A

# Acepromazine Maleate

ayss-proe´meh-zeen mal´ee-ate

**Trade and other names:** ACE, AceproJect, AceproTabs, Atravet, and PromAce; it sometimes is called acetylpromazine

**Functional classification:** Tranquilizer, phenothiazine tranquilizer

## Pharmacology and Mechanism of Action

Phenothiazine tranquilizer and sedative. Acepromazine inhibits central dopaminergic receptors to produce sedation and tranquilization. Acepromazine also has antimuscarinic action and blocks norepinephrine at adrenergic receptors (e.g., alpha-receptors). Because of the blockade of alpha-receptors on vascular smooth muscle, it also produces vasodilation. When administered as an anesthetic adjunct, it may produce a decrease in vascular resistance and lower blood pressure but usually does not decrease cardiac output. In horses, IV administration significantly increases the blood flow through digital arteries and laminae. The half-life in horses is approximately 2.5 hours.

## Indications and Clinical Uses

Acepromazine is used as a sedative, a tranquilizer, a pre-anesthetic, and an anesthetic adjunct. When used as an anesthetic pre-anesthetic, it induces muscle relaxation and lowers doses of anesthetic agents used concurrently. In pre-anesthetic protocols, it also may have some anti-arrhythmic effects. In small animals, duration of sedation can occur within 10 minutes and have a 4- to 6-hour duration. In small animals, acepromazine can produce antiemetic effects via dopaminergic blockade. Acepromazine produces arterial smooth muscle relaxation by inhibiting $alpha_1$ receptor–mediated constriction. This effect is used to increase blood flow to tissues, particularly in the metatarsal artery of horses, and produces increased blood flow to the palmar digital artery. This is used for the treatment of horses with laminitis.

Acepromazine has been used as a behavior-modifying agent in animals (e.g., to treat anxiety). However, there are other agents that are preferred for long-term management of behavior disorders in animals that have fewer adverse effects. It should not be used as a first choice to decrease stress in hospitalized animals because there are other preferred agents available. Acepromazine does not provide analgesic activity.

## Precautionary Information

### Adverse Reactions and Side Effects

Sedation and ataxia are common side effects. Extrapyramidal effects (involuntary muscle movements), twitching, dystonia, or Parkinson-like effects are rare but are possible with the administration of phenothiazines to animals. Acepromazine may produce paradoxical excitation, disinhibition, and aggression in some dogs.

Phenothiazines may produce excessive vagal tone in some animals. This may be especially prominent in brachycephalic breeds. Administration of atropine may be used to treat the signs of high vagal tone. Because of alpha-adrenergic antagonism, hypotension is possible in animals. Decreased vascular tone because of $alpha_1$ adrenergic blockade is a prominent effect of acepromazine. This may produce hypotension in susceptible animals.

Dogs with a mutation in the *ABCB1* gene may be deficient for the ABCB1 transporter (p-glycoprotein). These dogs may have increased sensitivity to the effects of acepromazine, resulting in greater sedation scores. Lower doses should be used in these dogs.

In horses, persistent penile prolapse has been reported from use. This effect in horses is unpredictable. Some resources indicate that it is dose dependent with increased likelihood as the dose is increased from 0.01 to 0.1 mg/kg IV. The duration of penile prolapse in horses may be as long as 4 hours with high doses. In rare cases, penile prolapse can lead to permanent paraphimosis. The mechanism is unknown but may be caused by the alpha-adrenergic blockade induced by acepromazine.

**Contraindications and Precautions**

It has been stated in some veterinary textbooks that acepromazine may increase the risk of seizures in animals, and it should be administered cautiously in animals that are prone to seizures. However, a risk of seizures in animals from administration of acepromazine has not been confirmed during clinical use. Seizures were not reported in retrospective studies in which animals prone to seizures were anesthetized and administered acepromazine as an anesthetic adjunct.

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

Dogs with a mutation in the *ABCB1* gene (previously listed as *MDR1*), which is the gene that codes for the p-glycoprotein membrane transporter, are likely to have prolonged and increased sedation after administration of acepromazine. In these dogs, the dose should be decreased or another sedative selected for use.

Phenothiazines can cause hypotension (via alpha-receptor blockade); therefore, use cautiously with other hypotensive drugs or in conditions that may exacerbate hypotension. When administered as a pre-anesthetic to dogs (0.05 mg/kg), it induces moderate hypotension but does not affect cardiac output significantly.

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

**Drug Interactions**

Specific drug interactions have not been reported from the use of acepromazine in animals. However, it exacerbates the effects of other sedative drugs and may potentiate other drugs that cause vasodilation. Acepromazine has been used to sedate dogs for glucose tolerance testing (0.1 mg/kg), without adversely affecting the results.

## Instructions for Use

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

## Patient Monitoring and Laboratory Tests

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

## Formulations

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

## Stability and Storage

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

## Small Animal Dosage

**Dogs**

- 0.025–0.1 mg/kg IM, IV, or SQ in a single dose (most common is 0.025 mg/kg). Do not exceed 3 mg total in dogs.
- Sedation: 0.5–2.2 mg/kg q6–8h PO.
- Anesthetic protocols: 0.01–0.05 mg/kg IV, administered with other agents.

**Cats**

- 0.025–0.1 mg/kg IM, IV, or SQ in a single dose.
- Sedation: 1.1–2.2 mg/kg q6–8h PO.
- Anesthetic protocols: 0.01–0.05 mg/kg IV, administered with other agents.

## Large Animal Dosage

**Horses**

- 0.04–0.1 mg/kg IM. It can be administered q6–12h, but such frequent dosing is not recommended, and an interval of 36–48 hours between doses is preferred. For perioperative use, 0.01–0.05 mg/kg, IM, SQ, or IV.
- Treatment of laminitis: 0.04 mg/kg, IV.

**Cattle**

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

**Pigs**

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

## Regulatory Information

Withdrawal times: There are no withdrawal times established in the United States. It has been estimated that for extralabel use, establish a withdrawal time of at least 7 days for meat and 48 hours for milk.
Canada: 7 days for meat; 48 hours for milk.
Racing Commissioners International (RCI) Classification: 3

# Acetaminophen

ah-seet-ah-mee´noe-fen

**Trade and other names:** Tylenol and generic brands. Known outside the United States as paracetamol.

**Functional classification:** Analgesic

## Pharmacology and Mechanism of Action

Analgesic drug. Exact mechanism of action is not known. There is evidence that acetaminophen inhibits centrally mediated pain transmission via inhibition of cyclo-oxygenase (COX)-3 a variant of COX-1 found in the central nervous system (CNS). Other evidence indicates that acetaminophen may inhibit prostaglandins in

### Patient Monitoring and Laboratory Tests
No specific monitoring is necessary.

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

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

### Small Animal Dosage
**Dogs and Cats**
- Treatment of coccidiosis: Add 1.25 g of 20% amprolium powder to daily feed or 30 mL of 9.6% amprolium solution to 3.8 L of drinking water for 7 days.

### Large Animal Dosage
**Calves**
- Prevention of coccidiosis: 5 mg/kg q24h for 21 days.
- Treatment of coccidiosis: 10 mg/kg q24h for 5 days PO.

### Regulatory Information
Withdrawal time for cattle (meat): 24 hours before slaughter.
A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal.

## Apomorphine Hydrochloride
ah-poe-mor´feen hye-droe-klor´-ide

**Trade and other names:** Apokyn and generic brands

**Functional classification:** Emetic

### Pharmacology and Mechanism of Action
Emetic drug. Apomorphine is opiate derivative that crosses the blood–brain barrier and stimulates dopamine ($D_2$) or chemoreceptor trigger zone receptors in the vomiting center. It promptly causes vomiting in dogs. Although it is easily absorbed from mucosal surfaces (e.g., conjunctiva of the eye), it is not absorbed orally because of first-pass effects.

### Indications and Clinical Uses
Apomorphine is indicated for inducing emesis in animals that have ingested toxic agents. After SQ administration, the onset of effect is 10 minutes or shorter. It is promptly effective for inducing vomiting in dogs but less so in cats. Apomorphine also is absorbed from mucosal administration after applying to the conjunctiva of the eye. Xylazine often is a more reliable emetic in cats. In dogs, 3% hydrogen peroxide (2.2 mL/kg) was equally effective for inducing emesis. (The dose of 3% hydrogen peroxide is typically 2.2 mL/kg or 1 mL/lb.)

## Precautionary Information

### Adverse Reactions and Side Effects

Apomorphine produces emesis before serious adverse effects can occur, but at higher doses (0.1 mg/kg), sedation can occur, which can mask the signs of some toxic agents. The hydrochloride salt of this formulation has a pH of 3–4 and can be irritating to the ocular conjunctival membranes. At high doses (1 mg/kg), excitement can occur, possibly via stimulation of dopamine ($D_1$ and $D_2$) receptors.

### Contraindications and Precautions

Apomorphine also may decrease vomiting stimulus in vomiting center; therefore, if the initial dose is not effective, emetic effects may be blocked during later attempts to induce vomiting. Use cautiously in cats that may be sensitive to opiates. (Xylazine is a more effective emetic agent in cats.)

### Drug Interactions

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

## Instructions for Use

Apomorphine should be available in most emergency practices for prompt treatment of poisoning. If not, consult local poison center or pharmacist for availability. Apomorphine can be administered IM, SQ, or to the mucosa (e.g., in the conjunctival sac of the eye). It should not be administered IV because the rapid diffusion to the CNS may block the emetic effects. In dogs, vomiting should occur within 3–10 minutes after administration. Limit administration to once. Consider other agent such as xylazine or dexmedetomidine to induce vomiting in cats.

## Patient Monitoring and Laboratory Tests

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

## Formulations

- Apomorphine is available in 6-mg tablets that can be hydrolyzed prior to use or is available in a 10-mg/mL concentration in a 2-mL ampule or 3-mL preloaded syringes.
- If apomorphine is not available from commercial sources, it has been prepared by compounding pharmacists. One approach is to mix 20 mg apomorphine in a sterile vial with 4.4 mL of sterile water to make a solution of 5 mg/mL. From this solution, drops may be added to the eye to induce vomiting.

## Stability and Storage

Store in a tightly sealed container at room temperature, protected from light. Solutions decompose when exposed to air and light. A green color indicates decomposition. One of the compounded formulations prepared in an aqueous solution (3 mg/mL) was stable at room temperature for 6 months after compounding.

## Small Animal Dosage

**Dogs and Cats (Less effective in cats.)**

- 0.03–0.05 mg/kg IM.
- 0.1 mg/kg SQ.

- Dissolve 6-mg tablet in 1–2 mL of 0.9% saline solution and instill directly in the conjunctiva of the eye. After animal vomits, the conjunctiva may be rinsed of residual drug with an eye wash solution.

### Large Animal Dosage

- No dose has been reported for large animals because they typically do not vomit.

### Regulatory Information

Do not administer to animals intended for food.
RCI Classification: 1

## Aprepitant

ap-reh´pih-tant

**Trade and other names:** Emend

**Functional classification:** Antiemetic

### Pharmacology and Mechanism of Action

Aprepitant is a centrally acting antiemetic. Aprepitant is a substance P/neurokinin 1 ($NK_1$) receptor antagonist, similar to the veterinary drug maropitant (Cerenia). It is used primarily in people to prevent vomiting from cancer chemotherapy, such as cisplatin. This drug is effective because chemotherapy drugs and other emetic stimuli release $NK_1$, which is highly emetic. It also blocks vomiting from other stimuli. The use in small animals has been somewhat limited because of the high expense and limited formulations for animals. In dogs, aprepitant is extensively metabolized after administration. Instead, the veterinary drug maropitant (Cerenia) is used much more often.

### Indications and Clinical Uses

Aprepitant is an effective antiemetic for people, particularly when used to treat vomiting associated with cancer chemotherapy. It may be used with corticosteroids (dexamethasone) and serotonin antagonists. However, despite its broad effects to decrease vomiting in people, there are no reports of effective use in dogs or cats. Instead, a similar-acting drug, maropitant (Cerenia), is used in dogs and cats and produces similar antiemetic effects.

### Precautionary Information

**Adverse Reactions and Side Effects**

There are no reported adverse effects in animals.

**Contraindications and Precautions**

No contraindications reported for animals.

**Drug Interactions**

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

### Instructions for Use
Calcium lactate contains 130 mg of calcium ion per gram.

### Patient Monitoring and Laboratory Tests
Monitor serum calcium concentrations.



### Formulations
- Calcium lactate is available in 325-mg (42.25 mg of calcium ion) and 650-mg (84.5 mg of calcium ion) OTC tablets.

### Stability and Storage
Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Do not mix with other compounds that may chelate with calcium.

### Small Animal Dosage
**Dogs**
- 0.5 g/day (500 mg) (in divided doses) PO.

**Cats**
- 0.2–0.5 g/day (200–500 mg) (in divided doses) PO.

### Large Animal Dosage
- No dose has been reported for large animals.

### Regulatory Information
No withdrawal times are available. Because this is a normal dietary supplement with little risk from residues, no withdrawal time is suggested for animals intended for food.

