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- and 45.5-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

Dogs and Cats

- Anthelmintic dosage: 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 for meat. Do not use in lactating dairy cattle. Sheep withdrawal time: 7 days for 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 United States.

Functional classification: Bronchodilator, beta-agonist

Pharmacology and Mechanism of Action

Beta$_2$-adrenergic agonist. Albuterol stimulates beta$_2$-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.

Albuterol exists as two chiral isomers. The R-isomer is the active bronchodilator form; the S-isomer is associated with adverse effects. The formulation levalbuterol is a formulation containing only the R-isomer.

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 doses. 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 was previously available as a metered-dose inhaler for horses (Torpex) for treatment of airway disease. It provided immediate relief of bronchospasm and bronchoconstriction in horses. However, the equine formulation is no longer commercially available. The human formulations can be used as a substitute.

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 $beta_2$-agonists will inhibit uterine contractions at the end of gestation in pregnant animals. High doses of $beta_2$-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/h.

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 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- and 4-mg tablets and 2-mg/5-mL syrup. Solutions for inhalation are 0.83 and 5 mg/mL. The equine formulation contained 6.7 g of formulated albuterol sulfate in a pressurized aluminum canister. This formulation is no longer commercially available for horses. Human metered-dose inhalers are available in various sizes ranging from 6.7 to 18 g, with 90 mcg per actuation.

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 PO, up to a maximum of 100 mcg/kg q6h.

Large Animal Dosage

Horses

- Deliver sufficient actuations of the metered-dose inhaler to administer 360 mcg per horse—equivalent to 4 actuations of a 90-mcg human metered-dose inhaler. This dose can be administered up to 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 and generic

Functional classification: Antihypercalcemic

Pharmacology and Mechanism of Action

Bisphosphonate drug. Drugs in this class include pamidronate, risedronate, zoledronate, and etidronate. New drugs approved to treat navicular syndrome in horses are tiludronate (Tildren) and clodronate (OSPHOS). 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 persistence of the drug in 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. Most doses for animals have been extrapolated from people (10 mg per person per day, or 70 mg once per week) because no animal-specific studies have identified the optimum dose.

In animals, alendronate is used to decrease calcium in conditions that cause hypercalcemia, such as hyperparathyroidism, 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 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.

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 www.FARAD.org.

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 adenosine monophosphate (cAMP). Other anti-inflammatory 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. The oral forms have mostly been discontinued, and only the injection forms remain. For oral administration, theophylline should be used. Consult the Theophylline section for more information on dosing.

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. GI adverse effects include nausea, vomiting, and diarrhea. CNS 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 PDE inhibitors such as sildenafil (Viagra) and pimobendan. Many drugs inhibit the metabolism of theophylline and potentially increase concentrations (e.g., cimetidine, erythromycin, fluoroquinolones, and propranolol). Some drugs 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. The oral forms have been discontinued, and the dosing listed applies to injection formulation. For oral administration, use theophylline.

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 25-mg/mL injection. A dose of 25 mg/mL of anhydrous aminophylline is equivalent to 19.7 mg of anhydrous theophylline per milliliter. Oral forms have been discontinued; for oral administration, use theophylline instead.

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 IM or IV.

Cats

- 6.6 mg/kg q12h IM or IV.

Large Animal Dosage

Horses

- Treatment of recurrent airway obstructions: 12 mg/kg initial dose followed by 5 mg/kg q12h. Aminophylline administered IV to horses has caused transient excitement and restlessness. Give IV 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.
For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.
RCI Classification: 3

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. (This indication is controversial.)

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 www.FARAD.org.
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 second-generation calcium-channel blocker of the dihydropyridine class. It decreases calcium influx in cardiac and vascular smooth muscle. However, its greatest effect is on vascular smooth muscle by blocking the L-type calcium channels. Through this mechanism, it acts as a vasodilator for treating hypertension.

Pharmacokinetics: It has a high volume of distribution and slow systemic clearance, resulting in a half-life of approximately 30 hours. It is well-absorbed orally.

Indications and Clinical Uses

In both dogs and cats, amlodipine is effective for lowering systemic blood pressure. Therefore, it is used to treat systemic hypertension (high blood pressure). Amlodipine has been considered the drug of choice for many years by clinicians for treating hypertension in cats. Hypertension in cats has been defined as systolic blood pressure greater than 190 mm Hg and diastolic pressure greater than 120 mm Hg. By comparison, angiotensin-converting enzyme (ACE) inhibitors are less effective in cats, and they respond better to amlodipine than to ACE inhibitors. Amlodipine reduces blood pressure in hypertensive cats and can reduce proteinuria but may not improve survival in cats with hypertensive kidney disease. Beta blockers may be added to therapy for cats (e.g., atenolol) to control the heart rate in hypertensive and hyperthyroid cats, but beta blockers do not have a direct anti-hypertensive effect in cats.

Although amlodipine has traditionally been considered the anti-hypertensive drug of choice for cats, recently, the angiotensin II blocker telmisartan has become a preferred agent because of proof of efficacy and available veterinary formulations (see Telmisartan for more information).

Precautionary Information

Adverse Reactions and Side Effects

The most common adverse effect is hypotension. In dogs and cats, gingival hyperplasia has been observed, which may be caused by an up-regulation of circulating androgens or inhibition of transglutaminase. Other mechanisms may be involved but are speculative. Gingival hyperplasia usually resolves after discontinuation of the medication and replacement with another drug (e.g., hydralazine or telmisartan).

In both dogs and cats, amlodipine may activate the renin–angiotensin–aldosterone system (RAAS). When this occurs, ACE inhibitors may be somewhat effective in reducing activation of RAAS, but addition of this medication also may increase risk of hypotension and may decrease renal glomerular pressure. Less common adverse reactions include lethargy, decreased appetite, azotemia, mild hypokalemia, and weight loss. Reflex tachycardia can occur with excessive decrease in blood pressure.

Amlodipine is a calcium-channel blocker, and although the action is more specific for vascular smooth muscle, it may depress the heart in some patients. Therefore, use carefully in patients with heart block or compromised cardiac contractility.

For treatment of a toxic overdose, administer calcium (e.g., calcium gluconate) and vasopressors.

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. Concurrent use with ACE inhibitors may increase the risk of hypotension and decreased glomerular pressure.

Instructions for Use

In cats, efficacy has been established at 0.625 mg/cat once daily. If cats are large size (greater than 4.5 kg) or refractory, increase dose to 1.25 mg/cat q24h PO. In some cats, addition of a beta blocker to slow heart rate may be indicated. The goal of treatment is to decrease systolic pressure to less than 150/90 (systolic/diastolic). See the Patient Monitoring and Laboratory Tests section.

Patient Monitoring and Laboratory Tests

Monitoring the patient's blood pressure is essential to proper treatment. Cats with high blood pressures of systolic 160–190 mm Hg and diastolic 100–120 mm Hg should be considered at risk of clinical effects from hypertension. When using amlodipine, the target blood pressure should be less than 160 mm Hg. If this is not achieved, increase the dose to 1.25 mg per cat, but maximum dose per cat should not exceed 2.5 mg per cat.

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 0.1–0.5 mg/kg q24h PO. The higher dose of 0.5 mg/kg may be needed in refractory cases to reduce blood pressure.

Cats

- 0.625 mg/cat initially q24h PO and increase if needed to 1.25 mg/cat. The dose of 0.625 mg is one eighth of a 5-mg human tablet. The 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 www.FARAD.org.
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 urinary tract infections (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 kidney 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.

Stability and Storage
Stable if stored in manufacturer's original vial.

Small Animal Dosage
Dogs (Two-dose regimens have been used.)
- 400 units/kg SQ or IM weekly.
- 10,000 units/m^2 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 drug

Pharmacology and Mechanism of Action
Nonsteroidal anti-inflammatory drug. Anti-inflammatory action is caused by inhibition of prostaglandins. Aspirin binds irreversibly to the COX enzyme in tissues to inhibit synthesis of prostaglandins. At low doses, it is more specific for COX-1 than COX-2. The sensitivity of COX-1 over COX-2 is the explanation for low aspirin doses used as antiplatelet treatment. However, in some animals, even low-dose aspirin does not inhibit platelet aggregation, possibly because COX-2 can be an additional source of thromboxane (TXA2). 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 nuclear factor kappa-β.

Pharmacokinetics: The pharmacokinetics are variable in animals with a half-life that ranges from 1 hour in horses, 6 hours in pigs, and 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. Aspirin has a long history of use for treating pain and inflammation, especially associated with osteoarthritis. Although it may be effective in animals, other agents specifically approved for animals are much more commonly used nowadays for osteoarthritis and other painful conditions.

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 to inhibit platelets and prevent thromboemboli formation. Inhibition of platelets is justified for some diseases because as platelets become hyper-reactive, they can release serotonin and other mediators that may exacerbate vascular diseases and produce blood clots. Although these low doses of aspirin are often used for antiplatelet therapy, aspirin

does not provide complete inhibition of platelet stimulation. Low doses (e.g., 1–5 mg/kg) produce inconsistent platelet inhibition in dogs and cats. Some animals are refractory (*aspirin resistance*). Addition of other antiplatelet drugs such as clopidogrel (Plavix) provides more effective inhibition.

Aspirin has been used to prevent complications from heartworm disease (thromboemboli). However, there is no convincing evidence that there is a clinical benefit from this treatment. Some evidence indicates that aspirin may be contraindicated in heartworm disease.

In cats, exposure of feline platelets in vitro to aspirin can have an inhibitory effect. Platelets collected from cats ex vivo after treatment with aspirin (5 mg/kg) had decreased TXA2 production, but platelet aggregation was not affected.

Although aspirin has been available for many years, it is not registered by the Food and Drug Administration (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 may inhibit 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 disease). Do not administer to animals prone to GI ulcers.

Drug Interactions

Some animals are more susceptible to the gastric effects of aspirin if corticosteroids are included in the protocol. 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 potent and prolonged effect of aspirin on platelets. The dosing section lists “antiplatelet” doses for aspirin in dogs and cats, but the efficacy of these doses has not been verified through clinical studies. Results from research animals have produced varied results. In some studies, 5–10 mg/kg was considered a consistent antiplatelet dose for dogs; in other studies, 1 mg/kg inhibited platelets in only one third of dogs; and in research dogs, doses as low as 0.5 mg/kg q12h impaired platelet aggregation.

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 farther 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 (T_4, T_3, and free T_4) 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 a 240-grain bolus (14,400 mg) and 3.9-, 15.6-, and 31.2-g tablets.
- Extended-release form for antiplatelet treatment (Durlaza): 16.2 mg capsule. (Do not open or break capsule.)

Stability and Storage

Store in a tightly sealed container at room temperature. After exposure to moisture, it decomposes 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.

Cats

- 10 mg/kg q48h PO.

Anti-inflammatory

Dogs

- 20–25 mg/kg q12h PO.

Cats

- 10–20 mg/kg q48h PO.

Antiplatelet

Dogs

- Typical doses are in the range of 1–5 mg/kg but have been as high as 5–10 mg/kg q24–48h PO to obtain a greater response. (Convincing evidence of a consistent antiplatelet clinical benefit in dogs is lacking.)

Cats

- 80 mg/cat q48h PO. Doses have ranged from 5 mg per cat q72h to 80 mg per cat (one tablet) q72h. No clinical studies have documented efficacy from either dose.

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 $beta_1$-receptor. Atenolol is a water-soluble beta blocker and relies on the kidneys for clearance. (By comparison, drugs such as propranolol and metoprolol are more lipophilic and rely on the liver for clearance.)

Pharmacokinetics: In dogs and cats, oral absorption is 90%. In cats, the half-life is approximately 4–5 hours, with a peak concentration of 1.4–1.9 mcg/mL after a dose of 2.5 mg/kg.

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. Although it is commonly administered to cats with hypertrophic cardiomyopathy to improve clinical signs, it did not slow progression of the disease. In dogs, it has been used for congenital cardiac conditions such as subaortic stenosis and pulmonary stenosis (0.5–1 mg/kg q12h).

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 it is 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. Although plasma and serum concentrations are not typically monitored, a concentration above 0.26 mcg/mL has been proposed as a target threshold for effective adrenergic beta-receptor blockade.

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. Studies using a compounded flavored oral paste and oral suspension formulation for cats produced similar beta-adrenergic blocking effects as a commercial tablet (2.5 mg/kg). Stability studies 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 and can be mixed with other water-based vehicles.

Small Animal Dosage

Dogs

- 6.25–12.5 mg/dog q12–24h (or 0.25–1.0 mg/kg q12–24h) PO. Start with 1 mg/kg PO q12h initially and lower dose as needed to maintain optimum heart rate. However, doses in dogs also 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 dosage is 6.25–12.5 mg/cat q12–24h PO (one quarter or one half tablet).

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 www.FARAD.org.
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

Alpha$_2$-antagonist. It binds to alpha$_2$-receptors to antagonize other drugs that act as agonists, such as dexmedetomidine, medetomidine, and xylazine. Other alpha$_2$-antagonists include yohimbine, but atipamezole is more specific for the alpha$_2$-receptor.

Indications and Clinical Uses

Atipamezole is used to reverse alpha$_2$-agonists such as dexmedetomidine (Dexdomitor), medetomidine (Domitor), detomidine, 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. In horses, it provides a satisfactory but incomplete reversal of detomidine.

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.
- CRI: 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 to overcome excess vagal stimulation associated with some clinical conditions. Atropine is used during cardiac arrest to overcome vagal influences. Atropine is also used as an antidote for organophosphate intoxication. In horses, atropine (single dose) may be used to relieve bronchoconstriction in horses with recurrent airway obstruction, also known as equine asthma syndrome. For this use, only a single dose is recommended. N-butylscopolammonium bromide (Buscopan) also is used for this indication.

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 increases oxygen demand.

Drug Interactions

Do not mix with alkaline solutions. Atropine antagonizes 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 with lower doses, in dogs, 0.06 mg/kg was more effective than 0.02 mg/kg. 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 cardiopulmonary resuscitation, up to 0.04 mg/kg.
- Cardiac arrest: 0.04 mg/kg IV (with other supportive measures).

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; repeat as needed.
- Equine asthma syndrome and recurrent airway obstruction: 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; 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 the United States. The manufacturer of large animal products lists 0 days for milk and meat; however, it is listed as 3 days for milk and 14 days for meat in the United Kingdom.
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 observed by some clinicians that this product (oral) is not as effective as injectable products such as aurothioglucose.

Auranofin has activity against some protozoan parasites, but the efficacy for treating protozoa, or optimum dose, has not been established in animals.

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.

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. The use in animals is based on anecdotal experience and small observational reports.

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 but has been discontinued by some manufacturers.

Stability and Storage

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

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

Angiotensin-converting enzyme (ACE) inhibitor. Inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and also produces sympathetic stimulation, renal hypertension, and synthesis of aldosterone. The inhibition of aldosterone decreases sodium and water retention. Benazepril, like other ACE inhibitors, produces vasodilation and decreases 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 (85% eliminated through the bile), and clearance is not affected in animals with kidney disease. Duration of ACE-inhibiting action is 16–24 hours, despite a short plasma half-life, because of high-affinity binding to ACE.

Pharmacokinetics: The half-life in cats is 16–23 hours, which results in once-daily dosing.

Indications and Clinical Uses

Benazepril, like other ACE inhibitors, is used to treat hypertension and congestive heart failure (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 reduces blood pressure in some cats with kidney disease but is less effective in cats with spontaneous hypertension. Therefore, ACE inhibitors such as benazepril are not considered a primary treatment for hypertension in cats. Benazepril has been used in cats to treat proteinuria and hypertension in cats with chronic kidney disease. However, a survival benefit in cats with chronic kidney disease is not demonstrated. 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. For cats with kidney disease and hypertension, other agents are preferred such as amlodipine or telmisartan.

In dogs, it produces similar benefits to animals with kidney disease (decreased proteinuria, increased GFR, and lower blood pressure), but it does not increase survival. Despite these limitations, some renal experts recommend including an ACE inhibitor (benazepril or enalapril) in the initial treatment for dogs with proteinuria caused by glomerular disease.

Precautionary Information

Adverse Reactions and Side Effects

Benazepril has been well tolerated in dogs and cats with chronic renal failure. However, it 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. Benazepril, like other ACE inhibitors, may be used with other cardiovascular drugs and furosemide. However, it does not prevent increases in aldosterone (caused by activation of the renin–angiotensin–aldosterone system) in patients treated with furosemide. It is possible that if ACE inhibitors are administered with spironolactone, there may be increases in serum potassium, but this is a rare occurrence in dogs and cats.

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 dosages 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. Monitor serum creatinine because some patients will show an increase in creatinine concentrations. Slight increases in creatinine in cats with chronic kidney disease may be tolerable and not a reason to discontinue treatment.

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

- 0.25–0.5 mg/kg q12–24h PO (0.5 mg/kg q24h in most patients). Increase by 0.5 mg/kg if needed, to a maximum of 2 mg/kg q24h.

Cats

- Systemic hypertension: 0.5–1 mg/kg/day q24h PO. Alternative dosage for cats is 2.5 mg per cat per day for cats up to 5 kg of body weight PO.
- Chronic kidney disease: 0.25–0.5 mg/kg q24h PO.

Large Animal Dosage

- No dose has been reported for large animals.

Regulatory Information

Do not administer to animals intended for food.
Racing Commissioners International (RCI) Classification: 3

Betamethasone

bay-tah-meth′ah-sone

Trade and other names: Celestone, BetaVet, 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 those of 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. The equine formulation (BetaVet) is a combination of a slow-release component (betamethasone acetate) and a rapid-acting form (betamethasone sodium phosphate) in a combination for injection intra-articularly for control of pain and inflammation associated with osteoarthritis in horses.

