phosphate	C		C	C				C		C							C
Hydrocortisone Na succinate	C		C	C				C		C							C
Hydromorphone HCl	C		C	C				C		C					W		C
Imipenem-Cilastatin	C ⁴		C ⁴	C ⁴	C ⁴			C ¹⁰									
Insulin (regular)	C ^P		C ^P	C	C			C ^P		C							
Isoproterenol	C ^P		C ^P	C	C			C ^P		C							C
Kanamycin	C ^P		C ^P	C	C			C		C							
Lidocaine	C ^P		C ^P	C	C			C		C							
Magnesium sulfate	C		C	C				C		C							
Meperidine HCl	C		C	C				C		C							C
Meropenem	C ¹		C ¹	C ¹	C ¹			C ⁴		C ⁴						W	C
Metoclopramide HCl	C		C	C				C		C							C ²
Morphine	C		C	C				C		C							C

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Entries can be identified as follows: generic name (lowercase), Trade name (first letter capitalized).

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Atropine	*																							
Buprenorphine		*																						
Butorphanol			*																					
Chlorpromazine				*																				
Cimetidine					*																			
Codeine						*																		
Diazepam							*																	
Dimenhydrinate								*																
Diphenhydramine									*															
Fentanyl										*														
Glycopyrrolate											*													
Haloperidol lactate												*												
Heparin													I *											
Hydroxyzine														I *										
Mepidine															*									
Metoclopramide																*								
Midazolam																	*							
Morphine																		*						
Pentazocine																			*					
Pentobarbital																				*				
Prochlorperazine																					*			
Promethazine																						*		
Ranitidine																							*	

Based on information in Trissel LA: Handbook on injectable drugs, ed 11, American Society of Health-System Pharmacists, Inc. The syringe compatibility table provides physical compatibility information on ly for drugs mixed in a syringe. Therapeutic incompatibilities are not represented, therefore, professional judgment should be exercised when utilizing this table. C, compatible; I, incompatible; no entry, no documented information.