## Capromorelin
kap′roe-moe-rel′in

**Trade and other names:** Entyce

**Functional classification:** Appetite stimulant

### Pharmacology and Mechanism of Action
Capromorelin mimics the action of ghrelin, which is a natural hormone produced by the stomach. Dogs can have decreased appetite associated with chronic diseases (cancer, kidney disease, heart disease, and intestinal diseases). Capromorelin is approved in dogs for appetite stimulation. It is a ghrelin-receptor agonist (GRA) that acts on the hypothalamus to mimic the action of endogenous ghrelin to increase appetite in dogs and increase growth hormone. Capromorelin is a growth hormone secretagogue (GHS) with a stimulatory effect on appetite through central effects on the hypothalamus and peripheral pathways through the action on the vagus nerve. Ghrelin increases the insulin-like growth factor (IGF-1), which is stimulated by growth hormone and may reduce cachexia and increase lean muscle mass in animals with chronic diseases. A similar agent evaluated in people is anamorelin, but this has not been evaluated clinically in veterinary medicine.

Other uses for capromorelin have been considered but are not established at this time. Such uses include growth hormone deficiency, cancer, and GI problems.

*Pharmacokinetics:* After oral administration to dogs, it peaks at approximately 1 hour and has a half-life of 1.2 hours. The bioavailability in dogs is 44%, with a volume of distribution (VD) of 2 L/kg. The protein binding is approximately 50% in dogs. Shortly after oral administration, there is a rapid increase in growth hormone followed by an increase in IGF-1. The increase in IGF-1 serves as a negative feedback mechanism to attenuate large spikes in growth hormone. The increase in IGF-1 is maintained with once-daily dosing in dogs at a dose of 3 mg/kg.

## Indications and Clinical Uses

Capromorelin is used to increase appetite in dogs. It should be administered once daily at the approved dose, with no limit to the length of treatment. In severely ill dogs or those with multiple other problems, it may take a few days to see a response. Some dogs may not respond at all. Some clinicians have increased the dose by 1.5 times to obtain a more consistent positive response. If no response is seen in a few days, even with a higher dose, consider discontinuing the drug and pursuing other treatments. In the clinical studies performed to obtain Food and Drug Administration (FDA) approval, at the label dose, it significantly improved appetite and body weight compared with placebo treatment. Other agents that have been used to increase appetite are mirtazapine, cyproheptadine, corticosteroids, and anabolic steroids, but capromorelin is the first drug approved specifically for this indication in dogs.

The current approval is for dogs only. There are no clinical studies in sick cats that can be used to recommend treatment. In healthy research cats, it increased IGF-1, increased appetite, and increased body weight. Future studies may reveal optimum doses and determine safety. It is proposed that it may be useful to stimulate appetite in cats with CKD at a dosage of 2 mg/kg PO once daily. As for dogs, an increase by 1.5 times (3 mg/kg) can be considered in cats that do not respond to the initial dose.

## Precautionary Information

### Adverse Reactions and Side Effects

In the clinical field trials, the most common adverse effect was diarrhea, vomiting, polydipsia, and hypersalivation. In the target animal safety studies, it was tolerated at 17.5 times the label dose for 12 months in healthy dogs.

### Contraindications and Precautions

The safety in dogs with liver or kidney disease has not been evaluated. It is metabolized by cytochrome P450 (CYP450) enzymes, and it is possible that other drugs that affect the CYP450 enzymes could alter the pharmacokinetics. It is excreted in both the urine and feces; use with caution in dogs with renal insufficiency or liver disease. Safety has not been evaluated in dogs used for breeding or pregnant or lactating bitches.

The safety has not been evaluated in cats, but it was safe in healthy research cats. There are no known contraindications or restrictions for dogs. It can be used regardless of duration, weight of dog, or age. It can be administered as long as necessary as long as no adverse effects are observed.

### Drug Interactions

There are no known drug interactions.

## Instructions for Use

Capromorelin is available in a 30-mg/mL oral solution. Dispense the correct dose to pets using the syringe available in the packaging. Rinse the syringe with water between uses.

## Patient Monitoring and Laboratory Tests

Monitor the patient's body weight and appetite. Although guidelines are not available for cats, it is advised to monitor parameters for diabetes in treated cats until other information is available. If cortisol concentrations are measured, there is an increase in cortisol release seen approximately 1 hour after administration of capromorelin; it declines to baseline levels 4 hours after oral administration.

## Formulations

- Capromorelin is available as an oral flavored solution at a concentration of 30 mg/mL. It is available in sizes of 10-, 15-, and 30-mL bottles with a dispensing syringe.

## Stability and Storage

Store in a tightly sealed container, protected from light, at temperatures less than 30°C (86°F). Do not mix with other drugs if compatibility is not known.

## Small Animal Dosage

**Dogs**

- 3 mg/kg PO once daily.

**Cats**

- Safe clinical doses have not been established. Until a specific feline form is available, consider a dosage of 2 mg/kg PO once daily.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No withdrawal times are available. Because this is not approved for food animals, it should not be administered to animals intended for food.

# Captopril

kap′toe-pril

**Trade and other names:** Capoten

**Functional classification:** Vasodilator, angiotensin-converting enzyme inhibitor

## Pharmacology and Mechanism of Action

Angiotensin-converting enzyme (ACE) inhibitor. Captopril inhibits conversion of angiotensin I to angiotensin II, leading to vasodilation. Angiotensin II is a potent vasoconstrictor and will stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. ACE inhibitors limit the ability of aldosterone to cause sodium and water retention that contribute to congestion. Captopril, like other ACE inhibitors, causes vasodilation, but ACE inhibitors also contribute to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins (PGs).

## Formulations

- Cyclosporine is available in 10-, 25-, 50-, and 100-mg capsules (Atopica) and 25- and 100-mg microemulsion capsules.
- There is one FDA-approved generic formulation of cyclosporine for dogs, which has shown to be bioequivalent with the proprietary form (original brand). It is approved in the same size capsules as the original formulation.
- Atopica for cats is available as a 100-mg/mL oral solution as a microemulsion. This may be mixed with the cat's food if it does not affect their appetite.
- Human forms are also available as a 100-mg/mL oral solution (Neoral, for microemulsion); 100-mg/mL oral solution and 25- and 100-mg capsules (Sandimmune); and 0.2% ophthalmic ointment (Optimmune). Generic human capsules are available (e.g., Gengraf). The human generic formulations are therapeutically equivalent in people but have not been compared in dogs or cats to Atopica.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It does not require refrigeration but store below 30°C. Freezing capsules at –20°C for 28 days did not affect stability or oral absorption. Compounded ophthalmic products are stable at room temperature for 60 days, but do not refrigerate.

## Small Animal Dosage

**Dogs**

- 3–7 mg/kg/day PO. The typical starting dosage is 5 mg/kg/day PO. After the induction period, some dogs with atopic dermatitis have been controlled with dosages as low as 5 mg/kg every other day to every third day.
- For perianal fistulas and immune-mediated diseases (e.g., IMHA), higher doses and more frequent administration have been used (5–8 mg/kg q12h). When a response is observed, the dose and frequency can be reduced.
- For immune suppression associated with organ transplantation, doses should be higher (e.g., 7–10 mg/kg q12h PO).
- IBD: 5 mg/kg PO q12h; then reduce the frequency to q24h after a response is observed.
- Idiopathic chronic hepatitis: 5–8 mg/kg/day, PO.

**Cats**

- 7.5 mg/kg per day PO. Some cats can be controlled with administration of this dose every other day or twice weekly. Administer on a small amount of food or at the time of feeding, but if mixed with food, some cats may refuse to eat.
- For immune suppression associated with organ transplantation, doses should be higher (e.g., 3–5 mg/kg q12h PO).

## Large Animal Dosage

- Only local administration has been used in horses (ocular). No other dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it may have mutagenic potential.

# Cyproheptadine Hydrochloride

sih′proe-hep′tah-deen hye-droe-klor′ide

**Trade and other names:** Periactin

**Functional classification:** Antihistamine

## Pharmacology and Mechanism of Action

Cyproheptadine is a phenothiazine with antihistamine and antiserotonin properties. It is not used as a serotonin antagonist in animals but has been used as appetite stimulant (probably by altering serotonin activity in appetite center).

## Indications and Clinical Uses

A common use of cyproheptadine is to stimulate the appetite in sick animals, especially cats, although, evidence based on controlled studies to demonstrate efficacy is not available. For dogs and cats, other appetite stimulants are preferred: mirtazapine for cats and capromorelin for dogs.

Cyproheptadine is used in some cats for treatment of feline asthma if serotonin is considered a component of the airway inflammation. However, in cats with hyperresponsive airways, cyproheptadine failed to reduce eosinophilic inflammation (8 mg per cat q12h). It has been used in some instances for treating inappropriate urination (urine spraying) in cats. Cyproheptadine has been used to treat head shaking in horses. Cyproheptadine has been used to treat equine pituitary pars intermedia dysfunction (Cushing syndrome) at 0.6–1.2 mg/kg, but results have been controversial. It is not effective for treatment of canine pituitary-dependent hyperadrenocorticism (Cushing syndrome). It has been considered as a treatment for animals that have "serotonin syndrome" from antidepressant drugs, although efficacy has not been documented for this use.

## Precautionary Information

### Adverse Reactions and Side Effects

Cyproheptadine may stimulate hunger. It can cause polyphagia and weight gain. Cyproheptadine also has antihistamine effects, antiserotonin effects, and antimuscarinic effects. In some cats, it has stimulated hyperactivity. In horses, it has been used at high doses without adverse effects.

### Contraindications and Precautions

None reported for animals.

### Drug Interactions

There are no drug interactions reported for small animals.

## Instructions for Use

Clinical studies have not been performed in veterinary medicine. Use is based primarily on empiricism and extrapolation from human results. Syrup contains 5% alcohol.

## Patient Monitoring and Laboratory Tests

Monitor weight gain in animals.

## Formulations Available

- Cyproheptadine is available in 4-mg tablets and 2-mg/5-mL syrup.

## Stability and Storage

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

## Small Animal Dosage

### Dogs and Cats

- Antihistamine: 0.5–1.1 mg/kg q8–12h PO or 2–4 mg/cat PO q12–24h.
- Appetite stimulant: 2 mg/cat PO.

- Feline asthma: 1–2 mg/cat PO q12h.
- Use for inappropriate urination: 2 mg/cat q12h PO; then reduce dosage to 1 mg/cat q12h PO.

### Large Animal Dosage

**Horses**

- 0.5 mg/kg q12h PO.
- Head shaking: 0.3 mg/kg q12h, PO.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.
RCI Classification: 4

## Cytarabine

sye-tare′ah-been

**Trade and other names:** Cytosar, Ara-C, and cytosine arabinoside

**Functional classification:** Anticancer agent

### Pharmacology and Mechanism of Action

Cytarabine is an anticancer agent that is also used for immunosuppressive treatment. Cytarabine (Cytosar) is a compound isolated from a sea sponge. It has also been referred to as *cytosine arabinoside* and *Ara-C*. Cytarabine is metabolized to an active drug that inhibits DNA synthesis. Cytarabine is an antimetabolite synthetic nucleoside analogue. Cytarabine A inhibits DNA polymerase in mitotically active cells and produces topoisomerase dysfunction and prevents DNA repair. This action produces the anticancer effects and immunosuppressive properties.

*Pharmacokinetics:* The half-life in dogs is approximately 70 minutes. When administered to dogs, the terminal half-lives of cytarabine are 1.35 hours and 1.15 hours after SQ and CRI, respectively. Peak concentrations are 2.9 mcg/mL and 2.8 mcg/mL after SQ and CRI administration, respectively.

### Indications and Clinical Uses

Cytarabine has been used for lymphoma, leukemia, and myelogenous leukemia in various anticancer drug protocols. It is usually administered as an IM or SQ injection because it has a short half-life (≈20 minutes) when administered IV.

It has also been administered to dogs for treatment of granulomatous meningoencephalomyelitis as an alternative to corticosteroids. Cytarabine penetrates the blood–CSF barrier of dogs and has been reported to improve the temporary and long-term remission and prognosis for dogs diagnosed with meningoencephalitis. Two protocols are used for this indication (see the dosing section). When administered via CRI to dogs, it maintains steady-state concentrations better than a SQ injection.

### Precautionary Information

**Adverse Reactions and Side Effects**

Cytarabine is bone marrow suppressive and can cause granulocytopenia, especially when delivered via CRIs. In addition, it may cause nausea and vomiting.

# Diphenhydramine Hydrochloride

dye-fen-hye´drah-meen hye-droe-klor´ide

**Trade and other names:** Benadryl and generic

**Functional classification:** Antihistamine



## Pharmacology and Mechanism of Action

Antihistamine ($H_1$ blocker). Similar to other antihistamines, it acts by blocking the $H_1$ receptor (H1) and suppresses inflammatory reactions caused by histamine. Other commonly used antihistamines include clemastine, chlorpheniramine, and hydroxyzine.