Precautionary Information

Adverse Reactions and Side Effects

There are many side effects from corticosteroids, which include polyphagia, polydipsia/polyuria, and hypothalamic–pituitary–adrenal axis suppression. Adverse effects include gastrointestinal (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 demodicosis, toxoplasmosis, fungal infections, and urinary tract infections. In horses, some equine clinicians have suggested that the use may increase risk of laminitis, but this has not been supported with clinical research.

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, and pregnant animals. Do not inject equine product intra-articular if there are signs of infection in the joint.

Drug Interactions

No drug interactions are reported in animals. However, co-administration with other drugs may increase risk of adverse effects. For example, administration with NSAIDs may increase the risk of GI problems.

Butorphanol Tartrate

byoo-tor′fah-nole tar′trate

Trade and other names: Torbutrol, Dolorex, Butorphine, and Torbugesic

Functional classification: Analgesic, opioid

Pharmacology and Mechanism of Action

Opioid analgesic. Butorphanol is an opiate that acts as kappa-receptor agonist and weak mu-receptor antagonist. As a kappa agonist, butorphanol produces sedation and analgesia in animals. It is considered a mild analgesic compared with 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. It is considered a weak analgesic compared with drugs that are pure mu-receptor agonists, and some of the observed effects may be caused by sedation rather than analgesia. It can be used, often with other agents, for sedation in patients with anxiety or when sedation is needed. In dogs, at doses of 0.4 mg/kg, butorphanol produces analgesia for a duration of 1 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 horses, it may be administered IV, IM, and as a CRI. CRI has been shown effective in controlled studies for relief of abdominal pain in horses.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are similar to other opioid analgesic drugs, but without significant mu-receptor effects. Sedation is common at analgesic doses. Respiratory depression can occur with high doses. Lethal dose in dogs (LD_{50}) is 20 mg/kg, which is much higher than clinical doses. 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 q2–4h).

Drug Interactions

Butorphanol is compatible with many other analgesics and is 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, hydromorphone, 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 little justification 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. Torbugesic is available as a 10 mg/mL injection; Butorphine for cats is available as 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

- Antitussive: 0.055 mg/kg q6–12h SQ, 0.011 mg/kg IM, or 0.5–1 mg/kg q6–12h PO.
- Pre-anesthetic or sedative use: 0.2–0.4 mg/kg IV, IM, or SQ. May be used with other sedatives such as acepromazine.
- 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/h.

Cats

- Analgesic: 0.2–0.8 mg/kg q2–6h IV or SQ or 1.5 mg/kg q4–8h PO.
- Sedation: 0.2–0.5 mg/kg IV or IM. Often administered with other sedative agents. When combined with other agents for short-term use, use the lower dose of 0.2 mg/kg.
- CRI: Loading dose of 0.2–0.4 mg/kg IV, followed by 0.1–0.2 mg/kg/h.

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. Low 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/h (0.013–0.024 mg/kg) 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

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. Oral disintegrating tablets are available as 0.125-, 0.25-, 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, exhibits 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. Clopidogrel is metabolized to an active metabolite that exerts its antiplatelet effect. This metabolite blocks ADP from binding to the $P2Y_1$ and $P2Y_{12}$ receptor in a competitive manner, which leads to decreased platelet activity. Binding of ADP to $P2Y_1$ and $P2Y_{12}$ activates a G-protein, which inhibits adenyl cyclase and decreases cyclic adenosine monophosphate (cAMP). Because this mechanism is different from the aspirin-inhibiting effect on platelets, clopidogrel is more effective than aspirin alone. In dog, cats, and horses, oral administration has produced significant inhibitory effects on platelets that are superior to aspirin. Clopidogrel administration also decreased serotonin release from platelets, which may be important in cats because they have highly reactive platelets and serotonin release may contribute to clinical signs of thromboemboli in cats. A related drug is ticlopidine.

Pharmacokinetics: In horses the half-life of clopidogrel was 6 hours, but the active metabolite (CAMB) was only 0.5 hours. In dogs, the parent drug (clopidogrel) is not detected in the blood, and the antiplatelet effects are caused by the active metabolite.

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 inhibits mechanisms that are not affected by aspirin alone. It has been used currently with aspirin treatment, but combined treatment is usually not necessary. Although clopidogrel is more consistently reliable as an antiplatelet drug than aspirin, some animals may be nonresponders (e.g., 33% of horses, 15% of cats). Nevertheless, the consensus opinion by experts recommend that clopidogrel is preferred over aspirin for prevent of arterial thromboemboli in dogs and cats.

In cats, clopidogrel has been recommended to prevent cardiogenic arterial thromboembolism associated with heart disease. Treatment can be initiated in cats based on echocardiogram studies that demonstrate the presence of "smoke" in the left atrium. In cats, clopidogrel produces antiplatelet effects that persist for 3 days after discontinuation of the drug. 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 PO q24h, clopidogrel significantly suppressed platelet activity in horses, which persisted for 6 days after the last dose. However, not all horses respond, and effects may not be sustained for 24 hours. This may be caused by rapid elimination of the active metabolite in some horses.

A similar drug is ticlopidine (Ticlid), which should not be used in cats because it produces adverse reactions.

Precautionary Information

Avoid use in animals that have bleeding problems; use cautiously with other drugs that may inhibit platelets or blood clotting.

Adverse Reactions and Side Effects

Bleeding problems can occur in susceptible patients, but this has not been reported to be a clinical problem in dogs or cats. In people, pruritus and skin rash have been reported, but this has not been observed in dogs and cats. The taste is bitter, and some cats may refuse oral administration.

Contraindications and Precautions

Do not use in patients that have a high risk of bleeding. Discontinue several days prior to a planned surgical procedure.

Drug Interactions

Use cautiously with other drugs that may inhibit blood clotting, such as anticoagulants. In people, omeprazole (oral antiulcer agent) inhibits the conversion of clopidogrel to the active metabolite. This does not occur in dogs. It is not known if this interaction occurs in cats or horses with clinical use.

Instructions for Use

Administer with or without aspirin in patients prone to thrombi and emboli, but concurrent use with aspirin is not necessary. Because platelets are involved in arterial thromboembolism more than venous thromboembolism, the use for prevention of arterial thromboembolism is better established than the use for venous thromboembolism. 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. The dosage in dogs is usually 1–2 mg/kg q24h PO. At this dosage, the onset is 2 days, and steady-state is achieved in 5–7 days. Higher doses are often used initially in dogs for the first few days.

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

- 18.75 mg per cat (one fourth of tablet) q24h PO. The taste is bitter for cats, and fractions of the tablets may be placed in gelatin capsules.
- Smaller doses may be effective but have not been evaluated in cats.

Dogs

- 2 mg/kg q24h PO.
- An oral loading dose may be given at 2–4 mg/kg followed by 1–2 mg/kg q24h PO. In some cases, a higher oral loading dose of 10 mg/kg has been used.

Large Animal Dosage

Horses

- Loading dose of 4 mg/kg followed by 2 mg/kg q24h PO.

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 PG, structurally related to PGF_2-alpha that produces PGF_2-alpha effects. Synthetic prostaglandins are much more potent than natural PGs, and one should not use these at the same dose as natural PGs. PGF_2 analogues have a direct luteolytic action on the corpus luteum. After injection, cloprostenol causes functional regression of the corpus luteum (luteolysis). In nonpregnant cycling cattle, this effect will result in starting estrus 2–5 days after injection. In pregnant animals, it terminates pregnancy by inducing luteolysis and decreasing progesterone followed by increasing myometrial contraction and increased uterine evacuation. In animals with prolonged luteal activity that have pyometra, mummified fetuses, 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.

Precautionary Information

Adverse Reactions and Side Effects

There is only limited use in veterinary medicine, and adverse effects have not been reported. The hydroxyethyl starch compounds are used more often in veterinary medicine when colloids are needed for IV use. 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 IV fluid solutions, including 0.9% saline solution and 5% dextrose solution.

Instructions for Use

Used primarily in critical care situations, such as hypovolemic shock. It should be delivered slowly via CRI (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, 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: Benylin and other over-the-counter antitussive brands

Functional classification: Antitussive

Pharmacology and Mechanism of Action

Dextromethorphan is a centrally acting antitussive drug. Dextromethorphan shares similar chemical structure to opiates but does not affect opiate receptors and appears to suppress coughing by directly affecting the cough receptor. Dextromethorphan is the d-isomer of levorphan (the l-isomer of levorphan is an opiate with addictive properties, but the d-isomer is 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, but this is not a practical use in veterinary medicine. Pharmacokinetic studies in dogs indicated that dextromethorphan does not attain effective concentrations after oral administration. Even after IV 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. Pharmacokinetic data are available for dogs but have not been reported for cats or any other species.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects from oral administration are not reported in veterinary medicine. High overdose may potentially cause sedation. In healthy research dogs, dextromethorphan produced vomiting after oral doses and severe CNS reactions after IV 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 over-the-counter (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 or phenylpropanolamine, 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 P450 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. Many preparations are 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- to 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 www.FARAD.org.
RCI Classification: 4

Dextrose Solution
deks´trose

Trade and other names: D5W (5% dextrose) and 50% dextrose solution

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 IV 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 IV 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 has been administered as an emergency treatment to lower serum potassium in cases of hyperkalemia. It lowers potassium by inducing insulin release shifting of potassium from extracellular to intracellular stores.

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

Note: Digitoxin is no longer available commercially and not used clinically. It has been removed from this edition, but readers may consult earlier editions of this handbook for more detailed information on clinical use and dosages.

Digoxin

dih-joks´in

Trade and other names: Lanoxin and Cardoxin

Functional classification: Cardiac inotropic agent

Pharmacology and Mechanism of Action

Digoxin is a cardiac inotropic agent and also is used to regulate cardiac rate and rhythm. 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 reentrant cardiac arrhythmias via these neuroendocrine effects. An older drug, digitoxin, is no longer available. (Consult older editions of this handbook for information on digitoxin.)

Indications and Clinical Uses

The use of digoxin for animals in heart failure has declined significantly because pimobendan is more frequently used and is available in a veterinary formulation.

Digoxin has been used for treatment of heart failure in dogs, cats, and occasionally other animals. Because the use for an inotropic effect has declined, the most common use is to decrease the heart rate in animals. This property is used for treatment of 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 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. Heart block (AV block) is possible. 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. Because some animals may also be receiving diuretics, monitor the potassium concentrations during treatment. Digoxin is a substrate for cytochrome P450 enzymes and p-glycoprotein. Many drugs are capable of increasing digoxin concentrations, including quinidine, aspirin, clarithromycin (and other macrolides), and chloramphenicol (see Appendixes I and J for list of inhibitors). Administration of phenobarbital chronically may decrease digoxin concentrations by increasing clearance. Calcium-channel blockers and beta blockers 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 H_2 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 higher concentrations of to reduce heart rate to 140–160 bpm. Adverse effects are common at concentrations 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 less than 3). Do not compound oral tablets with other medications.

Small Animal Dosage

Dogs

- 0.005–0.011 mg/kg q12h PO (dose used by most cardiologists).
- Alternatively, doses have varied based on dog's body weight: dogs weighing less than 20 kg: 0.005–0.01 mg/kg q12h and if weighing greater than 20 kg: 0.22 mg/m^2 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 one fourth 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/h 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

Dihydrotachysterol

dye-hye-droe-tak-iss´ter-ole

Trade and other names: Vitamin D

Functional classification: Vitamin

Pharmacology and Mechanism of Action

Vitamin D analogue. Vitamin D promotes absorption and utilization of calcium.

Indications and Clinical Uses

Dihydrotachysterol 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. Calcitriol and calcium supplements are other drugs 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. Normal total calcium concentrations in dogs and cats are 9–11.5 mg/dL and 8–10.5 mg/dL, respectively, or 1.2–1.5 mmol/L and 1.1–1.4 mmol/L, respectively.

Formulations
- No formulations are currently available in the United States. 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 as high as 0.1–0.3 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 www.FARAD.org.

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
Diltiazem is a 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 (sinoatrial [SA] node and AV node) predominates over other effects. The effects on vascular smooth muscle—to reduce blood pressure—are not as great as other calcium-channel blocking drugs such as amlodipine.

Pharmacokinetics: Half-life in dogs is approximately 3 hours (range, 2.5–4 hours), and it is shorter in horses (1.5 hours).

Indications and Clinical Uses
Diltiazem is used primarily for control of supraventricular arrhythmias, atrial fibrillation, and hypertrophic cardiomyopathy. It also is used for atrial flutter, AV nodal reentry arrhythmias, and other forms of tachycardia. Diltiazem is more effective

on heart tissues (AV node and SA node) than on blood vessels. It can be used with digoxin and the action on cardiac rate and rhythm may be greater when used with digoxin. 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, diltiazem is considered one of the drugs of choice for treatment of feline hypertrophic cardiomyopathy. 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 multi-drug resistance [MDR] gene) substrates. (See Appendixes J and K.) Do not mix IV 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 the 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.
- Diltiazem is also available as 120-, 180-, and 240-mg extended-release capsules and in a 5-mg/mL injection solution.
- Extended-release capsules have three or four tablets in one unit. The capsule may be opened to release the individual tablets for oral dosing in dogs and cats.

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 IV fluids but should be discarded after 24 hours. Do not freeze.

Small Animal Dosage

Dogs

- For most uses: 0.5–1.5 mg/kg q8h PO. For atrial fibrillation, dosages as high as 5 mg/kg q12h PO have been used as monotherapy, or 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 every 5 minutes to effect.
- Supraventricular tachycardia: 0.25 mg/kg over 2 minutes IV (repeat if necessary). First, inject 0.25 mg/kg; then wait 20 minutes for response before repeating. To administer a CRI, inject 0.15–0.25 mg/kg IV over 2 minutes; then use a CRI of 0.1–0.2 mg/kg/h, up to a maximum of 0.4 mg/kg/h.
- Acute renal failure: 0.2 mg/kg IV (slowly) followed by 3–5 mcg/kg/min CRI.

Cats

- 1.75–2.4 mg/kg q8h PO. Most common dosage in cats with immediate-release formulations is 7.5–10 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 later).
- 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. 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 a 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 www.FARAD.org.
RCI Classification: 4

Dimenhydrinate

dye-men-hye´drih-nate

Trade and other names: Dramamine (Gravol in Canada)

Functional classification: Antihistamine

Instructions for Use
Doses for individual patients should be adjusted by monitoring serum calcium concentrations.

Patient Monitoring and Laboratory Tests
Monitor serum calcium concentration. Normal total calcium concentrations in dogs and cats are 9–11.5 mg/dL and 8–10.5 mg/dL, respectively, or 1.2–1.5 mmol/L and 1.1–1.4 mmol/L, respectively.

Formulations
- No formulations are currently available in the United States. 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 as high as 0.1–0.3 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 www.FARAD.org.

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
Diltiazem is a 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 (sinoatrial [SA] node and AV node) predominates over other effects. The effects on vascular smooth muscle—to reduce blood pressure—are not as great as other calcium-channel blocking drugs such as amlodipine.

Pharmacokinetics: Half-life in dogs is approximately 3 hours (range, 2.5–4 hours), and it is shorter in horses (1.5 hours).

Indications and Clinical Uses
Diltiazem is used primarily for control of supraventricular arrhythmias, atrial fibrillation, and hypertrophic cardiomyopathy. It also is used for atrial flutter, AV nodal reentry arrhythmias, and other forms of tachycardia. Diltiazem is more effective

on heart tissues (AV node and SA node) than on blood vessels. It can be used with digoxin and the action on cardiac rate and rhythm may be greater when used with digoxin. 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, diltiazem is considered one of the drugs of choice for treatment of feline hypertrophic cardiomyopathy. 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 multi-drug resistance [MDR] gene) substrates. (See Appendixes J and K.) Do not mix IV 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 the 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.
- Diltiazem is also available as 120-, 180-, and 240-mg extended-release capsules and in a 5-mg/mL injection solution.
- Extended-release capsules have three or four tablets in one unit. The capsule may be opened to release the individual tablets for oral dosing in dogs and cats.

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 IV fluids but should be discarded after 24 hours. Do not freeze.

Small Animal Dosage

Dogs

- For most uses: 0.5–1.5 mg/kg q8h PO. For atrial fibrillation, dosages as high as 5 mg/kg q12h PO have been used as monotherapy, or 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 every 5 minutes to effect.
- Supraventricular tachycardia: 0.25 mg/kg over 2 minutes IV (repeat if necessary). First, inject 0.25 mg/kg; then wait 20 minutes for response before repeating. To administer a CRI, inject 0.15–0.25 mg/kg IV over 2 minutes; then use a CRI of 0.1–0.2 mg/kg/h, up to a maximum of 0.4 mg/kg/h.
- Acute renal failure: 0.2 mg/kg IV (slowly) followed by 3–5 mcg/kg/min CRI.

Cats

- 1.75–2.4 mg/kg q8h PO. Most common dosage in cats with immediate-release formulations is 7.5–10 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 later).
- 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. 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 a 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 www.FARAD.org.
RCI Classification: 4

Dimenhydrinate

dye-men-hye´drih-nate

Trade and other names: Dramamine (Gravol in Canada)

Functional classification: Antihistamine

Cats

- 20 mg/m^2 (≈1.25 mg/kg) every 3 weeks IV. In some cats, higher doses of 25 mg/m^2 appear to be equally tolerated.

Large Animal Dosage

Horses

- 70 mg/m^2 (0.84–0.96 mg/kg) IV every 3 weeks for six 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 and 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

Doxycycline is a tetracycline antibiotic. The 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 many bacteria, some protozoa, *Rickettsia* spp., and *Ehrlichia* spp. Although it is a broad-spectrum antibacterial agent, resistance is common. Most of Enterobacteriaceae bacteria (e.g., *E. coli*) test clinically resistant. *P. aeruginosa* are resistant. *Staphylococcus* spp. may be susceptible, but susceptibility testing is needed to identify clinically susceptible strains.

Pharmacokinetics: In dogs, after oral administration, the half-life is 12.6 hours, the volume of distribution is 1.7 L/kg, and oral absorption is 66%, producing a peak concentration of 4.5 mcg/mL. Protein binding in dogs and cats is high (greater than 90%). In horses, oral doxycycline has an average half-life of 10 hours, a volume of distribution (V/F) of 2.3 L/kg, and clearance (CL/F) of 2.03 L/kg/h. The average peak concentration (C_{MAX}) after oral administration of 10 mg/kg is 0.5 mcg/mL. The oral absorption in horses is low at only 12%. Protein binding in horses is 70%–80%.

Indications and Clinical Uses

Doxycycline is usually the drug of choice for treating vector-borne diseases in animals, such as those transmitted by ticks and fleas. Efficacy has been demonstrated in research studies and in some clinical studies. It is used for treating infections caused by bacteria, some protozoa, *Rickettsia* spp., and *Ehrlichia* spp. Doxycycline administered to cats with infections caused by *Mycoplasma* spp. or *Chlamydophila 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, 5 mg/kg q12h PO for 3–4 weeks has cleared *Ehrlichia canis* from blood and tissues. Doxycycline is recommended by the American Heartworm Society to be added to treatment of canine heartworm disease and initiated 30 days prior to adulticide treatment. It is used for heartworm disease because of the activity against the organism *Wolbachia*. This 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 not only to treat

ehrlichiosis but also to treat other diseases (e.g., respiratory infections) when oral treatment is indicated. If doxycycline is too expensive or the availability is limited, other alternatives can be considered, such as minocycline hydrochloride, which has been shown to be an acceptable substitute and more active against some organisms (see Minocycline for more details).

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. Doxycycline is less likely to cause chelation with calcium and teeth discoloration than other tetracyclines. If administered for a short time, it has not caused teeth discoloration in children.

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 recommended 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

Ordinarily, tetracyclines should not be administered to young animals because it can affect bone and teeth formation. However, it has been better tolerated in children than other tetracyclines and has been used in children up to 8 years old. Doxycycline is less likely to discolor teeth if used for short-term treatment. If solid-dose forms are administered to cats, lubricate the tablet or capsule or follow with food or water to ensure passage into stomach. Do not administer rapidly IV. Do not administer solution directly IM or SQ. Do not administer IV to horses under any circumstances; acute death has been reported from this use.

Pregnancy precaution: avoid use during pregnancy if possible.

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. Doxycycline can bind to aluminum-containing products (e.g., sucralfate, antacids), which decreases its oral absorption.

Instructions for Use

To prepare doxycycline IV 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 100–1000 mL of lactated Ringer's solution, sodium chloride, or 5% dextrose. Infuse over 1–2 hours (see the Stability and Storage section).

Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI breakpoints for sensitive organisms are ≤0.25 mcg/mL for testing isolates from dogs. Breakpoints for cats are not established, but similar values are recommended. The breakpoint for testing isolates from horses is ≤0.12 mcg/mL using a dosage of 20 mg/kg PO twice daily. Do not test tetracycline as a surrogate for doxycycline in horses. For other animals, tetracycline can be used as a surrogate for testing. Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline or minocycline or both.

Formulations

- Doxycycline is available in a 10-mg/mL oral suspension; 20-, 50-, 75-, 100-, and 150-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. The vial should be diluted to 10 mg/mL initially and then to 1 mg/mL before slow IV infusion. Administer IV only and not via the SQ or IM routes.

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 IV injection will retain potency for 48 hours when diluted with sodium chloride or 5% dextrose solution to concentrations between 1 and 0.1 mg/mL if stored at 25°C (room temperature). Protect from direct light exposure, but exposure to fluorescent lights is acceptable for 48 hours. Reconstituted solutions may be stored up to 72 hours if refrigerated and protected from light. If frozen after reconstitution with sterile water, solutions of 10 mg/mL are potent for 8 weeks. If thawed, do not refreeze.

Doxycycline calcium or doxycycline monohydrate commercial oral suspension for people is stable for 2 weeks at room temperature if stored in light-resistant container after reconstitution with water. Doxycycline tablets may be crushed and mixed with drinks or food (milk or pudding), and are stable for 24 hours at room temperature. If doxycycline is prepared in a compounded formulation, it may be unstable. Doxycycline hyclate tablets formulated in Ora Plus and Ora Sweet as a suspension (50:50) retained potency for only 7 days; stability beyond 7 days cannot be assured. Other suspensions prepared for animals also may be unstable. Observe for dark color change (dark brown) as evidence of loss of potency. When doxycycline hyclate and doxycycline monohydrate was compounded in an oil-based suspension, it was stable for 180 days. However, the suspension precipitates in the container and vigorous mixing is suggested prior to administration.

Small Animal Dosage

Dogs and Cats

- 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.

- Hemoplasmosis (cats): 10 mg/kg, PO, once daily for 7 days.
- Heartworm treatment (dogs): 10 mg/kg q12h PO administered for 28 days prior to adulticide treatment. It may be administered in combination with ivermectin.

Birds

- Mix four 100-mg doxycycline hyclate capsules with 1 L of 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 for 3 weeks.

Large Animal Dosage

- Horses: 20 mg/kg q12h PO. (*Do not* administer IV.)
- For *Lawsonia intracellularis:* 20 mg/kg PO q24h for 3 weeks.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.

Dronabinol

droe-nab´ih-nole

Trade and other names: Marinol

Functional classification: Antiemetic

Pharmacology and Mechanism of Action

Dronabinol is an antiemetic from the cannabinoid class. In cannabis, there are many active chemicals, but one of the most significant is delta-9-tetrahydrocannabinol (delta-9-THC). This compound is believed to be the most pharmacologically active. Dronabinol is a synthetic form of delta-9-THC that can be administered orally. The site of action is unknown, but there is some evidence that the active ingredient (THC) may affect the CB-1 cannabinoid receptor or possibly opiate receptors or other receptors in the vomiting center.

Dronabinol has good oral absorption, but complete 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). This agent and another synthetic form of THC is used 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. The oral synthetic THC agents have not been effective for treatment of chronic pain.

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.
Racing Commissioners International (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

Enalapril is an angiotensin-converting enzyme (ACE) inhibitor. Like other ACE inhibitors, it inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and also stimulates 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, causes vasodilation and decreases 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 congestive heart failure (CHF). Efficacy for treating CHF has been established from clinical trials and can be used with other drugs such as pimobendan, furosemide, digoxin, and spironolactone. If aldosterone breakthrough occurs with administration of ACE inhibitors, spironolactone may be indicated. It is primarily used in dogs. In addition to its use for treatment of CHF, 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. An angiotensin-receptor blocking drug (e.g., telmisartan) or other vasodilators are preferred in cats.

Angiotensin-converting enzyme 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, but this effect is uncommon. Nevertheless, monitor renal parameters in patients receiving ACE inhibitors, especially if they are receiving 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 drugs known to cause hypotension. The use may exacerbate effects of diuretics. Nonsteroidal anti-inflammatory drugs (NSAIDs) may potentially decrease vasodilating effects, but this has not been shown in studies in animals.

Instructions for Use

The doses of enalapril are based on clinical trials conducted in dogs. For dogs, generally start with once-daily administration and increase to q12h if needed (see the dosing section). In some dogs with mild disease, start with 0.25 mg/kg q12h and then increase to 0.5 mg/kg q12h at the first recheck. Other drugs used for treatment of heart failure, such as pimobendan and spironolactone, 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 a 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/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

- Horses: Although enalapril has been examined in research horses, there are no clinical studies available to establish doses.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at www.FARAD.org.

RCI Classification: 3

Instructions for Use

Doses for fluralaner are established from the approved label dosing. Interval of dosing is based on efficacy studies. It is effective for treatment of fleas and most ticks for 12 weeks but not beyond 8 weeks for the Lone Star tick (*Amblyomma americanum*). It can eliminate sarcoptic mange with a single dose. In cats, it was effective for fleas and ticks for 12 weeks but not beyond 8 weeks for the American dog tick (*Dermacentor variabilis*).

The oral chew tablets can be administered with, or without food. To administer the topical solution, follow the instructions on the product label. The hair between the shoulder blades on dogs or behind the head on cats should be parted and the contents of the solution should be applied to the skin. Avoid contact with the application site until it has dried.

Patient Monitoring and Laboratory Tests

There is no routine monitoring required. Monitor response to treatment through clinical examination of skin at regular check-ups.

Formulations

- Fluralaner is available in a flavored chew tablet for dogs in 112.5-, 250-, 500-, 1000-, and 1400-mg sizes.
- Fluralaner is available as a topical solution with 280 mg of fluralaner per milliliter in each tube. Each tube is packaged separately in sizes of 112.5-, 250-, 500-, 1000-, and 1400-mg per tube.
- Fluralaner topical solution for cats. Each tube is formulated to administer a 40-mg/kg dose. Each milliliter contains 280 mg of fluralaner in sizes of 112.5-, 250-, and 500-mg per tube.
- Fluralaner and moxidectin topical solution for cats is available as 280 mg fluralaner and 14 mg moxidectin per milliliter.

Stability and Storage

Fluralaner should be stored in a dry place at controlled temperatures less than 25°C.

Small Animal Dosage

Dogs

- 25 mg/kg once every 12 weeks for either oral chew tablets or topical solution.
- Treatment of *Demodex* infection: 25 mg/kg at 12-week intervals.

Cats

- 40 mg/kg topical solution applied every 12 weeks.
- The combination of fluralaner and moxidectin for cats (Bravecto Plus) should be applied at a dose of 40 mg/kg fluralaner and 0.9 mg/kg moxidectin every 2 months.

Large Animal Dosage

No large animal doses have been established.

Regulatory Information

No withdrawal times are established for animals intended for food (extralabel use).

Fluticasone Propionate

floo-tik′ah-sone proe-pee-oe-nayt

Trade and other names: Flovent

Functional classification: Corticosteroid

Pharmacology and Mechanism of Action

Fluticasone is a potent glucocorticoid anti-inflammatory drug with potency 18 times that of dexamethasone. It is usually administered as a topical (local) application, most often for inflammatory airway disease. 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. Glucocorticoids decrease the synthesis of inflammatory mediators such as prostaglandins, leukotrienes, and platelet-activating factor, which also may be important in these diseases. 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 fewer 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 (MDI). 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 seconds) 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 dosage of 44 mcg twice daily was as effective as 110 or 220 mcg twice daily.

In horses, the most common use is for equine asthma syndrome characterized by RAO.

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 NSAIDs will increase the risk of GI injury.

Instructions for Use

The use is based on administration of fluticasone for treatment of airway diseases. It is delivered via an MDI. These inhalers can be used in animals if special adaptations,

such as a spacer device, which are available for cats, dogs, and horses, are used. When treating dogs and cats, doses listed in the dosing section can be used initially and are 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 ACTH stimulation test if it is necessary to monitor adrenal function. Fluticasone, although minimally absorbed systemically, will suppress the ACTH response.

Formulations

- MDI at 44, 110, or 220 mcg per puff.

Stability and Storage

Store in original container (MDI). 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 delivered with an MDI. As patient is stabilized, decrease dose gradually to 110 mcg per dose, lower if possible.

Cats

- Start with 44 mcg per dose (1 puff from a 44-mcg inhaler) twice daily. Increase the dose as needed to 110 mcg and then to 220 mcg.

Large Animal Dosage

Horses

- 1–2 mg per horse (6–12 puffs from 220-mcg inhaler) twice daily for airway disease.
- For long-term management in horses, start with 2 mg per horse q24h; then gradually taper to 1.5 mg per horse every other day.

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 Antizol (human preparation)

Functional classification: Antidote

Pharmacology and Mechanism of Action

Fomepizole, which is also known as 4-methylpyrazole, 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.

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, or alternatively, reflex bradycardia).

Contraindications and Precautions

Use in animals with cardiovascular disease is not recommended.

Drug Interactions

No specific drug interactions are reported. However, ephedrine potentiates 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 and other agents to treat urinary incontinence (e.g., phenylpropanolamine).

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm in patients.

Formulations

- Most formulations of ephedrine have been removed from the market. Previously available as 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.

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

Epinephrine is a prototype for an adrenergic agonist. Also called adrenaline. Epinephrine is a nonselective agonist for alpha-adrenergic and beta-adrenergic receptors. The alpha-adrenergic effects increase vascular resistance and act as a potent vasopressor. The $beta_1$-receptor effects stimulate the heart. The $beta_2$–adrenergic effects increase bronchodilation and decrease inflammatory mediators in the airways. Epinephrine is a potent adrenergic agonist with a prompt onset and a short duration of action. Compared with norepinephrine, epinephrine has more profound beta-receptor activity. As a result, compared with norepinephrine, epinephrine is more likely to cause increases in heart rate and tachyarrhythmias than norepinephrine.

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 as a vasopressor in some cardiopulmonary resuscitation (CPR) 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

An overdose of epinephrine causes 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 to prevent excessive adrenergic receptor stimulation.

Drug Interactions

Epinephrine interacts 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, but the doses and protocols are developed from the experience of clinical use. IV doses are ordinarily used, but endotracheal administration is acceptable when IV access is not available. When the endotracheal route is used, the dose is higher (up to 10 times the IV dose for CPR), and the duration of effect may be longer than with IV administration. When administering an endotracheal dose, one can dilute the dose in a volume of 2–10 mL of saline. The intraosseous route also has been used, and doses are equivalent to IV doses. There appears to be no advantage to intracardiac injection compared with IV 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 IM use. Avoid the SQ route of administration because the vasoconstriction produced delays absorption from this site.

For CPR, the doses have been controversial (see the dosing section). There is a low dose (10 mcg/kg or 0.01 mg/kg) and a high dose (100 mcg/kg or 0.1 mg/kg). Generally, start with the low dose every 3–5 minutes IV in CPR; then use the high dose after prolonged CPR.

Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during treatment.

Formulations

- Epinephrine is available in a 1-mg/mL (1:1000) injection solution and 0.1-mg/mL (1:10,000) injection solution. The 1:10,000 is 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 the pH of the solution is greater than 5.5, it becomes unstable.

Small Animal Dosage

- Cardiac arrest: 10–20 mcg/kg IV or 100–200 mcg/kg (0.1–0.2 mg/kg) endotracheal (may be diluted in saline before administration). The low dose of 10–20 mcg/kg IV initially may be used and increased to 100 mcg/kg IV for prolonged CPR.
- Anaphylactic shock: 5–10 mcg/kg IV or IM 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; if no response, use high dose.
- Constant-rate infusion (CRI): 0.05 mcg/kg/min IV.
- During emergency use, the dose may be repeated every 5–15 minutes, but the maximum doses in dogs are 0.3 mg total for dogs weighing less than 40 kg and 0.5 mg total for dogs weighing more than 40 kg body weight.

Large Animal Dosage

- 1 mg/mL (1:1000) solution most often used.
- Anaphylactic shock (cattle, pigs, horses, and sheep): 20 mcg/kg (0.02 mg/kg) IM or 1 mL/45 kg (1 mL/100 lb). 5–10 mcg/kg (0.005–0.01 mg/kg) IV or 0.25–0.5 mL/45 kg (100 lb).

Regulatory Information

No withdrawal times are established. Epinephrine is rapidly metabolized after administration, and zero days is recommended for withdrawal.
RCI Classification: 2

Epoetin Alfa (Erythropoietin)

ee-poe´eh-tin

Trade and other names: Procrit, Eprex, and Erythropoietin

Functional classification: Hormone

Pharmacology and Mechanism of Action

Epoetin alfa is a human recombinant form of erythropoietin. Erythropoietin is a hematopoietic growth factor that stimulates erythropoiesis. It is used in clinical patients where stimulation of red blood cell production is needed.

Indications and Clinical Uses

Epoetin alfa 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.

Patient Monitoring and Laboratory Tests
No specific monitoring is necessary.

Formulations
- Furazolidone has been discontinued in the United States. It may be available through some compounding pharmacies. The 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 extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.

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 $Na^+/K^+/2Cl^-$ cotransporter in the ascending thick loop of Henle. It is often called *a high-ceiling diuretic* 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^{2+} and Ca^{2+}. 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. Torsemide is another diuretic in the same class as furosemide. It has greater potency than furosemide and can be used in refractory cases.

Pharmacokinetics: The plasma half-life in animals is short (1.5–3 hours); therefore, this is a short-acting drug, with a maximum onset of effect of 1–2 hours and a duration of 2–4 hours. Oral absorption can be highly variable but in dogs is as high as 77%. SQ absorption is as high as other injectable routes. 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, including pulmonary edema, liver disease, heart disease, and vascular disease. It is recommended in dogs with clinical signs of stage C heart disease, to be used initially, until the patient's clinical signs have improved. Furosemide increases potassium and calcium excretion and is used to treat hyperkalemia and hypercalcemia.

The use of furosemide for AKI treatment has no benefit or effect on patient outcome based on available evidence. Furosemide promotes urine output by decreasing reabsorption of sodium but does not increase glomerular filtration rate.

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). The efficacy to reduce EIPH has been controversial in horses, but there is reported evidence to support this effect. 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. Because of short duration, CRIs can produce greater efficacy in some animals.