Note that diphenhydramine (Benadryl) and dimenhydrinate (Dramamine) are essentially the same drug. Dimenhydrinate contains diphenhydramine and chlortheophylline. (See Dimenhydrinate for more details.)

## Indications and Clinical Uses

Diphenhydramine, like other antihistamines, blocks histamine type 1 ($H_1$) receptors to prevent action of histamine. It is used to prevent acute allergic reactions and for pruritus therapy in dogs and cats. However, success rates for treatment of pruritus have not been high. Diphenhydramine has been used to treat acute allergy episodes caused by mast cell release, allergy, insect bites, and so on. In addition to the antihistamine effect for treating allergies, these drugs block the effect of histamine in the vomiting center, vestibular center, and other centers that control vomiting in animals. This may control some types of vomiting in dogs but not likely in cats. There are other more effective antiemetics available for dogs and cats that are preferred.

## Precautionary Information

### Adverse Reactions and Side Effects

Sedation is the most common side effect. Sedation is the result of inhibition of histamine N-methyltransferase. Sedation may also be attributed to blockade of other CNS receptors such as those for serotonin, acetylcholine, and alpha-receptors. Antimuscarinic effects (atropinelike effects) also are common, including dry mouth and decreased GI secretions. Excitement has been observed in cats and other animals at high doses. Although it may induce some changes in cardiovascular parameters in some animals with IV administration, this has not been shown to be a problem when injected IV in dogs undergoing mast cell removal surgery.

### Contraindications and Precautions

Antimuscarinic effects (atropinelike effects) are common. Do not use in conditions for which anticholinergic drugs may be contraindicated, such as glaucoma, ileus, or cardiac arrhythmias. Discontinue administration a minimum of 7 days prior to allergen-specific allergy testing in dogs.

### Drug Interactions

There are no specific drug interactions. However, because of anticholinergic (atropinelike) effects, it may counteract drugs that are administered for a parasympathomimetic action (e.g., drugs used to stimulate intestinal motility).

### Instructions for Use
Antihistamine used primarily for allergic disease in animals. These drugs also can be used to treat or prevent vomiting in animals, but antihistamines are not effective antiemetics in cats. Clinical studies documenting efficacy have been limited. Most use is empirical with doses extrapolated from human use.

### Patient Monitoring and Laboratory Tests
No specific monitoring is necessary.

### Formulations
- Diphenhydramine is available OTC in a 2.5-mg/mL elixir, 25- and 50-mg capsules and tablets, and 50-mg/mL injection.

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

### Small Animal Dosage
**Dogs**
- 2.2 mg/kg q8–12h PO, IM, or SQ. For large dogs, this is equivalent to an oral dose of 25 or 50 mg per dog.

**Cats**
- 2–4 mg/kg q6–8h PO.
- 1 mg/kg q8h IV or IM.

### Large Animal Dosage
- 0.5–1 mg/kg as a single dose, as needed, IM.

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

## Diphenoxylate
dye-fen-oks´ih-late

**Trade and other names:** Lomotil, also called Co-phenotrope

**Functional classification:** Antidiarrheal

### Pharmacology and Mechanism of Action
Diphenoxylate is an opiate agonist. It binds to mu-opiate receptors in intestine and stimulates smooth muscle segmentation in intestine, decreases peristalsis, and enhances fluid and electrolyte absorption. It has little centrally acting effect.

### Indications and Clinical Uses
Diphenoxylate is used for the acute treatment of nonspecific diarrhea. It has a primarily local effect. Loperamide (Imodium) has a similar action and has become more popular for this indication. An additional use, not often used in veterinary medicine, is as an antitussive.

### Instructions for Use
Antihistamine used primarily for allergic disease in animals. These drugs also can be used to treat or prevent vomiting in animals, but antihistamines are not effective antiemetics in cats. Clinical studies documenting efficacy have been limited. Most use is empirical with doses extrapolated from human use.

### Patient Monitoring and Laboratory Tests
No specific monitoring is necessary.

### Formulations
- Diphenhydramine is available OTC in a 2.5-mg/mL elixir, 25- and 50-mg capsules and tablets, and 50-mg/mL injection.

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

### Small Animal Dosage
**Dogs**
- 2.2 mg/kg q8–12h PO, IM, or SQ. For large dogs, this is equivalent to an oral dose of 25 or 50 mg per dog.

**Cats**
- 2–4 mg/kg q6–8h PO.
- 1 mg/kg q8h IV or IM.

### Large Animal Dosage
- 0.5–1 mg/kg as a single dose, as needed, IM.

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

## Diphenoxylate
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### Indications and Clinical Uses
Diphenoxylate is used for the acute treatment of nonspecific diarrhea. It has a primarily local effect. Loperamide (Imodium) has a similar action and has become more popular for this indication. An additional use, not often used in veterinary medicine, is as an antitussive.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects have not been reported in veterinary medicine. Diphenoxylate is poorly absorbed systemically and produces few systemic side effects. Excessive use can cause constipation.

### Contraindications and Precautions

Do not use in patients with diarrhea caused by infectious causes. Opiates should not be used for chronic treatment of diarrhea.

### Drug Interactions

There are no specific drug interactions reported. However, use cautiously with other opiates and other drugs that may cause constipation (e.g., antimuscarinic drugs).



## Instructions for Use

Doses are based primarily on empiricism or extrapolation of human dose. Clinical studies have not been performed in animals. Diphenoxylate contains atropine, but the dose is not high enough for significant systemic effects.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Diphenoxylate is available in 2.5-mg tablets that also contain 0.025 mg atropine.
- Oral solution: 2.5 mg plus 0.025 mg atropine in 5 mL of solution (cherry flavored, with 15% alcohol).

## Stability and Storage

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

## Small Animal Dosage

**Dogs**

- 0.1–0.2 mg/kg q8–12h PO.
- Antitussive use: 0.2–0.5 mg/kg q12h PO.

**Cats**

- 0.05–0.1 mg/kg q12h PO.

## Large Animal Dosage

- No use in large animals is reported.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org. Schedule V controlled drug. RCI Classification: 4

# Dipyridamole

dye-peer-id´ah-mole

**Trade and other names:** Persantine

**Functional classification:** Anticoagulant

**Contraindications and Precautions**
Reduce dose in animals with compromised renal function. Safety in pregnant cats has not been studied.

**Drug Interactions**
No interactions identified.

### Instructions for Use
The dose listed for cats is based on limited studies in which 62.5 mg per cat was studied initially, but later evidence suggested that a more effective dosage is at least 125 mg per cat (or higher) q8–12h PO. Duration of treatment is undetermined, but generally 2 weeks may be needed.

### Patient Monitoring and Laboratory Tests
Monitor blood urea nitrogen (BUN) and creatinine during use.

### Formulations
- Famciclovir is available in 125-, 250-, and 500-mg tablets. It has been compounded into smaller tablets for kittens. A compounded oral suspension may be made by mixing 20 of the 500 mg famciclovir tablets (10 g), with 100 mL of a 1:1 mixture of Ora-Plus and Ora-Sweet. The final oral suspension is 100 mg/mL and is stable for 90 days if stored in a refrigerator. Label to indicate that it should be well shaken before use. Other compounded formulations for animals have not shown consistent quality or strength.

### Stability and Storage
Store tablets and capsules in tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage
**Cats**
- Treatment of feline herpes virus: The preferred dose is 90 mg/kg q12h, and some experts recommend q8h. Higher doses of 500 mg per cat (92–227 mg/kg) also have been used. Lower dosages should be used in kittens (30–50 mg/kg q12h PO).

### Large Animal Dosage
**Horses**
- No doses have been established.

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

## Famotidine
fah-moeʹtih-deen

**Trade and other names:** Pepcid and generic

**Functional classification:** Antiulcer agent

### Pharmacology and Mechanism of Action
Histamine$_2$ antagonist ($H_2$ blocker). Stimulation of acid secretion in the stomach requires activation of histamine type 2 receptors ($H_2$ receptor), gastrin receptors, and muscarinic

receptors. Famotidine and other $H_2$ blockers inhibit the action of histamine on the histamine $H_2$ receptor of parietal cells and inhibit gastric parietal cell gastric acid secretion. Famotidine increases stomach pH to help heal and prevent gastric and duodenal ulcers.

## Indications and Clinical Uses

Famotidine, like other $H_2$-receptor blockers, is used to treat ulcers and gastritis in a variety of animals. Although it is often used for animals with vomiting, there are no efficacy data to indicate that it is effective as an antiemetic. There are no efficacy data to support its use for preventing nonsteroidal anti-inflammatory drug (NSAID)–induced bleeding and ulcers. Famotidine has been used by veterinarians as a preferred $H_2$ blocker, but there is a lack of evidence to demonstrate superiority over other drugs in this class. Some studies have demonstrated efficacy at 1 mg/kg in dogs, while other studies have not demonstrated differences between famotidine and a placebo in dogs for increasing stomach pH. The target goal for stomach pH is greater than 3 for 75% of the dose interval or a pH greater than 4 for 67% of the dose interval. With oral doses, famotidine often does not meet these targets. Most evidence supports a lack of efficacy in dogs at a dosage of 1 mg/kg administered q12h, but it is more effective if administered as a constant-rate infusion (CRI) (1 mg/kg IV loading dose followed by 8-mg/kg/day infusion). In dogs, it may have short-term effects on acid suppression, but it had a diminished effect if administered for more than 12 days. It had less effect to maintain the stomach pH above 3 on day 1 of dosing compared with day 12. Therefore, if used, famotidine may be better for short-term use than long-term administration.

The use in large animals has received little attention. Omeprazole is preferred in horses for stomach acid suppression. In cattle, the half-life of famotidine is short and requires frequent administration (e.g., q6h) for effectiveness.

Proton pump inhibitors (PPIs) such as omeprazole, esomeprazole, and others are more effective for consistently suppressing stomach acid secretion and are preferred over histamine $H_2$ antagonists for dogs, horses, and cats.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects usually are seen only with decreased renal clearance. In people, central nervous system (CNS) signs may occur with high doses. The IV solution contains benzyl alcohol, aspartic acid, and mannitol. Give IV injections slowly to cats (over 5 minutes) because rapid IV injections may cause hemolysis.

### Contraindications and Precautions

Intravenous solutions contain benzyl alcohol. IV injections to small animals, especially cats, should be done slowly.

### Drug Interactions

Famotidine and other $H_2$-receptor blockers block secretion of stomach acid. Therefore, they interfere with oral absorption of drugs dependent on acidity, such as ketoconazole, itraconazole, and iron supplements. Unlike cimetidine, famotidine is not associated with inhibition of microsomal P450 enzymes.

## Instructions for Use

Administer with food for best absorption. Clinical studies for famotidine have not been performed; therefore, optimal doses for ulcer prevention and healing are not known. Dose recommendations are extrapolated from human use, studies in experimental animals, or from anecdotal experience. Experimental studies in dogs

have shown that doses of 0.1–0.2 mg/kg may inhibit stomach acid secretion, but most other studies have shown that higher doses of 1.0 mg/kg are needed to suppress stomach acid. Even at this dose, it has not been effective for reaching therapeutic targets in dogs but is more effective if administered as a CRI. For IV use, dilute with IV solutions (e.g., 0.9% saline) to a total volume of 5–10 mL.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Famotidine is available in 20- and 40-mg tablets, 8-mg/mL oral suspension, and 10-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Famotidine is soluble in water. Compounded formulations in cherry syrup have been stable for 14 days. Diluted IV solutions in saline are stable for 48 hours at room temperature.

### Small Animal Dosage

**Dogs**

- 0.5 mg/kg q12h PO, IV, SQ, or IM. A dosage of 40 mg/dog q12h has been used empirically. Higher dosages of 1 mg/kg q12h have been recommended for more reliable suppression of stomach acid.
- CRI: 1 mg/kg IV loading dose followed by 8 mg/kg/day CRI.

**Cats**

- 0.2 mg/kg q24h, up to 0.25 mg/kg q12h IM, SQ, PO, or IV (slowly over 5 minutes).

### Large Animal Dosage

**Horses**

- 1–2 mg/kg q6–8h PO or 0.2–0.4 mg/kg IV q6h.

**Cattle**

- 0.4 mg/kg IV q6h.

### Regulatory Information

No restrictions on use in animals not intended for food.
Racing Commissioners International (RCI) Classification: 5

## Febantel

feh-ban′tel

**Trade and other names:** Rintal and Vercom. Drontal Plus also contains two other drugs.

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Febantel is an antiparasitic that interferes with carbohydrate metabolism in parasitic worms. It suppresses mitochondrial reactions via inhibition of fumarate reductase and interferes with glucose transport. It is metabolized to a benzimidazole compound that binds to structural protein tubulin and prevents polymerization to

# Fenbendazole

fen-ben′dah-zole

**Trade and other names:** Panacur and Safe-Guard

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Fenbendazole is a benzimidazole antiparasitic drug. Like other benzimidazoles, fenbendazole produces a degeneration of the parasite microtubule and irreversibly blocks glucose uptake in parasites. Inhibition of glucose uptake causes depletion of energy stores in the parasite, eventually resulting in death. Mammals are spared from adverse effects because there is no effect on glucose metabolism in mammals.