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. When administered to dogs at a dosage of 2 mg/kg q12h, it significantly increased RAAS activity by day 5 of treatment. When the RAAS is activated, increased concentrations of aldosterone can have persistent and deleterious effects on vasculature and cardiac remodeling. SQ injection may cause irritation (stinging) at the injection site.

Contraindications and Precautions

Administer conservatively in animals receiving 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 NSAIDs with furosemide may diminish the effect. The pH of solution is 8–9.8. Furosemide is stable with alkaline drugs but it should not be mixed with acidifying drug solutions with a pH less than 5.5.

Instructions for Use

Recommendations for use of furosemide 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 to 2 hours and a duration of approximately 2–4 hours. CRIs 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. A 2-g bolus is available for large animals, but oral absorption is uncertain.

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 for IV administration. These solutions are stable for 8 hours. It is more soluble if the pH is greater than 8, but it readily precipitates when pH is less than 5.5. Compounded oral formulations in syrups and other flavorings are stable if kept at alkaline pH or in alcohol. However, lower pH results 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 in which 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/h for 8 hours. Alternatively, a dose of 2 mg/kg in 5% glucose can be infused over an 8-hour period IV.

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 250–500 mg/horse at 6- to 8-hour intervals IM or IV.
- CRI: 0.12 mg/kg IV followed by 0.12 mg/kg/h IV.
- Prevention of EIPH: 0.5 or 1 mg/kg IV, administered 4 hours prior to exercise or administered 24 hours preracing. Consult local racetrack jurisdiction for restrictions on administration.

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 IV injection no later than 4 hours before racing post time. In most horses, this does not produce violations above 100 ng/mL urine threshold at 4 hours. Check local racetrack jurisdiction for restrictions for administration on race day.

Glycopyrrolate

glye-koe-peer′oe-late

Trade and other names: Robinul-V

Functional classification: Anticholinergic

Pharmacology and Mechanism of Action

Glycopyrrolate is an anticholinergic agent (blocks acetylcholine effect at muscarinic receptor), parasympatholytic. Glycopyrrolate produces atropine-like effects systemically. However, glycopyrrolate may have less effect on the central nervous system (CNS) compared with atropine because of lower penetration to CNS. It may produce a longer duration of action than atropine. The major use is as an adjunct to anesthetic agents to decrease secretions or increase heart rate.

Indications and Clinical Uses

Glycopyrrolate is used to inhibit vagal effects and increase heart rate in animals. It also decreases respiratory, salivary, and GI secretions. It may be used as an adjunct to anesthesia when it is necessary to override vagal stimulus. In horses, glycopyrrolate has a half-life of 7–19 hours, but this varies depending on the breed of horse.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are attributed to antimuscarinic (anticholinergic) effects. Side effects of therapy include xerostomia, ileus, constipation, tachycardia, and urine retention. CNS effects are less than with atropine.

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, antagonizes 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 such as glycopyrrolate 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. A common dose is 1 mg per horse.

Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.
RCI Classification: 3

Gold Sodium Thiomalate

gold soe′dee-um thye-oh-mah′late

Trade and other names: Myochrysine

Functional classification: Immunosuppressive

Pharmacology and Mechanism of Action

Gold sodium thiomalate is a gold salt uses for diseases that respond to gold therapy (chrysotherapy). The 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 (e.g., 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, and the use is based only on anecdotal experiences and extrapolation of the use in people. Its use in animals is uncommon. Other immunosuppressive drugs are used more frequently.

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

Complete blood count (CBC) should be monitored periodically during treatment.

Hydralazine Hydrochloride

hye-drahl′ah-zeen hye-droe-klor′ide

Trade and other names: Apresoline

Functional classification: Vasodilator

Pharmacology and Mechanism of Action

Hydralazine is a vasodilator used when patients have become refractory to other vasodilators. 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 NO 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 congestive heart failure (CHF), valvular disease of the heart, and other cardiovascular disorders characterized by high peripheral vascular resistance. It may be used with other cardiac drugs such as angiotensin-converting enzyme (ACE) inhibitors and pimobendan. Use in animals has been primarily derived from empirical use and small observational studies. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. The most common use is as a vasodilator when canine patients have become refractory to other common cardiovascular agents such as ACE inhibitors and pimobendan. Candidates for hydralazine treatment are typically those in stage C or D of heart failure. Hydralazine is recommended by experts when afterload is needed in severe cases (0.5–2.0 mg/kg PO), starting at a low dose and titrating to effect.

Because of the availability of other agents, the use is not as common for routine treatment compared with several years ago. It is more common to use other vasodilator drugs, such as the ACE inhibitors, pimobendan, and calcium-channel blocking drugs.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects are attributed to excess vasodilation and subsequent hypotension, which results in reflex tachycardia. Hydralazine may dangerously decrease cardiac output if not monitored carefully. 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; therefore, consider adding an ACE inhibitor, spironolactone, or both to patients that become refractory to treatment.

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, ACE inhibitors, and diuretics. The optimum 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-, 25-, 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. 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
- IV dose: 0.5–3 mg/kg IV bolus q12h or after initial bolus; follow with CRI of 1.5–5 mcg/kg/min IV.
- Oral dose: 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 www.FARAD.org.
RCI Classification: 3

Hydrochlorothiazide
hye-droe-klor-oh-thye′ah-zide

Trade and other names: HydroDIURIL, Hydrozide (for cattle), and generic

Functional classification: Diuretic

Pharmacology and Mechanism of Action
Hydrochlorothiazide is a 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 the most water has already been reabsorbed), their diuretic effects are not as great compared with loop diuretics such as furosemide. Thiazide diuretics are used commonly as a first-line agent in people to control hypertension, but they are

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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.

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not used commonly in animals. Other agents are preferred as diuretics (e.g., furosemide) or to control hypertension.

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 oxolate uroliths). The use in small animals has been primarily derived from anecdotal experience or small observational studies. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. In cattle, hydrochlorothiazide is approved for use in dairy cattle as an aid in the treatment of postparturient udder edema.

Precautionary Information

Adverse Reactions and Side Effects

Hydrochlorothiazide may cause electrolyte imbalance such as hypokalemia.

Contraindications and Precautions

Do not use in patients with high serum calcium. Thiazide diuretics 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. Monitor calcium in patients that may be prone to hypercalcemia. When used in cattle, animals should be regularly and carefully observed for early signs of fluid and electrolyte imbalance.

Formulations

- Hydrochlorothiazide is available in 10- and 100-mg/mL oral solution and 25-, 50-, and 100-mg tablets. The combination of hydrochlorothiazide and spironolactone is Aldactazide. The cattle formulation is 25 mg/mL 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

- 2–4 mg/kg q12h PO.
- Antihypertensive dose: 1 mg/kg q12h PO.

Cats

- To decrease excretion of calcium in urine: 1 mg/kg q12h PO.
- To alkalinize urine: 2 mg/kg, q12h PO.
- Congestive heart failure: 1–2 mg/kg q12–24h PO.

Large Animal Dosage

Cattle

5–10 mL (125–250 mg) IV or IM once or twice a day. After onset of diuresis, treatment may be continued with an orally administered maintenance dose. For oral treatment, use chlorothiazide boluses.

Regulatory Information

Withdrawal time for cattle: 72-hour (6 milkings) milk withdrawal; no withdrawal time for slaughter is established. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.
RCI Classification: 4

Hydrocodone Bitartrate

hye-droe-koe′done bye-tar′trate

Trade and other names: Hycodan, Vicodin, Lortab, and generic

Functional classification: Antitussive, analgesic

Pharmacology and Mechanism of Action

Hydrocodone is an 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 (e.g., substance P). Hydrocodone is metabolized to other metabolites, including hydromorphone, which has approximately six times the potency of morphine. Central sedative and euphoric effects are related to mu-receptor effects in the brain. Other opioids used in animals include hydromorphone, codeine, oxymorphone, meperidine, and fentanyl. Hycodan also contains homatropine, which is added to decrease abuse by people. Hydrocodone formulations used for antitussive action may also contain guaifenesin or acetaminophen.

Pharmacokinetics: Hydrocodone is metabolized in people to hydromorphone. In dogs, this conversion to a more active form is minimal but is unknown in other animals.

Indications and Clinical Uses

Hydrocodone is an opiate agonist that has antitussive, analgesic, and sedative properties. In people, the combinations of hydrocodone and acetaminophen (e.g., Vicodin) and hydrocodone and aspirin are often prescribed as oral treatments for pain. However, in animals, the efficacy of these medications for treating pain has not been established.

The most common use of hydrocodone in dogs has been as an antitussive for symptomatic treatment of airway diseases, and many clinicians believe (anecdotally) that it is an effective antitussive. There are no antitussive preparations marketed for use in the United States that do not contain atropine. (Canadian preparations

Cats

- To decrease excretion of calcium in urine: 1 mg/kg q12h PO.
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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 from opioids are predictable and unavoidable. Side effects include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses but is not documented from the use in animals. Paradoxical excitement may occur in some animals.

Contraindications and Precautions

Do not use in patients that may be sensitive to opioid effects or experience dysphoria. Because preparations for oral use contain atropine, do not use in animals in which atropine may be contraindicated. Many formulations for treating pain in people contain hydrocodone and acetaminophen or hydrocodone and aspirin. Do not administer to animals sensitive to these other ingredients. Acetaminophen-containing products should never be administered to cats. 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).

Drug Interactions

No specific drug interactions are reported for animals. However, other typical drug interactions that affect opioids should be considered.

Instructions for Use

Hydrocodone use in animals (primarily dogs) is derived from anecdotal experience and opinions from experts. It is most often used as an antitussive in dogs.

Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

Formulations

- There are many oral formulations for humans to treat pain that contain hydrocodone and other analgesics such as acetaminophen (e.g., Vicodin). Typically, these preparations contain 5 mg of hydrocodone and 500 mg of acetaminophen.
- Hydrocodone is also available as an antitussive (Hycodan) in 5-mg tablets and 1-mg/mL syrup combined with homatropine in a concentration of 1.5 mg in tablets and 0.3 mg/mL in syrup, respectively. Formulations in Canada do not contain homatropine.
- The extended-release formulations for people contain 10-, 15-, 20-, 30-, 40-, 50-, 60-, 80-, 100-, and 120-mg tablets) approved for use in people for treating pain. These extended-release formulations provide extended duration for once- or twice-daily administration but have not been evaluated for animals.

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 h PO. Increase the dose if needed for tracheal collapse in dogs but not above the dose of 1.5 mg/kg.
- Analgesic dose: 0.5 mg/kg q8–12 h PO. (Analgesic properties have not been established in dogs.)

Cats

- No dose has been established. Oral doses may be effective in cats, but caution should be used because many formulations contain acetaminophen.

Large Animal Dosage

- No large animal doses have been reported.

Regulatory Information

Hydrocodone is a Schedule II drug controlled by the Drug Enforcement Administration (DEA).
Hydrocodone is not recommended for food-producing animals. If administered to a food animal, consult FARAD for extralabel use withdrawal interval estimates (www.FARAD.org).
RCI Classification: 1. Do not administer to racing horses.

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

Hydrocortisone is a glucocorticoid anti-inflammatory and adrenal replacement 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. The most common use is to mimic the effects of cortisol when used in patients with hypoadrenocorticism (patients with adrenal insufficiency). 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 most often for adrenal corticosteroid replacement treatment in patients with adrenal insufficiency. It is less often used for its anti-inflammatory effects and not used as commonly as other corticosteroids such as prednisolone or dexamethasone except when hormone replacement to mimic the effects of cortisol is needed. Hydrocortisone sodium succinate is a rapid-acting injectable product that can be used when a prompt response is needed.

be split into 5 mg/kg q12h PO. Highly susceptible fungi such as some strains of *Blastomyces* spp. can be treated with lower doses of 5 mg/kg once daily.
- Dermatophytes: 3 mg/kg/day PO for 15 days.
- Cryptococcosis: 5 mg/kg q12h PO.
- *Malassezia* dermatitis: 5 mg/kg q24h PO for 2 days, repeated each week for 3 weeks.

Cats
- General infections: 5 mg/kg PO once daily. Alternatively, 50 mg (total dose) once per day or 100 mg per cat once every other day.
- Dermatophytes: 5 mg/kg PO once daily on alternating weeks for 3 cycles. For example, treat once daily during weeks 1, 3, and 5, but not on weeks 2 and 4. Some cats may need an additional course of therapy to eliminate the infection.

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. If itraconazole is administered to food animals, contact FARAD at www.FARAD.org for extralabel withdrawal time information.

Ivermectin

eye-ver-mek′tin

Trade and other names: Heartgard, 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

Ivermectin is an antiparasitic drug of the avermectin class. It is a prototype for this class of antiparasitic agents, which also includes eprinomectin and milbemycins (milbemycin and moxidectin). These drugs are macrocyclic lactones and share many 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.

Ivermectin has a prolonged half-life in all the animals studied, which allows for infrequent administration to achieve clinical effects.

Indications and Clinical Uses

Ivermectin is used in horses for the treatment and control of large strongyles (adult) (*Strongylus vulgaris, Strongylus edentatus,* and *Triodontophorus* spp.), small strongyles (adult and fourth-stage larvae) (*Cyathostomum* spp., *Cylicocyclus* spp., *Cylicostephanus* spp.), 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* spp.), and stomach bots (*Gastrophilus* spp.).

In cattle, it is used for treatment and control of GI nematodes (adults and fourth-stage larvae) (*Haemonchus placei, Ostertagia ostertagi*) (including inhibited larvae), *Ostertagia lyrata, T. axei, T. colubriformis, Cooperia oncophora, Cooperia punctata, Cooperia pectinata, Oesophagostomum radiatum, Nematodirus helvetianus* (adults only), *Nematodirus 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 eurysternus, 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, *Hyostrongylus rubidus*; nodular worm, *Oesophagostomum* species; threadworm, *Strongyloides ransomi* (adults only); somatic roundworm larvae (threadworm, *S. ransomi* [somatic larvae]); lungworms (*Metastrongylus* spp. [adults only]); lice (*H. 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. It has been recommended by the American 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 preventive doses. For optimal heartworm adulticide effect, it is often administered with oral doxycycline (10 mg/kg per day for 28 days). Treatment of *Demodex* infections is effective but requires higher doses than for any other indication. See Instructions for Use section later for instructions to treat *Demodex*.

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 (*ABCB1*, formerly *MDR1* gene) that codes for the membrane pump P-glycoprotein. This mutation affects the efflux pump in the blood–brain barrier. Therefore, ivermectin can accumulate in the brain of these 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 the *ABCB1* mutation) may exhibit toxicity at doses of 150–340 mcg/kg.

Retinopathy has also been observed in dogs administered high doses. In affected animals, a sudden onset of blindness, mydriasis, or both may occur, but dogs recover if the drug is discontinued.

Ivermectin at doses of 400 mcg/kg has produced neurologic toxicosis in Siamese kittens, and doses as low as 300 mcg/kg have been lethal in kittens. In horses, adverse reactions may include itching because of effects on microfilariae.

Treatment of intoxication: Administer activated charcoal from excessive doses administered orally. Symptomatic treatment includes ventilation support and control of seizures. An IV administration of lipid emulsion can be used at a dose of 1.5 mL/kg bolus of a 20% emulsion.

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 (other 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 during pregnancy 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 the *ABCB1* (*MDR*) mutation may also be sensitive to other drugs such as loperamide, milbemycin, moxidectin, and anticancer drugs. Ivermectin is excreted in milk.

Drug Interactions

Except for low doses used for heartworm prevention, 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. Do not administer with spinosad (Comfortis, Trifexis) because it may potentiate toxicity.

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. Products for heartworm prevention 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 intravenously. 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* infection), start with a low dose (50–100 mcg/kg) and 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). When the maintenance dose is achieved (300–600 mcg/kg PO), it should be administered once daily until 4 weeks after the second consecutive negative monthly skin scraping. When using extralabel formulations to treat dogs, the aqueous formulations have better palatability than the propylene-based formulations. They can be mixed with flavorings to improve palatability.

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), 2% (20 mg/mL), and 0.27% (2.7 mg/mL) injectable solution; 10-mg/mL oral solution; 5 mg/mL pour-on for cattle, 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 product 0.01% (0.1 mg/mL) is available in ampules in foil pouches for treating ear mites in cats.
- Compounded formulations: Ivermectin is chemically unstable at certain pH ranges and after exposure to water. Unless stability and strength are documented, compounded formulations are not recommended.

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 every 30 days PO.
- Prior to adulticide treatment: Administer preventative dose for 2 months, and up to 3 months prior to adulticide treatment.
- Heartworm treatment: Ivermectin administered at preventive doses combined with doxycycline at 10 mg/kg PO per day for 28 days.
- Ectoparasite therapy: 200–400 mcg/kg (0.2–0.4 mg/kg) IM, 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 every 7 days PO or every 14 SQ for 4–6 weeks.

Cats

- Heartworm preventive: 24 mcg/kg every 30 days PO.
- Ectoparasite therapy: 200–400 mcg/kg (0.2–0.4 mg/kg) IM, SQ, or PO, every 7 days or as needed based on skin scraping and clinical examination.
- 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. Oral solution dose is 1 mL per 50 kg (110 lb). Administer once or as needed as part of a comprehensive worming program.

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)/kg as a single dose SQ.
- Pour-on: 0.5 mg/kg or 1 mL/10 kg (22 lb) of 5 mg/mL solution.

Pigs

- 300 mcg (0.3 mg)/kg SQ as a single dose.

Sheep

- Injection solution: 200 mcg (0.2 mg)/kg as a single dose SQ.

- 200 mcg/kg PO.

Regulatory Information

Pigs' withdrawal time for meat: 18 days for SQ injection.
Cattle and calves' withdrawal time (meat): 35 days for SQ injection or 180 days for slow-release bolus. Forty-eight 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 is indicated for use in horses for treatment and control of tapeworms, large strongyles (including *Strongylus vulgaris, S. edentatus, Strongylus 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 the 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.

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 (0.01–0.06 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 T_4, and 1 tablespoon contains 36 mg of T_4. 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).
- Horses with pituitary pars intermedia dysfunction: 0.1 mg/kg (48 mg per horse) per day.

Regulatory Information

No regulatory information is available for animals intended for food. Because of a 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

Lidocaine is a common local anesthetic. Lidocaine inhibits nerve conduction via sodium channel blockade. Lidocaine is also a Class 1 antiarrhythmic and 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 IV 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. In dogs with GI compromise caused by gastric dilatation volvulus, it improved recovery by reducing the severity of ischemic reperfusion injury and inflammatory response.

Pharmacokinetics: The pharmacokinetics in dogs and cats are similar; however, cats have increased sensitivity to the cardiac effects. In dogs, the half-life is approximately 1 hour with a high clearance rate (30–40 mL/kg/min). In cats, the pharmacokinetics are different than dogs with a longer half-life and slower clearance, making cats more susceptible to adverse effects than dogs. In cattle, the half-life is approximately 1 hour. In horses, the half-life ranges from 40 to 80 minutes with a high, but variable, clearance rate.

Indications and Clinical Uses

Lidocaine is used commonly as a local anesthetic and for treatment and conversion of ventricular arrhythmias. Lidocaine should be used cautiously for treating supraventricular arrhythmias because it may increase cardiac conduction. Lidocaine has been used on a limited basis to treat seizures that are refractory to other drugs. Lidocaine also is used for pain management. It has been administered as a CRI in animals, especially in postsurgical patients to improve recovery after intestinal or gastric surgery. 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 (see dosing section for formula).

In horses, lidocaine infusions delivered by CRI may help to restore intestinal motility and are used to treat intestinal ileus. In dogs, when it was delivered as a CRI, there was no change in gastric emptying, and there were modest effects to increase intestinal motility.

Lidocaine has been applied to animals as a transdermal patch. The patch (designed for people) is 5% strength and used primarily for neuropathic pain (postherpetic neuralgia). This patch also has been applied for some conditions in dogs and cats with anecdotal accounts of some success. Absorption from the patch is low (less than 5%), which is far below the threshold for toxic effects.

Precautionary Information

Adverse Reactions and Side Effects

High doses of lidocaine cause CNS effects (tremors, twitches, and seizures) and vomiting, but the risk of lidocaine-induced seizures is low. IV use and CRIs in horses have caused muscle fasciculations, rapid eye blinking, anxiety, ataxia, weakness, and seizures. Lidocaine can produce cardiac arrhythmias, but it has greater effect on abnormal cardiac tissue than normal tissue.

Use lidocaine cautiously in cats. IV 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.

Contraindications and Precautions

Cats are more susceptible to adverse effects, and lower doses should be used. For example, the CRI in cats is lower than the rate in dogs. Absorption from lidocaine patches in cats is only 6.3% and is not expected to present a problem. In animals with decreased blood flow to the liver (e.g., animals under anesthesia), clearance may be reduced and the risk of adverse effects increased.

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 of sodium bicarbonate to 10 mL of lidocaine (use immediately after mixing). To prepare solutions for infusion in horses, mix 10 g of 2% lidocaine in 3 L of lactated Ringer's solution (0.33% solution).

For treating ventricular arrhythmia in horses, consider adding magnesium sulfate to the infusion. See dosing instructions below for the magnesium sulfate dose.

Patient Monitoring and Laboratory Tests

Monitor for signs of neurotoxicity (e.g., depression, muscle twitching, and seizures). Monitor the electrocardiogram 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 IV dose: 2–4 mg/kg IV (to a maximum dose of 8 mg/kg over a 10-minute period).
- Antiarrhythmic CRI dosage: 1 mg/kg initially followed by 50–75 mcg/kg/min IV CRI.
- Antiarrhythmic IM dosage: 6 mg/kg q1.5h IM.
- Epidural: 4.4 mg/kg of 2% solution.
- Adjunct to control pain and inflammation associated with surgery: 2-mg/kg IV bolus followed by 0.05 mg/kg/min CRI for 24 hours (added to patient's fluids).
- MLK: Mixed as 100 mg/mL ketamine (1.6 mL per 500 mL of fluids), 20 mg/mL lidocaine (30 mL per 500 mL of fluids), and 15 mg/mL morphine (1.6 mL per 500 mL of fluids) and infused at a rate of morphine, 0.24 mg/kg/h; lidocaine, 3 mg/kg/h; and ketamine, 0.6 mg/kg/h, administered as CRI for peri-operative analgesia.

Cats
- Antiarrhythmic IV dose: Start with 0.1–0.4 mg/kg initially and then increase to 0.25–0.75 mg/kg IV slowly if there has been no response.
- Antiarrhythmic CRI dose: Loading dose of 0.5–1 mg/kg IV followed by 10–20 mcg/kg/min (0.6–1.2 mg/kg/h) IV CRI.
- Epidural: 4.4 mg/kg of 2% solution.

Large Animal Dosage
Horses
- Ventricular tachycardia: Start with 0.25–0.5 mg/kg IV injection over 5–10 minutes, up to 1.3–1.5 mg/kg for refractory cases. Follow with 0.03–0.05 mg/kg/min (30–50 mcg/kg/min) CRI. Consider adding magnesium sulfate to the infusion to enhance the efficacy. Add 2.7 g of magnesium sulfate to 1 L of 0.9% sodium chloride solution and administer over 10 minutes IV for a dose of 2–6 mg/kg.
- 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.
Racing Commissioners International (RCI) Classification: 2

Lincomycin Hydrochloride, Lincomycin Hydrochloride Monohydrate
lin-koe-mye′sin hye-droe-klor′ide and lin-koe-mye′sin hye-droe-klor′ide mono-hye′drate

Trade and other names: Lincocin and Lincomix

Functional classification: Antibacterial

observational studies. Medroxyprogesterone acetate, an alternate progestin, may have fewer side effects than megestrol acetate.

When used for proestrus treatment, administer 2.2 mg/kg for 8 days administered orally. For anestrus treatment, administer 0.55 mg/kg/day for 32 days. Tablets can be administered intact or crushed and mixed with food. When therapy is started, the animal should be confined for 3–8 days or until cessation of bleeding because dogs in proestrus accept a male.

Patient Monitoring and Laboratory Tests

Because of risk of diabetes mellitus, monitor glucose concentrations during treatment periodically. Examination of vaginal smears is recommended to confirm detection of proestrus.

Formulations

- Megestrol acetate is available in 5- and 20-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 (early proestrus).
- Anestrus: 0.5 mg/kg q24h PO for 32 days.
- Treatment of behavior problems: 2–4 mg/kg q24h for 8 days (reduce dose for maintenance).

Cats

(See precautions listed above.)

- Dermatologic therapy or urine spraying: 2.5–5 mg/cat q24h PO for 1 week; then reduce to 5 mg once or twice a week per cat.
- Suppress estrus: 5 mg/day per cat for 3 days; then 2.5–5 mg once a week for 10 weeks (0.02 mg/kg). For long-term use (30 weeks), a lower dosage of 2.5 mg once per week should be used for greater safety.

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

Melarsomine is an organic arsenical compound, primarily for treating heartworm disease in animals. Arsenicals alter glucose uptake and metabolism to eliminate

heartworms. Melarsomine has replaced older arsenicals such as thiacetarsamide (Caparsolate) for treating heartworm disease.

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% and not recommended. 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 administration may lead to 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. To prevent adverse reactions of adulticide therapy, the American Heartworm Society recommends a three-dose protocol, whereby the first dose is administered after 2 months of a macrocyclic lactone (e.g., ivermectin) and doxycycline. To limit lung injury, administer prednisolone or prednisone at a dosage of 0.5 mg/kg q12h for the first week after adulticide treatment and 0.5 mg/kg q24h for the second week followed by 0.5 mg/kg every other day for 1–2 weeks.

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.

Killing adult heartworms in cats with adulticide treatment can cause anaphylactic reactions, thromboembolism, and fatal reactions in cats.

Contraindications and Precautions

Use cautiously in animals with high heartworm burden and use the three-dose protocol to reduce lung injury. Melarsomine may be contraindicated in dogs with class 4 (very severe) heartworm disease until the worm burden is reduced.

Melarsomine is not recommended for cats because adulticide treatment can produce severe and even fatal reactions.

Drug Interactions

No drug interactions are reported. Administration of prednisolone does not affect efficacy of melarsomine.

Instructions for Use

The most accurate and up-to-date treatment protocol is available from the American Heartworm Society (https://www.heartwormsociety.org). Follow the product insert carefully for instructions on proper injection technique. 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 the most severe and should not be treated with an adulticide before decreasing the heartworm burden.

The current three-dose protocol includes starting pretreatment with a macrocyclic lactone (e.g., ivermectin) and doxycycline (or minocycline) for 2 months and then allowing a 1-month waiting period starting on day 60. After this waiting period, administer melarsomine on day 60, wait another month, and administer the second and third doses of melarsomine on days 90 and 91. Each melarsomine dose is

2.5 mg/kg. This protocol will reduce lung and pulmonary vessel reaction associated with heartworm treatment.

Avoid human exposure by either washing hands after handling or wearing gloves. There should be strict exercise restriction in dogs during adulticide treatment.

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 IM injection. Follow guidelines from the American Heartworm Society for the safest and most effective use of melarsomine.
- Three-dose protocol: One injection on days 60, 90, and 91 after the initial diagnosis.

Cats

- Not recommended because of adverse reactions.

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, OroCAM, Meloxidyl, Loxicom (veterinary preparations), Mobic and Vivlodex (human preparation), Metacam suspension (equine preparation, Europe), and Mobicox (human formulation in Canada)

Functional classification: Anti-inflammatory

Pharmacology and Mechanism of Action

Meloxicam is an NSAID of the oxicam class. Like other NSAIDs, meloxicam has analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the 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

Mexiletine

meks-il′eh-teen

Trade and other names: Mexitil

Functional classification: Antiarrhythmic

Pharmacology and Mechanism of Action

Mexiletine is an antiarrhythmic drug used occasionally in dogs. Mexiletine is a Class IB antiarrhythmic agent. Mechanism of action is to block the fast sodium channel and depress Phase 0 of depolarization. Because lidocaine is not absorbed orally, mexiletine has been used when oral administration of a Class I antiarrhythmic agent is needed in dogs. It has a similar mechanism of action as lidocaine. It is absorbed approximately 90% in people without significant first-pass effects. It is presumed to have good absorption also in dogs, although this has not been studied.

An additional use of mexiletine is for treating chronic pain. It is used to treat pain caused by diabetic neuropathy and nerve injury at lower doses than the antiarrhythmic dose.

Indications and Clinical Uses

Mexiletine has been used to treat ventricular arrhythmias. Although lidocaine is often the first Class I antiarrhythmic agent used for injection in the hospital, when longer-term treatment with an oral drug is needed, mexiletine is often the first choice.

The doses used in dogs are derived from empirical use and extrapolation from human medicine. It is often used in combination with atenolol or sotalol (Class II and Class III antiarrhythmic agents, respectively) because it may have better electrophysiological effects when used in combination. It may also counteract the adverse effects of sotalol on the action potential duration.

Precautionary Information

Adverse Reactions and Side Effects

In dogs, the most common adverse effects are GI problems. 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 or monitor liver parameters during use.

Drug Interactions

Sotalol will increase plasma drug concentrations.

Instructions for Use

Results of controlled clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people, research studies in experimental dogs, or anecdotal experience in animals. Administer with food to decrease GI problems.

Patient Monitoring and Laboratory Tests

Monitor ECG during use. Effective plasma drug concentrations are 0.75–2.0 mcg/mL (extrapolated from people).

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
- 6 mg/kg q8–12h PO.
- Chronic pain caused by nerve injury: 4–10 mg/kg PO q8h.

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 www.FARAD.org.
RCI Classification: 4

Mibolerone
mih-bole′er-one

Trade and other names: Cheque Drops

Functional classification: Hormone

Pharmacology and Mechanism of Action
Mibolerone is an androgenic steroid drug. Mibolerone mimics androgens in the body to produce hormone effects that suppress estrus.

Indications and Clinical Uses
Mibolerone is used to suppress estrus in animals. The primary indication is to prevent estrus in adult female dogs. There are no other established indications.

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. Avoid administration in bitches before their first estrous period. 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. Continue treatment as long as needed, but it is not recommended to be used for more than 2 years. Mibolerone should not be used in bitches before the first estrous period. It is not intended for animals being used primarily for breeding purposes.

Formulations

- Midazolam is available in a 5-mg/mL injection.
- Midazolam intranasal spray (Nayzilam) is available as a single-dose 5 mg/0.1 mL spray.
- Midazolam oral syrup is available in a cherry-flavored syrup for children in a concentration of 2 mg/mL.

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 less than 4), it becomes more soluble. It can be mixed for short-term use with other water-soluble anesthetics if administered immediately after mixing. Midazolam and ketamine hydrochloride are compatible when mixed in the same syringe.

Small Animal Dosage

Dogs

- 0.1–0.25 mg/kg IV or IM.
- 0.1–0.3 mg/kg/h IV infusion.
- Status epilepticus: 0.1–0.2 mg/kg IV bolus or 0.2 mg/kg administered intranasal in a 5-mg/mL solution.
- Oral administration: midazolam syrup (2 mg/mL), 0.5–0.75 mg/kg for sedation (dose extrapolated from pediatric use).

Cats

- Sedation: 0.05 mg/kg IV.
- Induction of anesthesia: 0.3–0.6 mg/kg IV combined with 3 mg/kg of 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: 0.1–0.2 mg/kg (5–10 mg per foal) IV over 15–20 minutes or IM followed by 3 mg/h IV (range, 2–6 mL/h) CRI to control seizures. The infusion dose is prepared by adding 10 mL (5 mg/mL) to 100 mL of saline to make a solution of 0.5 mg/mL.
- Anesthetic adjunct in horses: 0.1 mg/kg IV administered with ketamine (2.2 mg/kg) or other anesthetics (e.g., xylazine).

Sheep

- 0.5 mg/kg IV or IM for short-term sedation.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.
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. It is combined with spinosad in Trifexis

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Milbemycin is a commonly used antiparasitic drug in animals. 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. 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 a heartworm preventative, miticide, and microfilaricide. It is also used to control infections of hookworm, roundworms, and whipworms. It 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 infections caused by *Demodex* in dogs (see dosing section). It is sometimes preferred over other macrocyclic lactones for treating *Demodex* infection because it is better tolerated at high doses. (Note: The isooxazolines afoxolaner, fluralaner, lotilaner, and sarolaner are preferred for treating *Demodex* infection.) Milbemycin is widely used in animals, and the efficacy and dosing regimens are established through the approvals and clinical studies by the sponsors.

Precautionary Information

Adverse Reactions and Side Effects

At doses of 5 mg/kg, it was well tolerated in most dogs (10 times the heartworm preventative dose). At 10 mg/kg (20 times the heartworm preventative 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 dosages as low as 1.5 mg/kg per day. Sensitive breeds include collies, Australian shepherds, Old English sheepdogs, longhaired whippets, and Shetland sheepdogs. In susceptible animals, the effects are 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 (*ABCB1 gene*) that regulates the membrane pump P-glycoprotein. This mutation affects the efflux pump in the blood–brain barrier. Animals with a gene mutation lack a functional membrane pump, and milbemycin can accumulate in the brains 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.

In cats, it is generally well tolerated. In cats treated for *Demodex* infection at high doses (1–2 mg/kg), some vomiting and diarrhea can be observed, but neurologic signs are rare.

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 J for a 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. For *Demodex* infection, use a protocol of 1 mg/kg/day until clinical cure followed by 3 mg/kg/wk for a parasitological cure. Treatment can be long because it may require 4 months for a clinical cure and 8 months for a parasitologic 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. It is also found in other combination products (e.g., with spinosad in Trifexis).

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/day until a clinical cure is observed followed by 3 mg/kg once per week until a parasitologic 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 every 30 days PO.
- Demodicosis in cats: 1–2 mg/kg q24h 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 www.FARAD.org.

Mineral Oil

Trade and other names: Generic brands

Functional classification: Laxative

- For mild pain, start with 0.1–0.2 mg/kg IV or IM q6h. For more severe pain, gradually increase to 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 alpha$_2$ agonist or another sedative.
- 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. If used in a food producing animal, consult FARAD at www.FARAD.org, for information on withdrawal times.

RCI Classification: 1

Moxidectin

moks-ih-dek′tin

Trade and other names: ProHeart, ProHeart 6, ProHeart 12 (canine), Coraxis, Quest (equine), and Cydectin (bovine and ovine)

Functional classification: Antiparasitic

Pharmacology and Mechanism of Action

Moxidectin is an 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. Moxidectin is 100 times more lipophilic than ivermectin. 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. However, 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 also be used and for the treatment and control of *A. caninum, U. stenocephala, T. canis, Toxascaris leonina,* and *T. vulpis.*

Moxidectin also has been used to treat *Demodex* infections in dogs at high doses. In cats, it is used for the prevention of heartworm disease caused by *D. immitis*; for the treatment and control of intestinal roundworms (*Toxocara cati*), and hookworms

(*Ancylostoma tubaeforme*). It is combined with fluralaner in a topical solution for cats (Bravecto Plus) to include treatment of fleas and ticks and in a combination tablet for dogs with sarolaner and pyrantel for treatment of roundworms, fleas, ticks, and heartworm prevention. In horses, it 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]), and small strongyles ([adults] *Cyathostomum* spp., *Cylicocyclus* spp., *Cyliocostephanus* spp., *Coronocyclus* spp., 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* [second and third instars] and *Gasterophilus nasalis* [third instars]). One dose also suppresses strongyle egg production for 84 days. Some formulations for horses also contain praziquantel. This increases the spectrum to include other intestinal parasites such as tapeworms.