## Indications and Clinical Uses

Fenbendazole is effective for treatment of numerous helminth intestinal parasites in animals, including *Toxocara*, *Toxascaris, Ancylostoma,* and *Trichuris* spp. In dogs, it is effective for most intestinal helminth parasites and against nematodes. In dogs, it also has been used for pulmonary helminths (lungworms), but a longer duration of treatment is needed. Fenbendazole has been effective for treatment of *Giardia* infection, but higher doses are needed and there may be failure rates as high as 50%. It is effective in cats for treatment of lungworms, flukes, and a variety of helminth parasites. In horses, it is used for the control of large strongyles, small strongyles, pinworms, and ascarids. In pigs, it is effective for lungworms, large roundworms, nodular worms, small stomach worms, and kidney worms. In beef and dairy cattle, it is effective for control of lungworms, stomach worms, barberpole worms, stomach worms, and various intestinal worms.

## Precautionary Information

### Adverse Reactions and Side Effects

Fenbendazole has a good safety margin, but vomiting and diarrhea have been reported. When evaluated at doses of three and five times the recommended dose at three times the recommended duration, fenbendazole was well tolerated, and no adverse effects were reported in the target species. It has been safe to use during pregnancy. There have been reports of pancytopenia associated with fenbendazole administration, but these are rare.

### Contraindications and Precautions

No known contraindications. It may be used in all ages of animals.

### Drug Interactions

There are no known drug interactions.

## Instructions for Use

Dose recommendations are based on clinical studies by the manufacturer. Granules may be mixed with food. Paste may be given to horses and cattle. Presence of food does not affect oral absorption. In studies for treatment of *Giardia* infection, it was safer than other treatments but less effective.

## Patient Monitoring and Laboratory Tests

Fecal monitoring may be performed to determine the efficacy of treatment for intestinal parasites.

## Formulations

- Fenbendazole is available in 22.2% (222 mg/g) (Panacur) granules, 10% oral paste (92 g/32 oz), and 100-mg/mL oral suspension. Some formulations (e.g., Panacur Plus) may contain other ingredients such as ivermectin and praziquantel.

## Stability and Storage

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

## Small Animal Dosage

**Dogs**

- 50 mg/kg/day for 3 days PO. Duration may be extended to 5 days for severe parasitic infestations. For pulmonary helminths (lungworms) in dogs, increase the duration of this dosage to 10–14 days.
- *Giardia* treatment: 50 mg/kg q24h for 3–5 days.

**Cats**

- 50 mg/kg/day for 3 days PO.
- Duration may be extended to 5 days for severe parasitic infestations.

## Large Animal Dosage

**Horses**

- Intestinal parasites, such as strongyles, pinworms, and ascarids: Panacur granules or paste is administered at a dose of 5.1 mg/kg (2.3 mg/lb) PO. Two packets of 1.15 g each will treat a 450-kg (1000-lb) horse. Panacur paste can be administered to horses at a dose of 5 mg/kg PO. Retreatment at 6–8 weeks may be necessary. For treatment of ascarids (*Parascaris equorum*) in horses, a higher dose of 10 mg/kg is recommended.

**Sheep and Goats**

- 5 mg/kg PO.

**Cattle**

- 5 mg/kg PO or 5 mg/kg/day provided in feed for 3–6 days.

## Regulatory Information

Cattle withdrawal time (meat): 8 days. There is no withdrawal period for milk. Goat withdrawal time: 6 days meat; 0 days milk. For additional withdrawal time information, contact FARAD at www.FARAD.org.

# Fenoldopam Mesylate

fe-nol′doe-pam

**Trade and other names:** Corlopam

**Functional classification:** Vasodilator

## Pharmacology and Mechanism of Action

Fenoldopam is a dopamine agonist. It is specific for the dopamine $D_1$ receptors, without effects on alpha- or beta-adrenergic receptors, and therefore has been used to produce smooth muscle relaxation and vasodilation in vascular beds that have $D_1$ receptors (peripheral arteries and kidneys). It has no activity on $D_2$ receptors and only a small effect on alpha-adrenergic receptors. Because of this activity, fenoldopam has more specificity than dopamine, which has been used for similar indications. The most common use of fenoldopam is for increasing renal perfusion to treat acute renal failure.

*Pharmacokinetics:* The half-life in animals is very short (1–7 minutes in dogs), with very high clearance (60 mL/min/h); therefore, it is usually administered via CRI.

DRUG MONOGRAPH

# Hydrogen Peroxide 3% (Oral)

*(**hye**-droe-jen per-**oks**-ide)*

**Drug class**: Oral Emetic

DOSAGES DOSAGE FORMS

**NOTE:** Also see the *Overdose and Toxin Exposure Decontamination Guidelines* in the ***Appendix***.

## Prescriber Highlights

- Topical antiseptic that is used orally as a home-administered emetic in dogs when clients cannot transport the patient to a veterinary hospital in a timely manner or when other emetics have failed or are unavailable.
- Can cause esophageal irritation or other gastric effects; aspiration is possible
- Not recommended for use in cats
- Many contraindications for use as an emetic
- Do not use hydrogen peroxide solutions greater than 3%; solution should not be expired

## Uses / Indications

Hydrogen peroxide 3% solution can be used as an orally administered emetic in dogs, pigs, and ferrets. It is reserved primarily for those cases when animals cannot be transported to a veterinary hospital promptly and immediate emesis is required; it may also be used in a clinic setting when other emetics have failed or are unavailable. A prospective observational study found that hydrogen peroxide 3% solution successfully induced emesis in 90% of treated dogs and was equally as effective as apomorphine at 94%.[1]

Hydrogen peroxide is not recommended in cats because of its unreliability as an emetic and because of potentially life-threatening adverse effects (eg, hemorrhagic gastritis,[2] acute respiratory failure[3,4]).

Apomorphine or ropinirole for dogs and alpha-adrenergic agonists (eg, dexmedetomidine) or hydromorphone for cats are preferred emetic agents for administration in a veterinary clinic.

## Pharmacology / Actions

Orally administered hydrogen peroxide 3% solution induces a vomiting reflex via direct irritant effects of the oropharynx and gastric lining. Emesis typically ensues within 10 to 15 minutes following oral administration to dogs.[1,5] It is estimated that an average ≈50% of ingested contents are recovered after inducing emesis with either apomorphine or hydrogen peroxide.[1]

## Pharmacokinetics

No pharmacokinetic information located. Emetic effects may persist up to ≈2 hours after administering PO to dogs.[1]

## Contraindications / Precautions / Warnings

Emesis with hydrogen peroxide should only be considered if preferred methods (eg, apomorphine, ropinirole) are not available and the benefits of decontamination outweigh the risks of its use.[2] Before inducing emesis, obtain a complete history of the ingestion and ensure that vital signs are stable.

If home administration of hydrogen peroxide is necessary, be sure that clients use only the 3% medical-grade solution and not another, more concentrated hydrogen peroxide product. Do not induce emesis with solutions that contain greater than 3% hydrogen peroxide, or that contain other active ingredients (eg, “accelerated” solutions, teat dips).

after ingestion of strychnine or other CNS stimulants may precipitate seizures.

Emetics generally do not remove more than 80% of the material in the stomach (usually 40% to 60%) and significant quantities of the ingested drug/toxin may remain or may have already been absorbed. Successful induction of emesis does not signal the end of appropriate monitoring or therapy.

Because aspiration and/or bradycardia are possible, animals should be closely observed after administration. Suctioning, respiratory support, and cardiovascular support (eg, atropine) should be available. Do not allow animal to re-ingest vomitus.

### Adverse Effects

In dogs, diarrhea, lethargy, and protracted nausea and vomiting are possible[1]; antiemetic agents administered after desired emesis occurs may alleviate nausea and vomiting in severely affected dogs. Hydrogen peroxide solution may be aspirated during administration or after inducing emesis. In an experimental study, significant visual and histopathologic gastric lesions occurred following administration of hydrogen peroxide 3% solution to dogs; less severe duodenal lesions were seen.[2] Gastric ulcers and gastric degeneration and necrosis were evident at 4 and 24 hours. Most gastroduodenal lesions were present for up to 1 week and resolved by 2 weeks. Gastric dilatation-volvulus in dogs has been reported following hydrogen peroxide administration.

Cats can be particularly susceptible to hemorrhagic gastritis or esophagitis.[6] Aspiration with life-threatening lung injury and acute respiratory failure has also been reported in a cat.[4]

### Reproductive / Nursing Safety

No specific information was located. Although orally administered hydrogen peroxide 3% solution is unlikely to cause reproductive harm, this drug should only be used when the maternal benefits outweigh the potential risks to offspring.

### Overdose / Acute Toxicity

Hydrogen peroxide 3% solution can cause significant injury to the GI tract (see ***Adverse Effects***) after oral ingestion. Hydrogen peroxide in concentrations of 10% or greater can be very corrosive (causing severe burns to oral/gastric mucosa) and in humans, can induce oxygen emboli after oral ingestion.[7]

For patients that have experienced or are suspected to have experienced an overdose, consultation with a 24-hour poison center specializing in providing veterinary-specific information is recommended. For general information related to overdose and toxin exposures, as well as contact information for poison control centers, refer to *Appendix*.

### Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving hydrogen peroxide 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.

- **ACETYLCYSTEINE**, **ORAL**: Hydrogen peroxide can oxidize acetylcysteine in the GI tract and, although clinical significance is unclear, alternative emetics (eg, apomorphine, hydromorphone, xylazine) are preferred to induce emesis in patients with acetaminophen overdoses.[8]
- **ANTIEMETICS** (eg, **maropitant**, **ondansetron**): Pre-administration or ingestion of these products may negate the emetic effects of hydrogen peroxide.

### Laboratory Considerations

- No specific concerns were noted.

### Dosages

**NOTE:** All dosages use hydrogen peroxide 3% solution. The solution should not be expired.

- **DOGS:**

  **Emetic** (extra-label): 1 – 2.2 mL/kg PO (recommended maximum 50 mL/dog [NOT mL/kg]9) once; a subsequent dose may be given after 10 to 15 minutes if emesis is not achieved.[1,10] Results are improved if there is a small amount of food in the stomach.[5,11]

- **POT-BELLIED PIGS:**

  **Emetic** (extra-label): 1 – 2 mL/kg PO not to exceed 50 mL/pig (NOT mL/pig). Mix with a small amount of milk to encourage voluntary ingestion.[12]

- Adverse effects (eg, prolonged nausea or vomiting, respiratory distress)
- Heart rate and respiratory rate/character, including thoracic auscultation after emesis
- Clinical signs associated with toxicity of the substance ingested
- Blood toxicant concentrations if applicable

## Client Information

- Use only under the direct instructions of your veterinarian or an animal poison control center.
- Only use hydrogen peroxide 3% solution; stronger concentrations can be very toxic. Do not use expired solutions.
- Do not shake bottle. Carefully administer to avoid your animal unintentionally inhaling the liquid.
- Monitor your animal after giving hydrogen peroxide. Do not allow your animal to re-ingest the vomited material.
- Save all vomited fluid and material for your veterinarian to examine.
- Your animal should be seen by your veterinarian as soon as possible.

## Chemistry / Synonyms

Hydrogen peroxide 3% solution is a clear, colorless liquid containing 2.5% to 3.5% w/v hydrogen peroxide. Up to 0.05% of the liquid may contain preservatives.

Hydrogen peroxide 3% solution may also be known as dilute hydrogen peroxide solution, hydrogen peroxide solution 10-volume (**NOTE**: **NOT** 10%), or hydrogen peroxide topical solution.

## Storage / Stability

Store hydrogen peroxide 3% solutions in airtight containers at controlled room temperature between 15°C to 30°C (59°F-86°F) and protected from light. If hydrogen peroxide is allowed to become alkaline or it comes into contact with oxidizable organic matter, it will decompose. Do not shake bottle.

Hydrogen peroxide 3% solution can deteriorate with time; outdated or improperly stored products may not be effective as an emetic.

## Compatibility / Compounding Considerations

No specific information noted. Any compounded emetic for home use should be made from hydrogen peroxide 3% solution and not stronger concentrations.

## Dosage Forms / Regulatory Status

**VETERINARY-LABELED PRODUCTS:**

Hydrogen peroxide 3% solution in 473 mL bottles and 3.8 L (1 gal) jugs; generic; (OTC). Not reviewed or approved by the FDA.

**HUMAN-LABELED PRODUCTS:**

Hydrogen peroxide 3% solution is readily available OTC from a variety of manufacturers. Not reviewed or approved by the FDA. It is usually sold in pint bottles.

## References / Revisions

*Monograph last updated June 2021*

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### Regulatory Information
Do not administer to animals that produce food.