In cattle, moxidectin injectable is used to treat intestinal 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. viviparous* 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, Teladorsagia trifurcata, Trichostrongylus axei, T. colubriformis, Trichostrongylus vitrinus, Cooperia curticei, C. oncophora, Oesophagostomum columbianum, Oesophagostomum venulosum, Nematodirus battus, Nematodirus filicollis,* and *Nematodirus spathiger.*

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, vision problems, coma, and death. Sensitivity to moxidectin occurs in certain breeds because of a mutation in the *ABCB1* gene that codes for the membrane pump P-glycoprotein. Animals with this mutation lack a functional p-glycoprotein 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 (10 times, 20 times, and 30 times the label dose) administered to ivermectin-sensitive collies , no adverse effects were 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 (ProHeart 6), this product was temporarily discontinued several years ago. However, this safety concerns has been addressed by reformulating the product, which is now available in 6- and 12-month forms. 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.

Neurologic toxicity in animals producing seizures can be treated with diazepam, barbiturates, or propofol.

Contraindications and Precautions

Do not use the 2.5% topical solution in cats. Do not use in dogs younger than 2 months of age. 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. Administration to foals younger than 6 months of age is not recommended. Do not apply the large animal 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 (see Appendix J).

Instructions for Use

Caution is recommended if the bovine or equine formulation is considered for use in small animals. Toxic overdoses are likely because these formulations are highly concentrated.

When applying the 2.5% topical solutions to dogs, ensure that dogs do not lick the application site. Avoid exposure to people after applying the topical solution.

The approved formulations for dogs vary in their concentration and duration. For example, there are immediate-release products, 6-month products (ProHeart-6), and 12-month products (ProHeart-12). Pay attention to specific mixing and labeling instructions when administering each product.

Patient Monitoring and Laboratory Tests

Animals should be checked for heartworm status prior to initiating treatment.

Formulations

- 30-, 68-, and 136-mcg tablets for dogs, or 2.5% topical solution for dogs.
- 20-mg/mL equine oral gel (2% gel). Quest Plus gel for horses contains 20 mg/mL (2%) plus 125 mg of praziquantel (12.5%).
- 5-mg/mL cattle pour-on; 1-mg/mL oral drench for sheep; 10-mg/mL injectable solution for cattle;
- 6-month long-acting formulation: The 6-month injectable (ProHeart 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.
- 12-month long-acting formulation: 10 mg of constituted suspension per milliliter. This product has two separate vials that require mixing prior to administration or use. One vial contains 10% moxidectin sterile microspheres and the second vial contains sterile vehicle for constitution; only this sterile diluent should be used for the constitution. The constituted suspension can be injected 30 minutes after mixing.
- Combination products: The formulation Advantage Multi for dogs 2.5% (25 mg/mL) includes 25% imidacloprid. Advantage Multi for cats 1% (10mg/mL) includes 10% imidacloprid. Moxidectin is combined with fluralaner in a topical solution for cats, with 280 mg of fluralaner and 14 mg moxidectin per milliliter. Moxidectin is combined with sarolaner and pyrantel in a chewable tablet for dogs (Simparica TRIO).

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. Topical heartworm prevention (Advantage Multi, or Coraxis) 2.5 mg/kg monthly.
- Moxidectin is combined with sarolaner and pyrantel in a chewable tablet for dogs (Simparica TRIO). The tablet is designed to deliver a dose of 1.2 mg/kg sarolaner, 24 mcg/kg moxidectin, and 5 mg/kg pyrantel, once a month oral.
- 6-month formulation: 0.17 mg/kg or 0.05 mL of the constituted suspension/kg (0.0227 mL/lb), administered as a single SQ injection once every 6 months. No more than 3 mL should be injected in a single site.
- 12-month formulation: 0.5 mg/kg (0.23 mg/lb) or 0.05 mL of the constituted suspension per kilogram (0.023 mL/lb) by SQ injection. This amount of suspension will provide 0.5 mg moxidectin per kilogram of body weight (0.23 mg/lb). To ensure accurate dosing, calculate each dose based on the dog's weight at the time of treatment.
- 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 one to four doses; alternatively, higher doses of 400 mcg/kg/day PO. Higher doses are used for refractory *Demodex* cases, with dosages of 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.

Cats

- Topical heartworm prevention with Advantage Multi is 1 mg/kg of moxidectin topically every 30 days.
- Topical solution for cats with fluralaner and moxidectin (Bravecto Plus): Administer as a single dose topically at a dose of 40 mg/kg fluralaner and 2 mg/kg moxidectin every 2 months.

Large Animal Dosage

Horses

- GI parasites: 0.4 mg/kg PO. Avoid use in young horses, small ponies, and debilitated animals.

Cattle

- 0.2 mg/kg SQ once.
- Intestinal parasites, lungworms, mites, grubs, and lice: Topical treatment (pour-on): 0.5 mg/kg (0.23 mg/lb or 45 mL per 1000 lb). 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 lb, or 0.2 mg/kg) 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

Moxifloxacin is a fluoroquinolone antibacterial with broader spectrum than some of the older antibiotics in this class such as ciprofloxacin. 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

Formulations

- Nitroglycerin is available in 0.5-, 0.8-, 1-, 5-, and 10-mg/mL injection; 2% ointment; 0.3-, 0.4-, and 0.6-mg sublingual tablets; translingual spray; and transdermal systems (0.2 mg/h patch).

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Nitroglycerin tablets are very heat and light sensitive and should be stored in a tightly sealed glass bottle.

Small Animal Dosage

Dogs

- 4–12 mg (up to 15 mg) topically as needed. In dogs, it has been used as one-fourths to three-fourths inch of 2% ointment q6h (1 inch equals 15 mg).

Cats

- 2–4 mg topically or typically one-eighth to one-quarter inch q4–6h.

Large Animal Dosage

Horses

- Treatment of laminitis: Apply 2% ointment to skin above the hoof. (Efficacy is 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

Nitroprusside is a nitrate vasodilator. Like other nitrovasodilators, it relaxes vascular smooth muscle (especially venous) via generation of NO. NO stimulates guanylate cyclase to produce GMP in smooth muscle, with a predominant effect of relaxing vascular smooth muscle. Nitroprusside is used only as an IV infusion in the hospital, 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 IV administration.

Indications and Clinical Uses

Nitroprusside is used for acute management of pulmonary edema and other hypertensive conditions. It is administered only by IV 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 or the opinions from clinical cardiology experts. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. The cost of nitroprusside has increased tremendously in recent years to as much as $750 per vial. Therefore, the high cost has discouraged use in animals.

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 (greater than 5 mcg/kg/min). At high infusion rates (greater than 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 but use cautiously with other drugs that produce vasodilation.

Instructions for Use

Nitroprusside is administered via IV infusion. IV solution should be delivered in a 5% dextrose solution. (For example, add 20–50 mg to 250 mL of 5% dextrose to a concentration of 80–200 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. (Note: Vials can be extremely expensive.)

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 www.FARAD.org.

DRUG MONOGRAPH

Norepinephrine

Noradrenaline, Levarterenol

(nor-epeh-**nef**-rin)

Trade name: Levophed®

Table of Contents

Prescriber Highlights

Prescriber Highlights

- Pressor agent for persistent, profound shock (after fluids replaced); potentially useful for isoflurane-induced hypotension.
- ICU drug, requires CRI and continuous monitoring.
- Extravasation injuries possible.

Uses / Indications

Norepinephrine (NE) is a direct-acting sympathomimetic vasopressor and cardiac inotrope that may be indicated for treating profound hypotension—especially septic shock, or post-cardiac arrest hypotension due to vasodilation. In patients with persistent shock after adequate fluid volume replacement, it can be used as a cardiac stimulant and to raise blood pressure. NE has been shown to decrease hypotension in dogs and foals secondary to isoflurane anesthesia.[1,2,3] Norepinephrine may also be useful when administered intragastrically or intraperitoneally for treating upper GI bleeding.

Pharmacology / Actions

Norepinephrine has strong affinity for $beta_1$-, $alpha_1$-, & $alpha_2$-adrenergic receptors.

Norepinephrine acts as a peripheral vasoconstrictor (alpha-adrenergic), inotropic cardiostimulant, and coronary artery dilator (betaadrenergic). Total peripheral resistance is increased, resulting in increased systolic and diastolic blood pressure. Perfusion to vital organs, skin, and skeletal muscle can be reduced especially at higher dosages.

Pharmacokinetics

When administered IV, norepinephrine's onset of action occurs within 1-2 minutes and persists for an additional 1-2 minutes. It can cause tissue damage and is poorly absorbed when given SC. After oral administration, norepinephrine is destroyed in the GI tract and not absorbed. After uptake by sympathetic nerve endings, it is rapidly metabolized via catechol-O-methyltransferase (COMT) and monoamine oxidase (MAO) to inactive metabolites.

Contraindications / Precautions / Warnings

Pressors are not a substitute for adequate blood, fluid, or electrolyte replacement. Norepinephrine should not be given to patients that are hypotensive from blood volume deficits except as an emergency measure to maintain coronary and cerebral artery perfusion until blood volume replacement therapy can be completed. If used in the absence of blood volume replacement, severe peripheral and visceral vasoconstriction, decreased renal perfusion and urine output, and poor systemic blood flow can occur despite normal blood pressures. NE should not be used if severe peripheral vasoconstriction exists since it may be ineffective and cause further reductions in blood flow to vital organs. Because it increases myocardial oxygen demand, risks of use during cardiac events may outweigh the drug's benefits.

Norepinephrine is a critical care (ICU) drug. Patients must be observed and dosage rates titrated. Avoid abrupt withdrawal of the infusion.

Do NOT confuse NOREPInephrine with EPInephrine. Norepinephrine is considered a high alert medication (medications that require special safeguards to reduce the risk of errors). Consider instituting practices such as redundant drug dosage and volume checking, and special alert labels.

Adverse Effects

liberally throughout the area, which is easily identified by its cold, hard, and pallid appearance. Sympathetic blockade with phentolamine causes immediate and conspicuous local hyperemic changes if the area is infiltrated within 12 hours. Therefore, phentolamine should be given as soon as possible after the extravasation is noted.

Reproductive / Nursing Safety

In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy *(Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans)*. In a separate system evaluating the safety of drugs in canine and feline pregnancy,[4] this drug is categorized as class ***C*** *(These drugs may have potential risks. Studies in people or laboratory animals have uncovered risks, and these drugs should be used cautiously as a last resort when the benefit of therapy clearly outweighs the risks)*.

It is not known if norepinephrine enters maternal milk.

Overdose / Acute Toxicity

Overdose with norepinephrine bitartrate can result in severe hypertension, reflex bradycardia, cardiac ischemia, increase in peripheral resistance with resulting decreased perfusion to vital organs, and decreased cardiac output.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving norepinephrine and may be of significance in veterinary patients. Unless otherwise noted, use together is not necessarily contraindicated, but weigh the potential risks and perform additional monitoring when appropriate.

- **ATROPINE**: May block the reflex bradycardia caused by norepinephrine and enhances the pressor response.
- **BETA-BLOCKERS** (eg, **propranolol**): May result in higher blood pressures secondary to blocking beta-2 arteriole dilation. Can antagonize cardiac stimulating effects; propranolol may be used to treat norepinephrine-induced cardiac arrhythmias.
- **DIGOXIN**: Increased risk for arrhythmias.
- **DIPHENHYDRAMINE**: May potentiate pressor effects.
- **DIURETICS** (eg, **furosemide**): May decrease arterial responsiveness to norepinephrine.
- **LINEZOLID**: Norepinephrine effects may be increased.
- **MAO INHIBITORS**: Hypertension can result.
- **TRICYCLIC ANTIDEPRESSANTS** (eg, **amitriptyline**, **clomipramine**): Hypertension, cardiac arrhythmias, tachycardia can result.

Dosages

Note: Dosages and drug concentrations are listed as norepinephrine base. Injectable product concentration is labeled as norepinephrine base. An online drip rate table generator is available at: http://www.globalrph.com/drip.htm.

- **DOGS/CATS:**

Persistent, profound hypotension after adequate fluid volume replacement (extra-label): An initial dosage of NE 0.05 – 0.1 micrograms/kg/minute IV CRI then titrated to desired effect; most recommend a maximum CRI rate of 1 – 2 micrograms/kg/minute. If using a 4 microgram/mL dilution (4 mg in a 1 liter bag of a dextrose 5% containing fluid), the initial rate would be 0.75 – 1.5 mLs/kg/hour. Often used in combination with dopamine, dobutamine, or vasopressin.

Isoflurane–induced hypotension (extra-label): In a study comparing 12 healthy beagles, the average effective dose was NE 0.44 micrograms/kg/minute. Doses ranged from 0.1 – 2 micrograms/kg/minute.[3]

- **HORSES:**

Hypotension in critically ill foals (extra-label): Initially, NE 0.1 microgram/kg/minute IV CRI then titrated to desired effect. If using a 4 microgram/mL dilution (4 mg in a 1 liter bag of a dextrose 5% containing fluid) the initial rate would be 1.5 mLs/kg/hour. Upper end of dosage range is approximately 1.5 microgram/kg/minute.[5] Use with dobutamine could be considered.[6]

Isoflurane–induced hypotension in neonatal foals (extra-label): In the study, hypotension was induced by isoflurane and norepinephrine, dobutamine and vasopressin were evaluated. NE was dosed at 0.3 and 1 micrograms/kg/min IV CRI. Norepinephrine improved cardiac index and O_2 delivery; high dosage significantly increased blood pressure. Authors concluded that norepinephrine and dobutamine are better alternatives than vasopressin for restoring cardiovascular function and maintaining

pressure increased with both doses. With the high dose, stroke volume index and pulmonary artery pressure also increased. Systemic vascular resistance was above baseline for both doses. Hemoglobin, PCV, arterial oxygen content, mixed venous oxygen content, and oxygen delivery were increased with both doses. There were dose dependent increases in oxygen content, oxygen consumption and oxygen delivery. It is recommended to titrate the dose starting at the lowest dose to avoid excessive vasoconstriction.[8]

- **SHEEP:**

Hypotension after adequate fluid volume replacement during septic shock (extra-label): NE 0.4 – 1 microgram/kg/minute has been safely used in experimentally induced sepsis in sheep.[5,9] NE in combination with dobutamine may be more effective than NE alone.[10]

Monitoring

Norepinephrine is a critical care (ICU) drug. Patients must be observed and dosage rates titrated. Avoid abrupt withdrawal of the infusion.

- Blood pressure. Preferably including central venous pressure or pulmonary arterial diastolic pressure. Maintain mean arterial pressure >65 mm Hg.
- Heart rate and rhythm
- Blood gases, if available.
- Urine output.

Client Information

- Must only be used by professionals in a setting where precise IV infusion and constant blood pressure monitoring can be performed.

Chemistry / Synonyms

Norepinephrine bitartrate (noradrenaline acid tartrate) occurs as a white or faintly grey, odorless, crystalline powder that slowly darkens on exposure to air and light. One part is soluble in 2.5 parts water. Solutions in water have a pH of ≈3.5. The bitartrate injection contains sulfites.

Norepinephrine may also be known as levarterenol, noradrenaline, or L-arterenol. A commonly known trade name is *Levophed*®.

Storage / Stability

Store at room temperature (25°C; 77°F). Excursions are permitted to 15°C-30°C (59°F-86°F). Protect from light.

Compatibility / Compounding Considerations

Avoid contact with iron salts, alkalis, or oxidizing agents. Norepinephrine is **not compatible** with aminophylline, sodium bicarbonate, ranitidine, or pantoprazole. Administer whole blood or plasma separately (via a Ytube and individual containers if given simultaneously).

The following drugs are listed as **compatible** with norepinephrine infusions: amikacin sulfate, calcium chloride/gluconate, ciprofloxacin, dimenhydrinate, dobutamine HCl, heparin sodium, hydrocortisone sodium succinate, magnesium sulfate, meropenem, methylprednisolone sodium succinate, multivitamins, potassium chloride, succinylcholine chloride, and verapamil HCl. Compatibility is dependent upon factors such as pH, concentration, temperature, and diluent used; consult specialized references or a hospital pharmacist for more specific information.

Dilute norepinephrine in dextrose 5% or D5W/NS. Administration in saline solution alone is not recommended as significant loss of potency can occur due to oxidation. Dextrose containing fluids can help prevent oxidation. A 4 mL vial (4 mg) is added to a 250 mL, 500 mL, or 1000 mL bag of a dextrose 5%-containing IV solution. Each mL of this dilution then contains either 16 micrograms/mL (250 mL bag), 8 micrograms/mL (500 mL bag), or 4 micrograms/mL (1 L bag) of norepinephrine bitartrate base. Do not use if solution color is pinkish, darker than slightly yellow, or if it contains a precipitate.

Dosage Forms / Regulatory Status

VETERINARY-LABELED PRODUCTS: None.

HUMAN-LABELED PRODUCTS:

Norepinephrine bitartrate for injection (must be diluted before use): 1 mg/mL in 4 mL vials; *Levophed*®, generic; (Rx). Concentrations are listed as norepinephrine base.

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9. Li YH, et al. Effects of vasoactive drugs on crystalloid fluid kinetics in septic sheep. PLoS One. 2017;12(2).
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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 www.FARAD.org.