## Loperamide Hydrochloride
loe-pare′ah-mide hye-droe-klor′ide

**Trade and other names:** Imodium and generic brands

**Functional classification:** Analgesic, opioid

### Pharmacology and Mechanism of Action
Loperamide is an opiate agonist, but its effects are limited to peripheral receptors, particularly those on the GI tract. Like other opiates, loperamide acts on the mu-opiate receptors of the GI tract, where it decreases propulsive intestinal contractions and increases segmentation (an overall constipating effect). It also increases the tone of GI sphincters. In addition to affecting motility, opiates have an antisecretory effect and stimulate absorption of fluid, electrolytes, and glucose. Their effects on secretory diarrhea are probably related to inhibition of calcium influx and decreased calmodulin activity. The difference between loperamide and other opioids is that the action of loperamide is limited to the intestine. CNS effects do not occur because it does not cross the blood–brain barrier, or if it penetrates the blood-brain barrier, it is removed by drug transporters (P-glycoprotein).



### Indications and Clinical Uses
Loperamide is used for symptomatic treatment of acute nonspecific diarrhea. It has been administered orally to dogs and cats. There are no clinical studies in animals, and the use is based on extrapolation from the human uses or anecdotal evidence in animals. Long-term use is discouraged because it may lead to constipation. It has been administered to large animals, but this is generally not recommended.

### Precautionary Information
**Adverse Reactions and Side Effects**

Loperamide can cause severe constipation with repeated use. In some dogs that have a mutation in the *ABCB1* gene (previously known as the *MDR* gene), they may lack P-glycoprotein in the blood–brain barrier. In these susceptible animals, loperamide crosses the blood–brain barrier and causes profound sedation. Such cases may be reversed with naloxone. Dogs most susceptible include collie breeds, Australian shepherds, Old English sheepdogs, longhaired whippets, and Shetland sheepdogs.

**Contraindications and Precautions**

Small dogs and collie-type dogs may be at higher risk of adverse effects.

**Drug Interactions**

Do not administer with drugs that may act as MDR1 (p-glycoprotein) membrane inhibitors, such as ketoconazole. (Other inhibitors are listed in Appendix J.) These inhibitors may increase blood–brain barrier penetration and cause depression.

### Instructions for Use
Doses are based primarily on empiricism or extrapolation of human doses. Clinical studies have not been performed in animals.

### Patient Monitoring and Laboratory Tests
No specific monitoring is necessary.

### Formulations
- Loperamide is available in 2-mg tablets, 2-mg capsules, and 0.2-mg/mL oral liquid (over the counter).

### Stability and Storage
Store in a tightly sealed container, protected from light, and at room temperature. Loperamide is slightly soluble in water but only at low pH. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

**Dogs**
- 0.12 mg/kg q8–12h PO.

**Cats**
- 0.08–0.16 mg/kg q12h PO.

### Large Animal Dosage
- No large animal doses have been reported. If administered to horses or ruminants, it may induce problems associated with decreased intestinal motility.

### Regulatory Information
Withdrawal times are not established for animals that produce food. If administered to food animals, consult FARAD for extralabel use withdrawal interval estimates, at www.FARAD.org.
RCI Classification: 4

## Lorazepam
lor-ay′zeh-pam

**Trade and other names:** Ativan and generic brands

**Functional classification:** Anticonvulsant

### Pharmacology and Mechanism of Action
Lorazepam is a benzodiazepine sedative and CNS depressant. As a central-acting CNS depressant, it has actions similar to diazepam and other benzodiazepines. The mechanism of action appears to be via potentiation of gamma aminobutyric acid (GABA) receptor–mediated effects in the CNS.

*Pharmacokinetics:* In animals, lorazepam does not undergo extensive hepatic metabolism, but it is glucuronidated before excretion. Therefore, it is not subject to the same effects from cytochrome P450 enzymes as other benzodiazepines. In dogs, lorazepam has a half-life of 0.9 hours, with systemic clearance less than half that of diazepam. Oral absorption is 60%. Therefore the oral formulation may be suitable in dogs for some conditions.

### Indications and Clinical Uses
Lorazepam acts as a traditional benzodiazepine and may be considered for anxiety disorders in animals, but it has not been used as commonly as other drugs such as diazepam, alprazolam, or midazolam. Lorazepam also is effective for treating seizures, but it is not used as often in animals as other anticonvulsants. In controlled studies, it has

bacteria that cause infections in horses, including gram-positive cocci. However, higher doses have not been tested.

**Calves**

- 2 mg/kg, IV, SQ, or IM in the neck once daily for 3–5 days or 8–10 mg/kg once IM.

**Pigs**

- 2 mg/kg once per day IM (neck) for 3–5 days or 8 mg/kg once.

### Regulatory Information

Marbofloxacin is prohibited from use in animals intended for food in the United States. There are no withdrawal times established because it should not be administered to animals that produce food. In the United States, it is illegal to administer fluoroquinolones to food animals in an extralabel manner. Outside the United States, withdrawal times have been established: 6 days withdrawal for meat in cattle at 2 mg/kg and 3 days at 8 mg/kg. Milk withdrawal is 36 hours at 2 mg/kg and 72 hours at 8 mg/kg. Withdrawal time for pigs is 4 days.

## Maropitant Citrate

mar-op′i-tent

**Trade and other names:** Cerenia

**Functional classification:** Antiemetic

### Pharmacology and Mechanism of Action

Maropitant is an antiemetic from the same group as the human drug aprepitant (Emend). These drugs act as antiemetics by blocking the neurokinin-1 (NK1) receptor (also known as substance P). NK1 is a neurotransmitter to simulate vomiting from the emetic center. It has less affinity for other neurokinin receptors (NK2 and NK3). Although NK1 receptors are involved in other physiologic and behavioral responses, at doses used to control vomiting, there were no adverse effects associated with blockade of other receptors. Maropitant can inhibit vomiting that is stimulated from both central and peripheral sources mediated by other neurotransmitters such as acetylcholine, histamine, dopamine, and serotonin. The NK1 receptor is also involved in transmission of pain (via substance P), and blockers of this receptor may have potential as adjunctive treatments for painful conditions.

Other drugs in this class used in people include aprepitant (Emend) and rolapitant (Varubi).

*Pharmacokinetics:* In dogs, the peak concentration is achieved approximately 45 minutes after SQ administration. The half-life was 4–8 hours, depending on the dose. Dose-dependent pharmacokinetics occur, with the clearance decreasing and half-life increasing with doses above 2 mg/kg. Because of nonlinear pharmacokinetics, accumulation is possible with repeated dosing. Oral absorption is 24% at 2 mg/kg and 37% at 8 mg/kg in dogs. Pharmacokinetics are not affected by feeding. In cats, the clearance is much lower than in dogs, and the half-life is longer than in dogs, at 13–17 hours. In cats, it has nearly complete SQ absorption and 50% oral absorption. In horses, oral doses produced similar concentrations as in dogs, with a half-life of approximately 11.6 hours.

### Indications and Clinical Uses

Maropitant is approved for use as an antiemetic in dogs to inhibit vomiting from both central and peripheral sources. It has been effective to inhibit vomiting from chemotherapy, GI disease, toxins, renal disease, vestibular stimuli (motion sickness), and circulating stimuli via the chemoreceptor trigger zone (CRTZ). After SQ injection, it has

a rapid onset with a peak concentration 45 minutes after injection and a duration of 24 hours. Maropitant also is approved for use in cats and has been used safely and effectively in cats to treat vomiting from a variety of sources, such as motion sickness and stimulation by emetogenic agents (alpha$_2$ agonists, opioids), with a duration of action of 24 hours.

Maropitant can be administered oral, SQ, or IV route. A recent change in labeling allows for administration IV. For dogs and cats with nausea and vomiting, other antiemetic agents can safely be added to the treatment. These agents include ondansetron, metoclopramide, and dopamine antagonists. In people, for highly emetogenic cancer chemotherapeutic agents, an NK1 receptor blocker is combined with a serotonin blocker (e.g., ondansetron) and dexamethasone. Although maropitant is an effective antiemetic agent, there are no studies to support the use for gastroesophageal reflux.

Blockade of the NK1 receptor may have potential as an adjunctive treatment for some types of pain (e.g., visceral pain). Experimental studies have shown effects, but at this time, there are no clinical studies to demonstrate analgesic effects from maropitant. Maropitant may have some antitussive properties. It has been examined in horses at an oral dose of 4 mg/kg, but clinical effects have not been reported. At a dosage of 2 mg/kg q48h, it can decrease coughing severity and frequency of coughing in dogs with chronic bronchitis but does not decrease airway inflammation.

## Precautionary Information

### Adverse Reactions and Side Effects

Maropitant may cause slight pain or irritation from SQ injection. It has been recognized that the pain is caused by alteration of the formulation, which may occur when the injectable formulation is stored at room temperature. The cyclodextrin complex of maropitant is preserved at cold temperatures and is more stable and intact when the formulation is refrigerated. Therefore, the adverse event associated with a painful injection can be reduced if injectable maropitant is stored in the refrigerator before use.

Safety studies have been conducted with maropitant in both preclinical and clinical trials. In experimental dogs, it was safe at three and five times the labeled dose. Adverse effects observed in trials included excess salivation and muscle tremors. In cats, it has been well tolerated at high doses (of a factor of 10 times) and is safe at 5 mg/kg for 15 consecutive days.

In horses, a dose of 4 mg/kg oral for 5 days produced bradycardia and heart block in some horses.

### Contraindications and Precautions

Decreased clearance and accumulation occur after repeated doses with higher doses. Therefore, because of risk of accumulation, the original label stated that it should not be administered for more than 5 consecutive days, and one should allow a 2-day washout period before instituting another course of treatment. However, follow-up studies and a new revised label indicate that it may be safely administered to dogs at 8 mg/kg for 14 consecutive days, and the label has been extended to indicate that it may be administered until the condition has been resolved in dogs 7 months of age and older. When treating protracted vomiting, veterinarians should attempt to identify any underlying disease whenever possible instead of relying on maropitant to control the clinical signs. Maropitant effects and pharmacokinetics are not affected by kidney disease.

### Drug Interactions

Single doses have been administered in an IV line, but precipitation may be observed if mixed with alkalinizing solutions. Maropitant is an NK1 inhibitor, and

other neurokinin receptors are affected to a lesser degree. Therefore, because of this unique mechanism of action, drug interactions have not been identified. Maropitant has been used safely with other drugs, including anesthetics, anticancer agents, and other antiemetic agents. Maropitant is highly protein bound, but it is not known if there are protein-binding interactions with other drugs.

## Instructions for Use

Clinical trials in dogs have outlined the appropriate protocols for the use of maropitant. It has been effective for a wide range of causes of vomiting in dogs. In dogs, it was more effective to prevent opiate-induced vomiting if administered at least 30 minutes prior to the opiate administration, but to prevent nausea, 60 minutes prior is suggested.

It is also approved in cats for prevention of vomiting. It has been effective for a variety of causes of vomiting, including motion sickness and stimulation from emetogenic agents. The effective dose in cats is 1 mg/kg, regardless of cause. Maropitant can be administered the day before a scheduled anesthetic procedure to reduce anesthetic-induced vomiting (see dosing section for protocol).

If maropitant alone is not sufficient to control nausea and vomiting, consider adding other antinausea agents such as ondansetron, metoclopramide, or dopamine antagonists.

## Patient Monitoring and Laboratory Tests

Monitor for clinical signs and disease that may be a cause for the vomiting. Other specific monitoring and tests are not needed to use maropitant safely.

## Formulations

- Maropitant is available in 16-, 24-, 60-, or 160-mg tablets and a 10-mg/mL injectable solution. The pH of the solution is 4.1–4.7.

## Stability and Storage

Store in a tightly sealed container, protected from light. The injectable formulation can be stored at room temperature and in the refrigerator, but as noted earlier, pain from injection can be reduced if the formulation is stored in the refrigerator. Discard vial after 28 days of first use.

## Small Animal Dosage

**Dogs**

- 1 mg/kg SQ or IV or 2 mg/kg PO once daily for up to 5 days in dogs 2–7 months of age and until the problem is resolved for dogs older than 7 months.
- Motion sickness: 8 mg/kg PO once daily for up to 2 consecutive days.
- To prevent opioid-induced vomiting: 2–4 mg/kg PO or 1 mg/kg SQ or IV prior to anesthetic procedure.

**Cats**

- 1 mg/kg once daily IV, SQ, or PO (same dose for all causes of vomiting, including motion sickness).
- To decrease vomiting from highly emetic agents in cats, administer at least 2–2.5 hours prior to the administration of another emetic drug.
- To decrease vomiting and nausea from kidney disease: 4 mg per cat per day PO.
- Prior to anesthesia: Administer 8 mg per cat (2.5 mg/kg) oral 18 hours prior to a scheduled anesthetic procedure to reduce anesthesia-induced vomiting. Alternatively, administer an SQ injection 20 hours prior to the scheduled anesthetic procedure.

### Large Animal Dosage

- No large animal doses have been identified.

### Regulatory Information

No regulatory information is available for food animals. There are no withdrawal times established, and it is not recommended to be administered to animals that produce food.

## Masitinib Mesylate

**Note:** Masitinib has been withdrawn from the market and is no longer available. Consult previous editions of this book for information on the pharmacology, clinical use, and dosing.

## MCT Oil

**Trade and other names:** Medium-chain triglycerides (MCT) oil

**Functional classification:** Nutritional supplement



### Pharmacology and Mechanism of Action

Medium-chain triglyceride (MCT) oil is an oil supplement used for animals. Specifically, MCT oil supplements triglycerides in animals.

### Indications and Clinical Uses

Medium-chain triglyceride oil is used to treat lymphangiectasia and as a component of enteral feeding formulas.

### Precautionary Information

**Adverse Reactions and Side Effects**

Adverse effects not reported in veterinary medicine. It may cause diarrhea in some patients.

**Contraindications and Precautions**

No contraindications reported.

**Drug Interactions**

No drug interactions reported.

### Instructions for Use

Results of clinical trials using MCT oil have not been reported. Many enteral feeding formulas contain MCT oil (many polymeric formulations).

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- MCT oil is available as an oral liquid.

**Cats**

- 10 mg/kg IM, SQ, or IV q12h.

### Large Animal Dosage

- No large animal doses have been reported. However, doses similar to the range used in small animals are suggested for foals.

### Regulatory Information

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

## Mesalamine

mez-ahl'ah-meen

**Trade and other names:** 5-aminosalicylic acid, Asacol, Mesasal, Pentasa, and Mesalazine

**Functional classification:** Antidiarrheal

### Pharmacology and Mechanism of Action

Mesalamine is also known as 5-aminosalicylic acid. It is the active component of sulfasalazine, which is commonly administered for treatment of colitis. (See Sulfasalazine and Olsalazine for additional information.) The action of mesalamine is not precisely known, but it appears to suppress the metabolism of arachidonic acid in the intestine. It inhibits both COX- and lipoxygenase-mediated mucosal inflammation. Systemic absorption is low; most of the action is believed to be local. Four formulations of mesalamine have been used:

1. Asacol. Asacol is a tablet coated with an acrylic-based resin. The resin dissolves at a pH of 7.0 and is designed to release 5-aminosalicylic acid in the colon.
2. Mesasal. Mesasal is a tablet coated with an acrylic-based resin that dissolves at a pH greater than 6.0. It is designed to release 5-aminosalicylic acid in the terminal ileum and colon. Approximately 35% of the salicylate is absorbed systemically. The dosage in people is 1–1.5 g/day.
3. Olsalazine sodium (Dipentum). Olsalazine is a dimer of two molecules of 5-aminosalicylic acid linked by an azo bond that is released by bacterial digestion in the colon. It is used in people who cannot tolerate sulfasalazine. Only 2% of the salicylate from this compound is absorbed systemically. The most common adverse effect in people from this preparation has been watery diarrhea.
4. Pentasa. Pentasa contains microgranules of mesalamine coated with ethyl cellulose, which releases 5-aminosalicylic acid into the small and large intestine gradually, regardless of pH.

### Indications and Clinical Uses

Mesalamine is used for treatment of inflammatory bowel disease, including colitis, in animals. Most often sulfasalazine is used; however, in some animals, especially those sensitive to sulfonamides, mesalamine may be indicated. Use in animals has been primarily derived from empirical use, anecdotal experience, and recommendations from clinical experts. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### Precautionary Information

**Adverse Reactions and Side Effects**

Mesalamine alone has not been associated with side effects in animals. Adverse effects associated with sulfasalazine are caused by the sulfonamide component. (See Sulfasalazine for more information.)

**Contraindications and Precautions**

Drug interactions are possible, but they have not been reported in animals, probably because low systemic drug levels are achieved. Mesalamine, if absorbed sufficiently, can potentially interfere with thiopurine methyltransferase and therefore increase the risk of toxicity from azathioprine.

**Drug Interactions**

No drug interactions are reported in animals. Omeprazole can potentially increase absorption by increasing intestinal pH.

## Instructions for Use

Mesalamine usually is used as a substitute for sulfasalazine in animals that cannot tolerate sulfonamides.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Mesalamine is available in 400-mg tablets and 250-mg capsules. Delayed-release tablets are 400 mg (Asacol) and 1.2 g (film-coated Lialda). Controlled-release capsules are 250 and 500 mg (ethylcellulose-coated Pentasa).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is slightly soluble in water and ethanol. It should be protected from air and moisture. Darkening may occur after exposure to air. Do not crush coated tablets.

## Small Animal Dosage

- Veterinary doses have not been established. The usual human dosage is 400–500 mg q6–8h PO, and it has been used to extrapolate an animal dosage (e.g., 5–10 mg/kg q8h PO).

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No regulatory information is available. Because of a low risk of residues, no withdrawal times are suggested.
RCI Classification: 5

# Metaflumizone

met-ah-floo-mah-zone

**Trade and other names:** ProMeris

**Functional classification:** Antiparasitic

This product has been removed from the market. Consult previous editions of this handbook for information on pharmacology and clinical use.

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

### Small Animal Dosage
**Dogs**
- 5–25 mg/dog q24–48h PO.

**Cats**
- 2.5–5 mg/cat q24–48h PO.

### Large Animal Dosage
- No large animal doses have been reported.

### Regulatory Information
Do not use in animals intended for food.
Methyltestosterone is a Schedule III controlled drug.
RCI Classification: 4

## Metoclopramide Hydrochloride
met-oh-kloe-prah′mide hye-droe-klor′ide

**Trade and other names:** Reglan and Maxolon

**Functional classification:** Antiemetic

### Pharmacology and Mechanism of Action
Metoclopramide is an antiemetic and prokinetic drug that has been used in small animals for many years to control postoperative vomiting and stimulate GI motility. Metoclopramide stimulates motility of the upper GI tract and is a centrally acting antiemetic. The mechanism of action of metoclopramide is not completely understood. Among the proposed mechanisms is stimulation of 5-$HT_4$ (serotonin) receptors or an increase in the release of acetylcholine in the GI tract, possibly through a prejunctional mechanism. The affinity for 5-$HT_4$ receptors is low compared with other, more effective motility-modifying drugs. It inhibits gastric relaxation induced by dopamine, thus enhancing the cholinergic responses of gastric smooth muscle to increase motility. It also increases the tone of the lower esophageal sphincter. Metoclopramide acts centrally to inhibit dopamine in the CRTZ, which is responsible for antiemetic effects. The antiemetic effects occur primarily through dopamine ($D_2$) receptor blocking action.

Through $D_2$ receptor antagonism, metoclopramide increases prolactin, which has effects on the mammary gland and lactation.

*Pharmacokinetics* The half-life in dogs has ranged from less than 1 hour to 2 hours; effects on the esophageal sphincter persisted for only 30–60 minutes.

### Indications and Clinical Uses
Metoclopramide is used primarily for gastroparesis and treatment of vomiting. It is not effective for dogs with gastric dilation and should not be used in dogs with megaesophagus. In dogs, it is not very effective for decreasing gastroesophageal reflux or for increasing stomach emptying. One study demonstrated effects for gastroesophageal reflux in surgical patients at high doses of 1 mg/kg IV followed

by infusion of 1 mg/kg/h, but other studies showed no benefit. The primary effect in dogs appears to be via its antiemetic properties (dopamine antagonism in the vomiting center).

Because metoclopramide transiently increases prolactin secretion, there has been interest in using it for treating agalactia in animals. Metoclopramide increases prolactin and increases mammary gland development and lactation. In humans, it has been used as a galactagogue to increase lactation. This property also has been used in dogs to increase lactation in butches. At a dosage of 0.2 mg/kg PO q6h, it increases prolactin and milk lactose. Domperidone also has this activity and is preferred for this use in dogs and cats. (See Domperidone.)

In horses, it has been used to treat intestinal postoperative ileus, but adverse effects have limited the use. It is not effective in ruminants. In people, metoclopramide has also been used to treat hiccups and lactation deficiency.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are primarily related to blockade of central dopaminergic receptors. Adverse effects similar to those that are reported for other centrally acting $D_2$-receptor antagonists such as phenothiazines. In horses, undesirable side effects have been common and limit the therapeutic use. Adverse effects in horses include behavioral changes, excitement, and abdominal discomfort. Excitement from IV infusions can be severe. In calves at doses greater than 0.1 mg/kg, it produces neurologic effects.

### Contraindications and Precautions

Do not use in patients with epilepsy or with diseases caused by GI obstruction. Use cautiously in horses because dangerous behavior changes may occur. In people, it has been safe to use in the first trimester of pregnancy, but the effects on pregnancy in animals have not been studied. When used to increase lactation, metoclopramide is excreted into milk but not at a high enough level to harm newborn animals.

### Drug Interactions

Efficacy is diminished when administered with parasympatholytic (atropine-like) drugs.



## Instructions for Use

The use in animals is based primarily on studies in research animals, experience in people, or anecdotal experience in animals. There have been small observational studies in clinical patients to evaluate efficacy for gastroesophageal reflux. The most common use is for general antiemetic purposes, for which it has shown efficacy in dogs. Doses as high as 2 mg/kg have been used to prevent vomiting during cancer chemotherapy (higher doses may produce antiserotonin effects).

In recent years, other antiemetic agents have become more popular and widely used in small animals compared to metoclopramide. These agents include maropitant and serotonin antagonists (e.g., ondansetron).

In horses, there is some increase in intestinal motility at recommended doses, but little effect on the large bowel has been seen. In calves, metoclopramide had little effect on rumen motility.

## Patient Monitoring and Laboratory Tests

Monitor for signs of behavior disturbances from treatment, especially when IV doses are administered.

## Formulations Available

- Metoclopramide is available in 5- and 10-mg tablets, 1-mg/mL oral solution, and 5-mg/mL injection in 2-, 10-, and 30-mL vials.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is incompatible with other drugs when mixed in solution. Do not freeze. Stability is less than 24 hours if not protected from light. The solution has a pH of 4–5 and is stable over a pH range of 2–9. Individual doses may be stored in plastic syringes and are stable for 90 days in the refrigerator and 60 days at room temperature.

## Small Animal Dosage

**Dogs and Cats**

- Antiemetic dosage: 0.5 mg/kg q8h IV, IM, or PO.
- CRI: Administer a loading dose of 0.4 mg/kg followed by 0.3 mg/kg/h. In refractory cases, CRI dose may be increased up to 1.0 mg/kg/h. For antiemetic treatment with cancer chemotherapy, the dose used is up to 2 mg/kg per 24 hours.
- Dosage to stimulate lactation: 0.2 mg/kg PO q6h for 6 days.

## Large Animal Dosage

**Horses**

- Infusion of metoclopramide (0.125–0.25 mg/kg/h) added to IV fluids to reduce postoperative ileus in horses (see precautions regarding use in horses).

**Calves and cattle**

- Not recommended because it is not a suitable prokinetic agent in ruminants. At a dose of 0.1 mg/kg IV to cattle, it does not increase abomasal emptying. Adverse reactions develop at higher doses (0.3 mg/kg).

## 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

# Metoprolol Tartrate

meh-toe′proe-lole tar′trate

**Trade and other names:** Lopressor

**Functional classification:** Beta blocker

## Pharmacology and Mechanism of Action

Metoprolol is a $beta_1$-adrenergic receptor blocker. Metoprolol has similar properties to propranolol except that metoprolol is specific for $beta_1$ receptors, with less effect on $beta_2$ receptors. Metoprolol is a lipophilic beta blocker and relies on the liver for clearance. Lipophilic beta blockers such as metoprolol undergo high first-pass clearance, which reduces oral bioavailability and causes high interpatient variability in plasma concentrations and effects. An alternative $beta_1$ blocker used in animals is atenolol, which is water soluble and cleared by the kidneys.

# Metronidazole and Metronidazole Benzoate

meh-troe-nye′dah-zole

**Trade and other names:** Flagyl and generic brands

**Functional classification:** Antibacterial, antiparasitic

## Pharmacology and Mechanism of Action

Metronidazole is an antibacterial and antiprotozoal drug used frequently in small animals, primarily for GI problems. It is a second-generation nitroimidazole in which the activity involves generation of free nitro radicals via metabolism within protozoa and bacteria. Metronidazole disrupts DNA in the organism via reaction with intracellular metabolite. Its action is specific for anaerobic bacteria and protozoa. Resistance is rare. It is active against some protozoa, including *Trichomonas* spp., *Giardia* spp., and intestinal protozoal parasites. It also has in vitro activity against anaerobic bacteria and *Helicobacter* spp.

*Pharmacokinetics:* Metronidazole oral absorption is nearly complete in animals (75%–100% in horses and 60%–100% in dogs). Rectal absorption in horses is 30%. The half-lives are 2–4 hours in horses, 9–12 hours in foals, and 3–5 hours in dogs. Metronidazole benzoate is formulated for cats to improve palatability. In this form, the oral absorption (12.4 mg/kg of the base) is 64%, with a half-life of 5 hours.