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 PDE III. PDE 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 PDE V in the pulmonary circulation. The inotropic effects of pimobendan are attributed to its action as a calcium sensitizer rather than the PDE inhibition. By acting as a calcium sensitizer, it increases the interaction of troponin C with contractile proteins and acts as an inotropic agent. The benefits in heart failure are caused by both positive inotropic effects and vasodilating properties. Other beneficial effects may include anti-inflammatory activity, increased sensitivity of baroreceptors, increased lusitropy, and decreased platelet aggregation.

Pharmacokinetics: 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. Pimobendan is metabolized (demethylated) to desmethylpimobendan (DMP), which is an active metabolite with greater effect on PDE III activity. In dogs, the half-life is short, reported as 30 minutes to 1 hour, depending on the study. The oral absorption is 70%.

In cats, pimobendan produces much higher blood concentrations than dogs, and the half-life is almost three times longer than in dogs. Both pimobendan and the metabolite DMP act as calcium sensitizers, but cats are less responsive to DMP than dogs.

Indications and Clinical Uses

Pimobendan is indicated for use in dogs for treatment of congestive heart failure (CHF). It has been used in dogs with either valvular insufficiency or cardiomyopathy. It is recommended in consensus guidelines for any dog with valvular disease with stage B2 or higher and may delay onset of CHF. In dogs with heart failure caused by valvular disease, it decreased heart rate, decreased left ventricular and left atrial dimensions, reduced heart size, and reduced preload and natriuretic peptide concentrations. In dogs with stage C valvular heart disease, it has improved survival and quality of life. 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 (furosemide), spironolactone, and angiotensin-converting

enzyme (ACE) inhibitors. Pimobendan treatment has produced significant improvement compared with placebo in dogs treated with an ACE inhibitor and a diuretic. Pimobendan may be helpful for treating Doberman pinschers, and probably other breeds, with occult (asymptomatic) dilated cardiomyopathy by prolonging the onset of clinical signs, improving survival and overall outcome.

It has not been recommended to administer positive inotropic agents such as pimobendan to cats with hypertrophic cardiomyopathy. However, it has been associated with improvement in clinical signs and longer survival time in cats with heart failure associated with dilated cardiomyopathy as part of a therapeutic regimen that may include other drugs (e.g., furosemide). Although not FDA approved for cats, when administered at 1.25 mg/cat q12h (0.25 mg/kg), 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. At therapeutic doses, there has been negligible effect on platelet aggregation.

Contraindications and Precautions

Use pimobendan cautiously in animals prone to cardiac arrhythmias. Do not use in animals with obstructive cardiomyopathy or a fixed obstruction of the outflow tract. 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 PDE inhibitors such as theophylline, pentoxifylline, and sildenafil (Viagra) and related drugs. Sildenafil is a PDE V inhibitor, and theophylline is a PDE IV inhibitor. Pimobendan is insoluble unless in an acidic environment, and it is difficult to mix pimobendan into a solution.

Instructions for Use

Follow the approved label instruction for use. Evaluate stage of heart failure in animals before use. Consider the addition of other drugs such as 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 the 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. If administered with an ACE inhibitor, some dogs are managed on 0.125 mg/kg q12h PO.

Cats
- 1.25 mg/cat q12h PO (0.1–0.3 mg/kg q12h).

Large Animal Dosage
- No doses have been reported for large animals.

Regulatory Information
Do not administer to animals intended for food.

Piperacillin Sodium and Tazobactam
pih′per-ah-sill′in soe′dee-um taze′oh-back-tam

Trade and other names: Zosyn and generic; also referred to as "Pip-Taz"

Functional classification: Antibacterial, beta-lactam

Pharmacology and Mechanism of Action
Piperacillin is a beta-lactam antibiotic of the acylureidopenicillin class. Like other beta-lactams, piperacillin binds PBPs that weaken or interfere with cell wall formation. After binding to PBPs, 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 MIC values during the dose interval). Tazobactam is a beta-lactamase inhibitor. When administered in combination with piperacillin, it increases the spectrum to include beta-lactamase–producing strains of gram-negative and gram-positive bacteria.

Compared with other beta-lactam antibiotics, piperacillin–tazobactam has good activity against *Pseudomonas aeruginosa* and bacteria of the Enterobacterales, including some extended spectrum beta-lactamases (ESBL)–producing strains. It also has good activity against streptococci but is not active against methicillin-resistant *Staphylococcus* spp.

Pharmacokinetics: Pharmacokinetic data for dogs indicate a half-life of 0.55 hours, a volume of distribution of 0.27 L/kg, and clearance of 5.79 mL/kg/min. Protein binding in dogs is 18%. Because piperacillin has a short half-life in animals and must be given by injection (usually IV), the use is often limited to in-hospital use.

Indications and Clinical Uses
Piperacillin and tazobactam is one of the most popular IV antibiotics for in-hospital use in people. The use includes septicemia, UTIs, skin, soft tissue, respiratory infections, intra-abdominal infections, and gynecologic infections. Targeted organisms include bacteria of the Enterobacterales (*Escherichia coli, Klebsiella pneumoniae*) and *P. aeruginosa*. The activity includes some ESBL-producing strains of the Enterobacterales. The in vitro activity against some gram-negative bacteria is enhanced when administered

Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an ACTH stimulation test to monitor adrenal function. Corticosteroids can increase liver enzymes, especially ALP, because of enzyme induction, without inducing liver pathology. Prednisolone can increase WBC 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 intravenously.

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 for adrenal insufficiency: 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. IV dose should be given slowly over 30–60 seconds.
- Treatment of shock (although efficacy for treating shock has not been established): 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 www.FARAD.org.
RCI Classification: 4

Prednisone

pred′nih-sone

Trade and other names: Deltasone, Meticorten, and generic brands

Functional classification: Corticosteroid

Pharmacology and Mechanism of Action

Prednisone is the inactive form of prednisolone. After administration in most animals (except horses and cats), prednisone is converted to prednisolone, and the effects listed for prednisolone are expected.

Prednisone is a glucocorticoid anti-inflammatory drug. The effect of prednisone is attributed 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 is evidence of poor conversion of prednisone to prednisolone or poor absorption of prednisone in cats and horses. Prednisolone or another active drug (e.g., triamcinolone, dexamethasone) should be used instead for these animals. 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

There are many side effects from corticosteroids that include polyphagia, polydipsia and polyuria, behavior changes, and HPA axis suppression. Adverse effects include GI ulceration, diarrhea hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone (but not free T_4), 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 dogs, prednisolone administration increased vascular resistance, systolic blood pressure, and increase cardiac afterload. This could potentially exacerbate CHF in some dogs. Thus, in dogs with heart disease, prednisolone should be used carefully.

Contraindications and Precautions

Use corticosteroids cautiously in patients with a risk of GI ulcers or infections and 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 NSAIDs increases the risk of GI injury. Corticosteroids may inhibit conversion of T_4 thyroid hormone to the active form T_3. However, in dogs, the concentration of total T_4 , but not free T_4, is decreased. Therefore, the effect on thyroid status in a canine patient is expected to be minimal.

Instructions for Use

Prednisolone and prednisone can be used interchangeably in dogs. However, cats and horses may have problems converting prednisone to the active prednisolone or problems with oral absorption of prednisone, and prednisolone should be used instead. (Alternatively, methylprednisolone or triamcinolone can be used.) As for

prednisolone, the doses vary across a broad range based on severity of the underlying condition. Consult the dosing section for the range of doses administered for each condition.

Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an ACTH stimulation test to monitor adrenal function. Corticosteroids can increase liver enzymes, especially ALP, without inducing liver pathology. Corticosteroid administration may decrease conversion of thyroid hormones to active form. However, in dogs receiving anti-inflammatory doses of prednisone, total T_4 concentrations, but not freeT_4, may be decreased.

Formulations

- Prednisone oral forms: 1-, 2.5-, 5-, 10-, 20-, 25-, and 50-mg tablets; 1-mg/mL syrup (Liquid Pred in 5% alcohol); and 1-mg/mL oral solution (in 5% alcohol)
- Prednisone for injection: 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 and 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, per day, which may be divided into twice-daily treatments, IM, or PO initially; then taper to q48h at a dose of 0.3–0.5 mg/kg.
- Immunosuppressive: 2.2–6.6 mg/kg/day IV, IM, or PO initially; then taper to 2–4 mg/kg q48h. Initial doses rarely need to exceed 4 mg/kg per day.
- Replacement therapy for adrenal insufficiency: 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/m^2 q24h for 7 days; then 20 mg/m^2 every other day PO.

Cats

- Not recommended for cats because of an inability to form active metabolite. However, if use is attempted, higher doses than used in dogs are needed.

Large Animal Dosage

Horses

- Prednisone suspension (Meticorten) (label dosage): 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 an 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 www.FARAD.org.
RCI Classification: 4

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
- 0.5–2 mg per dog q8–24h (as needed).

Cats
- 0.25–1 mg per cat (0.07 mg/kg or approximately 1 mg per 15 kg) q8–12h PO.
- Cats with urethral obstruction: 0.5 mg per cat PO q8h initially; then 0.25–0.5 mg per cat once daily.

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 www.FARAD.org.
RCI Classification: 3

Prednisolone, Prednisolone Acetate
Trade and other names: Delta-Cortef, PrednisTab, and generic brands

Functional classification: Corticosteroid

Pharmacology and Mechanism of Action
Prednisolone is one of the most widely used glucocorticoids. Prednisolone is the active form of prednisone. Prednisolone, like other glucocorticoids, produces anti-inflammatory and immunosuppressive effects. 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 intramuscularly or intraarticularly.

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 is used for treatment of equine asthma syndrome when recurrent airway obstruction (RAO) occurs. In cattle, corticosteroids have been used in the treatment of ketosis. The prednisolone and trimeprazine formulation (Temaril-P) has been effective for treating pruritus in dogs. (See Trimeprazine for further details.)

Precautionary Information

Adverse Reactions and Side Effects

There are many side effects from corticosteroids, which include polyphagia, polydipsia and 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 cats, there is a concern that corticosteroids such as prednisolone can exacerbate CHF through volume expansion secondary to steroid-induced hyperglycemia. This has occurred in susceptible cats after injections of methylprednisolone acetate. This has not been a clinical problem in otherwise healthy cats. In dogs, there was not an expansion of plasma volume, but short-term use can increase vascular resistance, systolic blood pressure, and increase cardiac afterload. This could potentially exacerbate CHF in some dogs. The mechanism is through increased sensitivity of the alpha receptors and angiotensin II. Thus, in both cats and dogs with heart disease, prednisolone should be used carefully.

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 and not supported by clinical evidence.

Contraindications and Precautions

Use cautiously in patients with a risk of GI ulcers or infection and in animals in which growing or healing is necessary. Use prednisolone cautiously in patients with kidney disease because it may increase azotemia. Use prednisolone cautiously in pregnant animals because fetal abnormalities have been reported in laboratory rodents. Use cautiously in dogs and cats with heart disease because in cats it can increase volume expansion in cats at risk of CHF, and in dogs, it can increase vascular resistance and blood pressure. 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 NSAIDs will increase the risk of GI injury. Corticosteroids may inhibit conversion of T_4 thyroid hormone to the active form T_3. However, in dogs, the concentration of total T_4 but not free T_4, is decreased. Therefore the effect on thyroid status in canine patients is expected to be minimal.

Instructions for Use

Doses for prednisolone are of a broad range and based on severity of underlying condition. Generally, after initial treatment, if the patient responds favorably, the doses for long-term maintenance treatment can be tapered to less than 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 ACTH stimulation test to monitor adrenal function. Corticosteroids can increase liver enzymes, especially ALP, without inducing liver pathology. Prednisone can increase white blood cell (WBC) 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, but free T_4 concentrations should be unaffected. Prednisolone and prednisone at high doses for several weeks may produce significant proteinuria and glomerular changes in some dogs.

Formulations

- Oral prednisolone is available in 5- and 20-mg tablets and 3-mg/mL syrup.
- Injection is available as a 25-mg/mL acetate suspension injection (10 and 50 mg/mL in Canada).
- Prednisolone sodium phosphate orally disintegrating tablets are available for people but not widely used in animals. These tablets are available in sizes of 5, 10, 15, and 30 mg.
- Prednisolone is also available in combination with trimeprazine (Temaril-P). (See Trimeprazine 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: The induction dose is 0.5–1 mg/kg, per day, which may be split into q12h doses, IM, or PO. Then taper the dose to 0.3–0.5 mg/kg, q48h, for long-term treatment.
- Immunosuppressive: 2.2–6.6 mg/kg/day IV, IM, or PO initially; then taper to 2–4 mg/kg q48h. Initial dosages rarely need to exceed 4 mg/kg per day.
- 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 for adrenal insufficiency: 0.2–0.3 mg/kg/day PO.
- Cancer therapy (e.g., CHOP protocol): 40 mg/m^2 q24h for 7 days; then 20 mg/m^2 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 United States. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.
RCI Classification: 4

Sildenafil Citrate

sill-den′-ah-fil

Trade and other names: Viagra and Revatio

Functional classification: Vasodilator

Pharmacology and Mechanism of Action

Sildenafil is used as a vasodilator. Sildenafil's vasodilator effects are specific for phosphodiesterase V. Sildenafil and similar drugs act to increase cyclic guanosine monophosphate (GMP) by inhibiting its breakdown by phosphodiesterase V (PDE V). Relaxation of smooth muscle occurs from generation of nitric oxide. There are two important locations of PDE V, (1) vascular smooth muscle of the lungs and (2) corpus cavernosum. The effects on the corpus cavernosum produce the desired clinical effects for treating erectile dysfunction in people. 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 dosage of 1–2 mg/kg q12h PO in dogs.

Sildenafil also relaxes smooth muscle in other sites, including portions of the GI tract, uterus, and gallbladder. Relaxation of the esophageal muscle may improve some dogs with clinical megaesophagus. Most of the esophagus in dogs is comprised of striated muscle, but the lower esophageal sphincter is made of smooth muscle, which can be relaxed by some agents.

Pharmacokinetics: In dogs, the half-life is approximately 5 hours.

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 and megaesophagus. In dogs, there is clinical evidence for the beneficial effects of sildenafil in patients with pulmonary hypertension. Results of prospective studies in dogs show that the response may be inconsistent but that many dogs have lower pulmonary artery pressure after treatment with sildenafil. On the other hand, some dogs do not respond. Sildenafil has been used to improve clinical signs in dogs with congenital idiopathic megaesophagus. This improvement occurs through relaxation of the lower esophageal sphincter muscle to facilitate emptying of the esophagus to the stomach.

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. When used for treating megaesophagus in dogs, it should not be used with cisapride or metoclopramide because they antagonize the effect.

Instructions for Use
The use in veterinary medicine has been based on studies in dogs with pulmonary hypertension and in dogs with megaesophagus. 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
- Pulmonary hypertension: 2 mg/kg q12h PO. Dose interval may range from 8–24 hours, and doses as high as 3 mg/kg have been administered to some dogs. There are variations in the dose range because of limitation in tablet sizes.
- Megaesophagus: 1 mg/kg PO q12h.

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 www.FARAD.org.

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 is a dietary supplement that contains silybin as the most active ingredient. It is also known as milk thistle, the plant 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 an antioxidant effect, in which it inhibits both peroxidation of lipid membranes and GSH oxidation. Experimental data have supported the hepatoprotective properties of silymarin as an antioxidant and a free radical scavenger.

Pharmacokinetics: One product (Marin) is complexed with phosphatidylcholine, which may increase oral bioavailability. The combination products contain vitamin E (aqueous alpha tocopherol, 10–100 IU/kg/day), which has also been advocated for its antioxidant effects.

The pharmacokinetics of silymarin have been studied in dogs, cats, and horses. After oral administration to cats, the half-life is 3.2 hours (±1.74) but the oral

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, which contains 100-mcg elemental iodide (118 mcg of sodium iodide) per milliliter 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 in another section of this book.

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 lb) slowly; repeat weekly.

Regulatory Information

Because of a low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Sotalol Hydrochloride

soe′tah-lole hye-droe-klor′ide

Trade and other names: Betapace

Functional classification: Beta blocker, antiarrhythmic

Pharmacology and Mechanism of Action

Sotalol is an antiarrhythmic agent that has effects as a nonselective beta-receptor ($beta_1$ and $beta_2$) adrenergic blocker (Class II antiarrhythmic). The action as a Class II antiarrhythmic is similar to propranolol (one-third potency); however, it has beneficial effects through additional 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. The benefit during treatment with sotalol is that the negative inotropic effects from beta-receptor antagonism is balanced by increased action potential duration, leading to a prolonged time for calcium reentry.

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 has been used as a preferred oral

antiarrhythmic agent administered to small animals, particularly dogs, there are no controlled studies to establish efficacy over other agents. The use and doses are derived primarily from small observational studies or anecdotal and clinical experience.

In horses, sotalol (2 mg/kg q12h) produces lower peak concentrations than comparable doses in people. However, it has decreased heart rate and increased the QT interval, which facilitates cardioversion in horses with atrial fibrillation.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have not been reported for animals but are expected to be similar to those of propranolol. In people, reported adverse effects include atrioventricular (AV) block, hypotension, dyspnea, bronchospasm, bradycardia, and QT interval prolongation. These effects are possible but not reported from the use in animals. Like many antiarrhythmic agents, sotalol may have some proarrhythmic activity. Negative inotropic effects may cause concern in some animals with poor cardiac contractility.

Contraindications and Precautions

Sotalol should be administered cautiously to patients with heart failure or AV block. Use cautiously in patients with poor cardiac reserve because it may decrease cardiac contractility. In dogs with ventricular arrhythmias, it produces a mild decrease in left ventricular function; otherwise, it has been well tolerated in dogs with atrial enlargement and systolic dysfunction.

Drug Interactions

Use cautiously with other cardiovascular drugs that may depress the heart. A full range of drug interactions is not known for dogs because the use is extralabel, and such records are not kept. However, drug interactions are possible from other medications that interfere with drug metabolism.

Instructions for Use

The beta-blocking effects occur at low doses; Class III antiarrhythmic effects occur at higher doses. In people, sotalol has been a more effective maintenance agent for controlling arrhythmias than other drugs, and this may be true in animals also.

Patient Monitoring and Laboratory Tests

Monitor heart rate during treatment. Monitor the electrocardiogram for response to 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

- 2 mg/kg q12h PO. (For medium- to large-breed dogs, begin with 40 mg per dog q12h; then increase to 80 mg per dog if no response.)

Cats

- 1–2 mg/kg q12h PO. A dosage of 10–20 mg per cat q12h also has been used.

Large Animal Dosage

Horses

- Treatment of atrial fibrillation: 2 mg/kg PO q12h for 3 days.
- Ventricular tachycardia: 1 mg/kg PO q12h up to 2–3 mg/kg PO q12h. (Increase dose as needed to control the response.)

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.
RCI Classification: 3

Spectinomycin and Spectinomycin Dihydrochloride Pentahydrate

spek-tih-noe-mye′sin

Trade and other names: Spectam, Spectogard, Prospec, Linco-Spectin, and Adspec

Functional classification: Antibiotic, aminocyclitol

Pharmacology and Mechanism of Action

Spectinomycin is an aminocyclitol antibiotic that shares similar features with the aminoglycoside class of antibiotics. However, it differs in that it does not contain amino sugars or glycosidic bonds. 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* spp. but with 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 *Escherichia coli* and as an injection for treatment of respiratory infections. Spectinomycin has been used in cattle to treat bovine respiratory disease infections caused by *Pasteurella* spp., *Mannheimia* spp., and *Histophilus somni*. It also has activity against *Mycoplasma* spp. It has been used in dogs, but this use is uncommon.

The approved indication for dogs is oral treatment "of infectious diarrhea and gastroenteritis caused by organisms susceptible to spectinomycin." The injectable or oral formulation is for "treatment of infections caused by gram-negative and gram-positive organisms susceptible to spectinomycin." However, these are outdated indications, and the use in small animals is uncommon. It is approved for pigs for treatment and control of infectious bacterial enteritis associated with *E. coli* in pigs younger than 4 weeks of age. It is also approved for poultry to be added to drinking water.

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 IV injection. This solution has produced severe pulmonary edema and death.

Drug Interactions

No drug interactions are reported.

Formulations
- Spinosad is available in five chewable tablet sizes containing 140, 270, 560, 810, or 1620 mg.
- Spinosad + milbemycin chewable tablets are available as 140 mg of spinosad and 2.3 mg of milbemycin oxime, 270 mg of spinosad and 4.5 mg of milbemycin oxime, 560 mg of spinosad and 9.3 mg of milbemycin oxime, 810 mg of spinosad and 13.5 mg of milbemycin oxime, and 1620 mg of spinosad and 27 mg of milbemycin oxime.

Stability and Storage
Store in blister packs and at room temperature.

Small Animal Dosage
Dogs
- 30 mg/kg (13.5 mg/lb) PO administered once per month.

Cats
- 50–100 mg/kg PO once per month. (The approved dosage in some countries for cats is 50 mg/kg once per month.)

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 www.FARAD.org.

Spironolactone
speer-one-oh-lak′tone

Trade and other names: Aldactone and Prilactone (Europe)

Functional classification: Diuretic

Pharmacology and Mechanism of Action
Spironolactone is considered a potassium-sparing diuretic, but it also acts as an aldosterone antagonist. The action of spironolactone is to interfere with sodium reabsorption in distal renal tubules by competitively inhibiting the action of aldosterone. Aldosterone mediates retention of water and sodium. Spironolactone 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 because it does not produce a significant diuretic action. Because aldosterone may have direct effects on remodeling of cardiac muscle cells and vascular endothelium, spironolactone may act by blunting aldosterone-induced myocardial remodeling and myocardial fibrosis. There are minor antiandrogenic effects produced; therefore, a related drug, eplerenone (Inspra), has been used in people because it produces fewer antiandrogenic effects compared with aldosterone. But the endocrine effects and antiandrogenic effects are not as much of a problem in dogs compared with people, and spironolactone is still the preferred agent in this class.

Pharmacokinetics: In dogs, the oral absorption is 50% but is increased to 80%–90% when administered with food. At the currently recommended dose in dogs (2 mg/kg), it produces approximately 88% inhibition of 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 (CHF) caused by valvular disease. (Other treatments can include pimobendan, digoxin, angiotensin-converting enzyme [ACE] inhibitors, and furosemide.) Spironolactone is not recommended for routine use to delay the onset of heart failure in patients with valvular disease (stage B2). Spironolactone may also be used with angiotensin-converting enzyme (ACE) inhibitors to achieve a synergistic effect for treatment of heart failure in animals. The addition of spironolactone to traditional cardiac therapy can reduce the risk of cardiac morbidity and mortality in dogs with valvular disease. The proposed benefit of spironolactone treatment 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. Despite treatment with ACE inhibitors, some animals may still exhibit aldosterone synthesis, which has been known as *aldosterone breakthrough*. Spironolactone may be effective to decrease the effects caused by aldosterone breakthrough.

Spironolactone has also been used for managing hepatic cirrhosis because it inhibits 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 for more information on cats).

Precautionary Information

Adverse Reactions and Side Effects

Spironolactone can produce hyperkalemia in some patients. Facial dermatitis has been reported from administration of spironolactone to cats, which may limit its clinical use in these animals. The mechanism of these reactions is not known. High doses and long-term use may produce some steroid-like side effects, but this has not been a significant clinical problem in dogs. However, in people, these endocrine effects have been associated with antiandrogenic effects such as gynecomastia, hirsutism, and impotence. The only antiandrogenic effects reported from its use in animals is prostatic atrophy, which 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 ACE inhibitors and does not ordinarily produce adverse changes in potassium concentrations. However, in some animals, the dual treatment with spironolactone and an ACE inhibitor may increase the risk of kidney injury and may increase the risk of hyperkalemia. Therefore, some monitoring is advised to avoid this problem. Use cautiously with other drugs that can increase potassium concentrations such as trimethoprim and NSAIDs. Other cardiac treatments have been safely administered with spironolactone such as pimobendan, digoxin, and furosemide.

Instructions for Use
Spironolactone usually is administered with other drugs (e.g., ACE inhibitors, inotropic agents, vasodilators) for treating CHF.

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. In Europe, there is an approved formulation for animals. In the United States, the human generic formulation is used.
- Oral suspension: 5 mg/mL.

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 dosage for dogs is 2 mg/kg/day.

Cats
- Use in cats is controversial because it may produce dermatitis and because the efficacy is questionable. However, dosages 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 www.FARAD.org.
RCI Classification: 4

Stanozolol
stan-oh′zoe-lole

Trade and other names: Winstrol-V

Functional classification: Hormone, anabolic agent

Pharmacology and Mechanism of Action
Stanozolol is an anabolic steroid. Stanozolol is a derivative of testosterone. These anabolic agents are designed to maximize anabolic effects while minimizing androgenic action. Other anabolic agents include boldenone, nandrolone, oxymetholone, and methyltestosterone.

Large Animal Dosage
No doses have been reported for large animals.

Regulatory Information
Because of a low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

Tegaserod Maleate
teg-ah-ser′odd mal′ee-ate

Trade and other names: Zelnorm

Functional classification: Gastrointestinal stimulant

Note: In 2007, tegaserod was removed from the US market and was made available to physicians only through a restricted distribution program from the manufacturer. Beginning in April 2008, tegaserod was no longer available through the restricted distribution program; therefore the US Food and Drug Administration (FDA) has decided to make tegaserod available only to physicians for patients in emergency situations that are life threatening or require hospitalization.

Thus this drug is no longer available to veterinarians. For information on the pharmacology, use, and dosing for tegaserod, please consult previous editions of this book.

Telmisartan
tel′ mi sar′ tan

Trade and other names: Semintra (veterinary form) and Micardis (human form)

Functional classification: Vasodilator

Pharmacology and Mechanism of Action
Telmisartan is a vasodilator that functions as an angiotensin II receptor blocker (ARB). Angiotensin II acts primarily on the type 1 and type 2 receptors, but telmisartan has high affinity and selectivity for the angiotensin II subtype 1 (AT-1) receptor and preserves the beneficial effects from the AT-2 subtype (angiotensin II, subtype 2 receptor). Compared with angiotensin-converting enzyme (ACE) inhibitors, it directly blocks the receptor, rather than inhibits synthesis of angiotensin II. Angiotensin II is produced in animals with heart disease and kidney disease and in response to an activated renin–angiotensin–aldosterone system (RAAS). Telmisartan has a long binding affinity for the angiotensin II receptor, producing long-lasting effects and is capable of blocking the AT-1 receptor, regardless of the source of angiotensin; therefore it is effective in states of *angiotensin breakthrough*. Telmisartan and other ARBs have been used in people who cannot tolerate ACE inhibitors. ARBs have the advantage of being less likely to induce hyperkalemia and are more easily tolerated in people.

In cats, telmisartan has an approved indication for treating hypertension in cats and has been shown to be superior to ACE inhibitors for this use. It was approved for use in cats by the FDA in May 2018. Hypertension in cats is a common problem that often occurs with chronic kidney disease (CKD) and hyperthyroidism. Proteinuria has been associated with renal hypertension, and telmisartan can be helpful to decrease proteinuria.

In dogs, telmisartan does not have an FDA-approved indication but is used to treat hypertension when other agents have been ineffective. It may produce a more complete blockade of aldosterone production than ACE inhibitors.

Telmisartan may have some anticancer properties through activation of a receptor that can induce apoptosis of cancer cells The application of this property in animals has so far been unexplored.

Pharmacokinetics: Telmisartan has a longer half-life and is more lipophilic than other ARBs. In dogs, the half-life is approximately 5 hours. In cats, the oral bioavailability is approximately 33%. Oral absorption is lower with feeding, but it may be administered with a small amount of food if necessary, without decrease in efficacy. Peak concentration occurs in 15–30 minutes after administration. The half-life in cats is approximately 8–8.5 hours. By comparison, the half-life in people is 20–24 hours.

Indications and Clinical Uses

Telmisartan is the only ARB that has been rigorously tested in cats. It was more effective than ACE inhibitors, irbesartan, and losartan. Compared with placebo, it significantly lowers the systolic blood pressure in cats after 14 days of treatment. In cats, the approved indication is for treatment of hypertension and proteinuria caused by CKD. In cats, it can be considered a first choice for treating hypertension and has been preferred over ACE inhibitors such as benazepril.

The use in dogs is based on less rigorous studies, but studies in experimental animals and anecdotal experience support the use. In dogs, it is generally used for hypertension and proteinuria when other agents such as ACE inhibitors (e.g., enalapril, benazepril) are ineffective or not tolerated. In experimental dogs, telmisartan (1 mg/kg) was more effective than enalapril. It has also been administered concurrently with other antihypertensive agents in dogs. A related drug, irbesartan (30 mg/kg q12h), has also been shown to block angiotensin II receptors in dogs, but losartan is less potent because it relies mostly on an active metabolite that dogs do not produce (see Losartan for more details). Because telmisartan is more active than losartan in dogs and easily available to veterinarians, it should be a preferred if an angiotensin II blocker is needed.

Precautionary Information

Adverse Reactions and Side Effects

Adverse effects have been uncommon, but clinical trials in cats have shown vomiting, hypersalivation, weight loss, diarrhea, lethargy, anemia, and hypotension. Drugs that act on the RAAS can produce a decrease in red blood cell count. If hypotension is observed, a dose adjustment is appropriate. If severe hypotension is observed, treat with fluid therapy until the patient is stabilized; then re-evaluate the dose or the drug regimen.

In cats, there was no increase in creatinine even in cats with stage 2 or 3 CKD. During safety studies, up to five times the approved dose was administered to cats for 6 months, and adverse effects were not observed other than those listed earlier, which included hypotension and decreased red blood cell count.

Contraindications and Precautions

No specific contraindications have been reported for animals. Safety in breeding, pregnant, or lactating animals has not been established.

Drug Interactions

Combined use of an ARB and an ACE inhibitor may increase the risk of kidney injury because of dual blockade. This may be associated with increased risks of hypotension, hyperkalemia, and changes in kidney function.

Instructions for Use

In cats, the dose protocols are based on the FDA-approved indications and label instructions for treating proteinuria in cats with CKD. The oral solution is well tolerated in cats and can be administered directly or with small amounts of food. It should not be mixed in with food but can be given simultaneously with a meal. When using the dosing syringe, rinse with water between treatments. In dogs, the use is based more on anecdotal experience and studies in research dogs but is an accepted use by most cardiologists.

Patient Monitoring and Laboratory Tests

Monitor blood pressure in treated animals. Typically, the blood pressure should be checked within 7–10 days of initiating treatment. If the patient is stable, blood pressure measurements can be performed at the same time as regular checkups. If blood pressure is too low (defined as less than 120/60 mm Hg) with clinical signs of weakness, syncope, or tachycardia, the dose should be lowered by 0.5-mg/kg increments. Monitor the complete blood count (CBC) periodically during treatment because of a risk of lower red blood cell count.

Formulations

- Telmisartan is available for cats as a 10-mg/mL oral solution in a 35-mL bottle.
- Tablets: formulation for people in sizes of 20-, 40-, and 80-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

- 1 mg/kg once per day PO as a starting dosage. Increase to 3 mg/kg once per day and then to twice daily if needed.

Cats

- 1.5 mg/kg PO q12h initially for the first 14 days. Thereafter, 2 mg/kg PO q24h. For the oral solution, this is equivalent to 0.2 mL/kg. May be administered directly or with small amount of food, but not mixed in with food. Adjust the dose by 0.5-mg/kg increments by monitoring the blood pressure. Cats that are hypotensive from 2 mg/kg are usually adjusted down to 1 mg/kg.

Large Animal Dosage

- No large animal doses have been reported.

Regulatory Information

Do not administer to animals intended for food.
Racing Commissioners International (RCI) Classification: 3

Tepoxalin

tep-oks′ah-lin

Trade and other names: Zubrin

Functional classification: Anti-inflammatory

Large Animal Dosage

Horses

- 30 mg/kg PO q12h. However, there are no studies to demonstrate efficacy in horses.

Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at www.FARAD.org.

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

Terbutaline is a beta$_2$-adrenergic agonist. It is used primarily as a bronchodilator. Terbutaline stimulates beta$_2$-receptors to relax bronchial smooth muscle. Terbutaline is more beta$_2$ specific than drugs such as isoproterenol, which affect both beta$_1$- and beta$_2$-adrenergic receptors. Other beta$_2$-specific drugs include albuterol and metaproterenol. In addition to the beta$_2$ effects to relax bronchial smooth muscle and relieve bronchospasm, the beta$_2$ agonists may inhibit release of inflammatory mediators from mast cells.

Indications and Clinical Uses

Terbutaline, like other beta$_2$-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. Is has been useful as an injection to rapidly relieve bronchospasm in small animals associated with inflammatory airway disease or clinical procedures.

It has been used in horses for short-term administration, by injection, to relieve bronchoconstriction associated with recurrent airway obstruction (RAO), which is a component of equine asthma syndrome. The use in animals has been primarily derived from empirical use, experience in humans, and recommendations from clinical experts. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness in animals. 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 PO route in horses; therefore, it is not effective in horses for PO administration. Clenbuterol usually is the first drug of choice for oral administration in horses. (See Clenbuterol.)

Terbutaline (and other beta$_2$-agonists) have also been used during pregnancy to delay labor. (The dosage in people is 2.5 mg q6h PO.)

Precautionary Information

Adverse Reactions and Side Effects

Excessive beta-adrenergic stimulation from terbutaline at high doses can produce tachycardia and muscle tremors. Arrhythmias are possible with high doses. All $beta_2$ agonists inhibit uterine contractions at the end of gestation in pregnant animals. High doses of $beta_2$ agonists can lead to hypokalemia because they stimulate Na^+-K^+-ATPase and increase intracellular potassium while decreasing serum potassium and producing hyperglycemia. Treatment consists of potassium chloride (KCl) supplement at a rate of 0.5 mEq/kg/h.

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

Terbutaline may be administered PO, IM, or SQ. Other $beta_2$ agonists used in animals for relief of bronchoconstriction include albuterol and salmeterol, and clenbuterol in horses. Animals with acute bronchoconstriction may also benefit from corticosteroid treatment and oxygen therapy. Caution should be used when administering repeated SQ doses. The maximum SQ 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 vials with a concentration of 1 mg/mL for injection.

Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Terbutaline sulfate is soluble in water and can be diluted in sterile water prior to administration. 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 remained 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 (one quarter of a 2.5-mg tablet) q12h PO.
- 5–10 mcg/kg (0.005–0.01 mg/kg) q4h SQ or IM. The most common dose in cats is 0.05 mg per cat (equivalent to 0.05 mL) injected SQ.

Large Animal Dosage

Horses

- Not absorbed orally. Use IV for treatment of chronic 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. Testosterone is used to supplement testosterone in deficient animals. It also produces anabolic effects in debilitated animals and increases weight gain. Testosterone esters are administered intramuscularly to avoid first-pass effects that occur from PO administration. Esters in oil are absorbed more slowly from IM 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 to enhance athletic performance and increase muscle development.

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. In men who take excessive testosterone supplements, there are cardiovascular risks.

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.