## Indications and Clinical Uses

Metronidazole is not approved for use in animal animals, and the use is derived from small observational studies, anecdotal experience, and opinions from experts. It has been used to treat diarrhea and other intestinal problems caused by intestinal protozoa such as *Giardia, Trichomonas,* and *Entamoeba* spp. It may be used in small animals and horses for treatment of a variety of anaerobic infections. Common uses in horses include treatment of infections caused by *Clostridium* spp., and *Bacteroides fragilis*. Metronidazole has been used for immune-modulating activity in the intestine of animals and administered for inflammatory bowel disease in animals. However, evidence of a direct immune-modulating effect or immunosuppressive effect is lacking. A common use of metronidazole is for short-term treatment of acute nonspecific diarrhea in animals. Clinical results have been mixed for this use. One controlled study in dogs showed that there is no benefit from this treatment compared to placebo. In another study, the duration of diarrhea was decreased by approximately 1.5 days compared to placebo treatment in dogs. The diarrhea resolved in most dogs within several days, regardless of treatment. Metronidazole benzoate, an ester pro-drug of metronidazole, has been used in cats because it is more palatable.

## Precautionary Information

### Adverse Reactions and Side Effects

The most severe adverse effect is caused by toxicity to the CNS. It is highly lipophilic and readily crosses the blood–brain barrier. High doses have caused lethargy, CNS depression, ataxia, tremors, seizures, vomiting, and weakness. Most CNS toxicity caused from metronidazole in animals occurs at high doses (greater than 60 mg/kg/day). The CNS signs are related to inhibition of action of gamma-aminobutyric acid (GABA) and are responsive to benzodiazepines (diazepam 0.4 mg/kg q8h for 3 days).

In horses, adverse effects include peripheral neuropathy, hepatopathy, and decreased appetite, all of which are more likely with high doses. The drug has a longer half-life in foals, and foals may be more prone to adverse effects than adult horses.

Like other nitroimidazoles, metronidazole has the potential to produce mutagenic changes in cells, but the clinical significance of this effect is uncertain. There are no reports of increased rated of cancer in patients that have received metronidazole.

Like other nitroimidazoles, it has a bitter taste and can cause vomiting and anorexia. At a dose of 25 mg/kg in dogs, it may degrade the olfactory ability. This may affect the ability of working dogs (e.g., law enforcement dogs) to perform their duties to detect explosives, illegal drugs, and other agents. A total of 50% of the treated dogs had decreased olfactory ability in one study.

Metronidazole benzoate has been used in some cats safely at 25 mg/kg q12h for 7 days. However, there is a caution about the effect of benzoate salts in cats because it is a benzoic acid derivative. Benzoic acid can be toxic to cats and causes ataxia, blindness, respiratory problems, and other CNS disorders. Despite this concern, it is estimated that 500 mg/kg/day of metronidazole benzoate would be needed to provide a toxic dose of benzoic acid to cats. Nevertheless, any cat showing CNS or other signs of toxicity should have the metronidazole benzoate discontinued immediately.

**Contraindications and Precautions**

Fetal abnormalities have not been demonstrated in animals with recommended doses but use cautiously during pregnancy.

**Drug Interactions**

Like other nitroimidazoles, it can potentiate the effects of warfarin and cyclosporine via inhibition of drug metabolism.



## Instructions for Use

Metronidazole is one of the most commonly used drugs for anaerobic infections. Although it is effective for giardiasis, other drugs used for *Giardia* spp. include albendazole, fenbendazole, and quinacrine. CNS toxicity is a concern, but it is dose related. The maximum dose that should be administered is 50–65 mg/kg/day in any species.

Metronidazole is unpalatable and can produce a metallic taste. In cats, when the tablet is crushed or broken, the unpalatability is particularly a problem. Metronidazole benzoate has a bland taste and is better tolerated. Metronidazole benzoate is not commercially available in the United States. However, it may be available from compounding pharmacies. Because of the weight of metronidazole benzoate versus metronidazole hydrochloride, a factor of 1.6 times is used to convert a metronidazole hydrochloride dose to a metronidazole benzoate dose. Metronidazole benzoate is 62% metronidazole; therefore, 20 mg/kg of metronidazole benzoate delivers 12.4 mg/kg of metronidazole.

In horses, oral absorption of metronidazole is practically complete and not affected by feeding pattern (e.g., with or without food and similar with hay or concentrate). However, absorption from rectal administration to horses is low.

Metronidazole should not be injected directly; it is too acidic. See Stability and Storage section for mixing instructions.

## Patient Monitoring and Laboratory Tests

Monitor for neurologic adverse effects. MICs for anaerobic bacteria are typically 2–4 mcg/mL, or less. The CLSI breakpoint is ≤8 mcg/mL.

## Formulations

- Metronidazole is available in 250- and 500-mg tablets, 375-mg capsules, 50-mg/mL suspension, and 5-mg/mL injection.
- Metronidazole benzoate is a formulation not available in the United States but has been compounded for veterinary use. Metronidazole benzoate is 62% metronidazole. It has been formulated in Ora-Plus and Ora-Sweet (drug excipients) to a concentration of 16 mg/mL.

## Stability and Storage

The base is slightly soluble in water. The benzoate form is practically insoluble; the hydrochloride form is soluble in water. Metronidazole has been crushed and mixed with some flavorings to mask the taste. When mixed with some syrups or water, with exceptions listed here, decomposition occurs within 28 days.

Metronidazole benzoate prepared in vehicles such as Ora-Plus or Ora-Sweet was stable for 90 days. Metronidazole base (from tablets) also was mixed with these vehicles and was found to be stable for 90 days.

When reconstituted, metronidazole hydrochloride is too acidic (pH 0.5–2) for direct injection. Injection of 5 mg/mL should be further diluted with 100 mL (0.9% saline, 5% dextrose, or Ringer's solution) and neutralized with 5 mEq of sodium bicarbonate per 500 mg for a pH of 6–7. Reconstituted injectable forms are stable for 96 hours but after dilution should be discarded after 24 hours.

## Small Animal Dosage

### Dogs

- Anaerobic bacteria: 15 mg/kg q12h or 12 mg/kg q8h PO.
- Anaerobic bacteria: IV dose: 15 mg/kg IV via slow infusion over at least 30 minutes in a diluted form. Give slowly to avoid adverse CNS effects.
- *Giardia* infection: 12–15 mg/kg q12h for 5–7 days PO.

### Cats

- Anaerobic bacteria: 10–25 mg/kg q24h PO.
- *Giardia* infection: 17 mg/kg (one third tablet per cat) q24h for 8 days.
- Metronidazole benzoate (for treatment of *Giardia* infection): 25 mg/kg PO 12h for 7 days. Metronidazole benzoate is 62% metronidazole; therefore 20 mg/kg of metronidazole benzoate delivers 12.4 mg/kg of metronidazole.

## Large Animal Dosage

### Horses

- Treatment of anaerobic bacteria and protozoal infections: 10 mg/kg q12h PO. Note: Some clinicians have used higher doses (≤15–20 mg/kg q6h), but at these doses, side effects are more likely.
- Foals: 10–15 mg/kg IV or PO q12h.

### Cattle

- Treatment of trichomoniasis (bulls): 75 mg/kg q12h IV for three doses. (See Regulatory Information.)

## Regulatory Information

Do not administer to animals that produce food. Administration of nitroimidazoles to animals intended for food is prohibited. Treated cattle must not be slaughtered for food.

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

## Pharmacology and Mechanism of Action

Mineral is a lubricant laxative that has been widely used for many years. Mineral oil has nonspecific effects to increase water content of stool and act as a lubricant for intestinal contents.

## Indications and Clinical Uses

Mineral oil is administered orally (via stomach tube in horses) to increase passage of feces for treatment of impaction and constipation. It is primarily used in large animals (especially horses), and small animal use is uncommon.

### Precautionary Information

**Adverse Reactions and Side Effects**

Adverse effects have not been reported. Chronic use may decrease absorption of fat-soluble vitamins.

**Contraindications and Precautions**

Use caution when administering via stomach tube. Accidental administration into the lungs has produced fatal reactions.

**Drug Interactions**

No drug interactions reported. Chronic use may inhibit absorption of fat-soluble vitamins.

## Instructions for Use

Use is empirical. No clinical results reported.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Mineral oil is available in an oral liquid.

## Stability and Storage

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

## Small Animal Dosage

**Dogs**

- 10–50 mL/dog q12h PO.

**Cats**

- 10–25 mL/cat q12h PO.

## Large Animal Dosage

**Horses and Cattle**

- 500–1000 mL (1 pint to 1 quart) per horse or cow PO as needed. Up to 2–4 L per adult horse or cow PO (usually administered via stomach tube).

**Sheep and Pigs**

- 500–1000 mL PO as needed.

## Regulatory Information

No regulatory information is available. Because of a low risk of residues, no withdrawal times are suggested.

DRUG MONOGRAPH

# Mirtazapine

*(mir-**taz**-ah-peen)*

**Trade name**: Remeron®, Miratаz®

**Drug class**: 5-HT3 Receptor Antagonist, Tetracyclic Antidepressant

DOSAGES DOSAGE FORMS

## Prescriber Highlights

- Transdermal form is labeled for management of weight loss in cats. Also used in tablet form as an appetite stimulant and antiemetic in dogs and cats with chronic kidney disease (CKD)
- Can be used in conjunction with other antiemetics
- Primary adverse effect is sedation. In cats, vocalization and increased affection can be noted.
- The lowest effective dose should be used to reduce sedative properties. Doses should not exceed 30 mg/day in dogs when using for appetite stimulation.
- Owners handling transdermal mirtazapine should wear gloves. Humans and other animals in the household should avoid contact with the treated cat for at least 2 hours after transdermal administration.

## Uses / Indications

Transdermal mirtazapine is indicated in the management of weight loss in cats. In a study, average weight gain was 3.9% of body weight after a 2-week course of therapy.[1] In another study, cats ingested significantly more food when receiving mirtazapine tablets as compared with placebo.[2] No difference in food ingestion was noted between the 2 groups, but high doses (ie, 3.75 mg) of mirtazapine were associated with significantly more noticeable behavior changes.[2]

The drug is an effective appetite stimulant and has antiemetic activity in cats with CKD.[3] In a study of healthy dogs, mirtazapine accelerated gastric emptying and colonic transit without having an effect on small intestine transit.[4] Other potential veterinary uses of mirtazapine could include treatment of chemotherapy-induced nausea and vomiting, behavior-related conditions, congestive heart failure, GI disorders, liver disease, and neoplasia.

## Pharmacology / Actions

The antidepressant activity of mirtazapine appears to be mediated by antagonism at central presynaptic $\alpha_2$ receptors, which normally act as a negative feedback mechanism, inhibiting further norepinephrine (NE) release. By blocking these receptors, mirtazapine overcomes the negative feedback loop and causes a net increase in NE. This mechanism may also contribute to the appetite-stimulating effects of the medication, as NE acts at other α receptors to increase appetite. In addition, mirtazapine antagonizes several serotonin (5-HT) receptor subtypes. The drug is a potent inhibitor of the 5-$HT_2$, 5-$HT_3$, and histamine ($H_1$) receptors. Antagonism at 5-$HT_3$ receptors accounts for the antinausea and antiemetic effects of the drug, and its action at $H_1$ receptors produces prominent sedative effects. It is a moderate peripheral $\alpha_1$-adrenergic antagonist, a property that may explain the occasional orthostatic hypotension associated with its use; it is also a moderate antagonist of muscarinic receptors, which may explain the relatively low incidence of anticholinergic effects.

## Pharmacokinetics

After administration of oral mirtazapine at either 1.88 mg (low dose [LD]) or 3.75 mg (high dose [HD]) in a study of healthy cats, median elimination half-lives were 9.2 hours and 15.9 hours, respectively.[2] Mean clearance was 10.5 mL/kg/min (LD) and 18 mL/kg/min (HD). A single LD of mirtazapine was well tolerated and resulted in a half-life compatible with 24-hour dose intervals in healthy cats. Mirtazapine does not appear to have linear kinetics in cats.[2] A study in cats with CKD ($n = 6$) found that mean half-life was 15.2 hours and mean oral clearance was 0.6 L/hr/kg.[5] The authors concluded that the results were compatible with administration every 48 hours in cats with CKD.[5] Liver disease delays time to peak concentration (4 hours vs 1 hour) and prolongs elimination half-life (14 hours vs 7 hours) in cats.[6]

Transdermal mirtazapine bioavailability is ≈65%, and peak drug concentration is reached ≈ 16 hours after administration of a single dose and ≈ 2 hours after repeated administration.[7] Half-life is 21 to 27 hours,[7] although a shorter half-life (10-11 hours) may reflect both topical and oral (ie, grooming) exposure. In healthy cats, transdermal mirtazapine has been shown to reach steady state within 14 days. Transdermal time to maximum concentration is 6 hours, with a peak plasma concentratic ($C_{MAX}$) of 32.1 ng/mL.

appears to be ~70% to 72% in mice, rats, and dogs, whereas in humans and rabbits, it is ~85%. Despite the interspecies differences in PPB, no displacement interactions or dose adjustments for mirtazapine are expected due to its large therapeutic window and nonspecific, relatively low affinity for plasma proteins. Mirtazapine is metabolized via multiple pathways and varies by species. In all species tested (ie, humans and laboratory animals), the drug is metabolized via the following mechanisms: 8-hydroxylaton followed by conjugation, *N*-oxidation, and demethylation followed by conjugation. Humans and guinea pigs also produce metabolites via $N^+$-glucuronidation, whereas mice are the only species that have been found to use demethylation followed by $CO_2$ addition and conjugation and 13-hydroxylation followed by conjugation as methods of mirtazapine breakdown. These processes are conducted primarily by CYP2D6, CYP1A2, and CYP3A4, but mirtazapine exerts minimal inhibition on these cytochromes. Several metabolic pathways of mirtazapine involve conjugation with glucuronide (glucuronidation). Because cats have a limited capacity for glucuronidation, mirtazapine is cleared less rapidly from the system; therefore, extended dosing intervals may be required.

In humans, elimination occurs via urine (75%) and feces (15%). Renal impairment may reduce elimination by 30% to 50% as compared with normal subjects, and hepatic impairment may reduce clearance by up to 30%. The elimination half-life of mirtazapine ranges from 20 to 40 hours across age and gender subgroups, so dose increases should occur no more frequently than every 7 to 14 days. Females (both human and animal) of all ages exhibit significantly longer elimination half-lives than males (in humans, mean half-life of 37 hours for females versus 26 hours for males).

## Contraindications / Precautions / Warnings

Mirtazapine is contraindicated in patients hypersensitive to it and in those that have received monoamine oxidase inhibitors (eg, selegiline) in the past 14 days. Transdermal mirtazapine should not be administered orally or in the eye.

Mirtazapine has been associated with orthostatic hypotension in humans and should therefore be used with caution in patients with known cardiac disease or cerebrovascular disease that could be exacerbated by hypotension. Patients with renal impairment, renal failure, or hepatic disease may require lower doses of mirtazapine and should be closely monitored while receiving mirtazapine. Mirtazapine has rarely been associated with hyponatremia in humans; caution should be used in patients receiving a diuretic or other medication that could decrease sodium levels.

Abrupt discontinuation of mirtazapine after long-term administration has resulted in withdrawal symptoms such as nausea, headache, and malaise in humans. In general, antidepressants may affect blood glucose concentrations due to their indirect effects on the endocrine system; caution should be used in patients with diabetes mellitus.

Mirtazapine exhibits very weak anticholinergic activity; consequently, vigilance should be used in patients that might be more susceptible to these effects (eg, those with urinary retention; prostatic hypertrophy; acute, untreated closed-angle glaucoma or increased intraocular pressure; GI obstruction or ileus). Effects of mirtazapine may also be additive to anticholinergic medications.

Extra care should be taken in active animals, as mirtazapine may impair concentration and alertness. Although extremely rare, mirtazapine has been associated with blood dyscrasias in humans and should be used cautiously in patients with pre-existing hematologic disease, especially leukopenia, neutropenia, and/or thrombocytopenia. Prolongation of the QT interval has been reported, and risk may increase with other QT-prolonging drugs.

## Adverse Effects

Mirtazapine appears to be well tolerated in both dogs and cats at the appropriately prescribed dosages. In a study evaluating the adverse effects of mirtazapine in cats, the 10 most common adverse effects seen (listed from most frequent to least frequent) were vocalization (56%), agitation (31%), vomiting (26.2%), abnormal gait/ataxia (16.7%), restlessness (14.3%), tremors/trembling (14.3%), hypersalivation (13%), tachypnea (11.9%), tachycardia (10.7%), and lethargy (10.7%). Only one cat that received the 1.88 mg dose had adverse effects, whereas 25 cats that received a dose of 3.75 mg displayed adverse effects. Other adverse effects reported during the study included anorexia, disorientation, dyspnea, hypothermia, mouth breathing/panting, mydriasis, behavior changes, depression/sedation, fasciculations, hyperactivity, hypertension, pacing, dysphoria, inappropriate elimination, polyphagia, circling, discomfort, hiding, inappetence, seizures, and weakness.[10] Increases in liver enzymes have been reported in some cats receiving mirtazapine. In a study, cats experienced more adverse effects with 3.75 mg doses as compared with 1.88 mg doses.[10]

Transdermal mirtazapine may cause application site reactions (eg, erythema, crusting/scabbing, residue) in ≈ 10% of cats.

## Reproductive / Nursing Safety

The FDA categorizes mirtazapine as category ***C*** (*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*). Reproductive studies in rats, rabbits, and dogs have shown no evidence of teratogenicity. Additional studies in hamsters, rabbits, and rats have shown no evidence of fetal genetic mutation or reduction in parental fertility, although there were increases in postimplantation losses and pup deaths, as well as decreases in birth weight.

Mirtazapine is distributed in human breast milk and can be detected in the serum of breastfed infants; caution should be used in nursing dams.

## Overdose / Acute Toxicity

There were 235 single-agent exposures to mirtazapine reported to the ASPCA Animal Poison Control Center (APCC) between 2009 and 2013. Of the 58 dogs, 21 showed clinical signs, with 52% agitated, 29% lethargic, 19% vocalizing, 19% panting, and 14% tremoring. Of the 178 cats, 131 showed clinical signs, with 57% vocalizing, 38% agitated, 23% vomiting, 21% tachycardic, 15% ataxic, and 11% lethargic.

theoretical in humans or animals receiving mirtazapine and may be of significance in veterinary patients. Unless otherwise noted, use together is not necessarily contraindicated, but the potential risks should be weighed and additional monitoring performed when appropriate.

- **BENZODIAZEPINES** (eg, **diazepam, midazolam**): Concurrent use has minimal effects on mirtazapine blood levels, but use together may cause additive impairment of motor skills.
- **BUPRENORPHINE**: Concurrent use with mirtazapine may increase risk for serotonin syndrome.
- **BUTORPHANOL**: Concurrent use with mirtazapine may increase risk for serotonin syndrome.
- **CIMETIDINE**: May increase mirtazapine exposure
- **CLONIDINE**: Concurrent use with mirtazapine may cause increases in blood pressure.
- **CNS DEPRESSANTS** (eg, **antihistamines, opioids**): Concurrent use with mirtazapine may increase risk for sedation and CNS depression.
- **CYPROHEPTADINE**: May negate the effects mirtazapine
- **ERYTHROMYCIN**: May increase mirtazapine exposure
- **KETOCONAZOLE**: May increase mirtazapine exposure
- **MONOAMINE OXIDASE INHIBITORS** (**MAOIs**; eg, **selegiline, amitraz, linezolid, methylene blue**): Increased risk for serotonin syndrome when used concurrently with mirtazapine. Concurrent use or use within 14 days is contraindicated.
- **SEROTONERGIC AGENTS, MISCELLANEOUS** (eg, **buspirone, lithium, metoclopramide, ondansetron**): Concurrent use with mirtazapine increases risk for serotonin syndrome.
- **SELECTIVE SEROTONIN REUPTAKE INHIBITORS** (**SSRIs**; eg, **fluoxetine, fluvoxamine**): Concurrent use with mirtazapine increases risk for serotonin syndrome.
- **TRICYCLIC ANTIDEPRESSANTS** (eg, **amitriptyline, clomipramine**): Concurrent use with mirtazapine increases risk for serotonin syndrome.
- **TRAMADOL**: Increased risk for serotonin syndrome when used concurrently with mirtazapine
- **WARFARIN**: May prolong prothrombin time (PT) when used concurrently with mirtazapine

## Laboratory Considerations

- No specific concerns noted

## Dosages

- **DOGS**:

**Appetite stimulant and/or antiemetic** (extra-label): There is little data on mirtazapine pharmacokinetics or efficacy in dogs. Anecdotal doses ranging from 3.75 – 30 mg (depending on dog size) PO every 24 hours have been suggested. Alternatively, 1.1 – 1.3 mg/kg PO every 24 hours.[11] Doses should not exceed 30 mg per dog per day.

- **CATS**:

**Management of weight loss; transdermal ointment** (FDA approved): 1.5-inch ribbon (≈2 mg/cat) applied to inner pinna of cat's ear every 24 hours for 14 days. Person applying medication should wear gloves. Alternate application of ointment between the left and right inner pinnae of the ears (Adapted from label information; *Mirataz*®).

**Appetite stimulant and/or antiemetic** (extra-label): 1.88 mg (practically, ¼ of a 7.5-mg tablet; ⅛ of a 15-mg tablet) per cat PO every 48 hours.[3] The optimal dose has not been determined, and although some advise higher doses or giving this dose every 24 hours in cats with normal renal function, the smaller doses mentioned here are more often indicated as the appropriate treatment in cats, and it has been suggested that higher doses are not more effective and actually have more adverse effects. Extending the dose interval may be appropriate in cats with liver disease.[6]

## Monitoring

- Clinical efficacy measured by the following parameters: increased appetite, decreased episodes of vomiting, and weight gain
- Liver enzymes in cats
- Adverse effects (eg, behavior, sedation)

- If your animal is receiving the orally disintegrating tablets, make sure your hands are dry before handling the tablet. Place the tablet under the animal's tongue and hold the animal's mouth closed for several seconds to allow it to dissolve (should occur quickly). After the tablet has melted, offer the animal water.
- Gloves should be worn when handling the transdermal formulation and disposed of afterward. After the medication is applied, wash hands with soap and water. Members of the household should avoid contact with the treated cat for 2 hours after administration, as mirtazapine can be absorbed through the skin.

## Chemistry / Synonyms

Mirtazapine, a member of the piperazinoazepine group of compounds, is classified as an atypical tetracyclic antidepressant and is not chemically related to other antidepressants. Mirtazapine occurs as a white to creamy white crystalline powder that is slightly soluble in water.

Mirtazapine may also be known as 6-azamianserin, Org-3770, mepirzapine, and *Remeron*®; many trade names for international products are available.

## Storage / Stability

Mirtazapine transdermal ointment should be stored at 25°C (77°F) and used within 30 days after opening.

The coated tablets and orally disintegrating tablets should be stored between 20°C and 25°C (68°F-77°F), with excursions permitted between 15°C and 30°C (59°F-86°F). Protect from light and moisture. The orally disintegrating tablets must be used once removed from the tablet blister and cannot be stored.

## Compatibility / Compounding Considerations

Compounded preparation stability: Mirtazapine 10 mg/mL oral suspension can be compounded from commercially available tablets. Triturate 10 mirtazapine 30 mg tablets with 15 mL of *Ora-Plus*® and qs ad to 30 mL with *Ora-Sweet*®. The resulting suspension retains 90% potency for 90 days stored at both 5°C (41°F) and 25°C (77°F). Compounded preparations of mirtazapine should be protected from light and shaken well before use.[12]

## Dosage Forms / Regulatory Status

**VETERINARY-LABELED PRODUCTS**:

Mirtazapine Transdermal Ointment: 100 mg/tube in 5-gram tube (20 mg per 1 gram); ***Miratаz***®, (Rx)

**HUMAN-LABELED PRODUCTS**:

Mirtazapine Oral Tablets: 7.5 mg, 15 mg, 30 mg, and 45 mg; *Remeron*®, generic; (Rx)

Mirtazapine Orally Disintegrating Tablets: 15 mg, 30 mg, and 45 mg; *Remeron SolTab*®, generic; (Rx). **NOTE**: Some generic ODTs may contain xylitol (unknown quantity).

## References / Revisions

*Monograph last updated by James A. Budde, PharmD, DICVP, August 2019. Reviewed by Todd M. Archer, DVM, MS, DACVIM, and Megan Flanigan, PharmD, FSVHP.*

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topical exposure. After application, care should be taken that people or other animals in the household do not come in contact with the treated cat for 2 hours because mirtazapine can be absorbed transdermally and orally. However, there are negligible residues are present at the application site and the body of the cat at 2 hours after dosing. There are no known contraindications in animals.

**Drug Interactions**

No drug interactions have been reported for animals. However, if possible, avoid use with SSRIs and MAOIs such as selegiline.

## Instructions for Use

Doses and recommendations are based on the clinical use in cats with chronic kidney disease through published evidence from clinical studies and the FDA-approved label. Other uses are anecdotal and not well documented.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Mirtazapine is available in 15-, 30-, and 45-mg tablets. There is also a rapidly disintegrating tablet in these sizes that dissolves easily in a pet's mouth.
- Transdermal formulation: Each gram of ointment contains 20 mg of mirtazapine (2%), supplied in a 5-g tube containing 100 mg (0.1 g) of mirtazapine.

## 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**

- 0.5–1 mg/kg q12h PO. Generally in the range of 3.75–7.5 mg per dog daily PO.

**Cats**

- 1.9 mg per cat PO. Doses have ranged from 3.75–7.5 mg per cat per day PO (one fourth to one half of a 15-mg tablet). In healthy cats, it can be administered once daily. In cats with chronic kidney disease, increase the interval to q48h.
- Transdermal formulations: Apply a 1.5-inch ribbon of ointment (approximately 2 mg/cat or 0.5 mg/kg) on the inner pinna of the cat's ear once daily for 14 days.

## Large Animal Dosage

No large animal doses are available.

## Regulatory Information

No withdrawal time information is available for food-producing animals.

# Misoprostol

mee-soe-pross'tole

**Trade and other names:** Cytotec

**Functional classification:** Antiulcer agent

## Pharmacology and Mechanism of Action

Misoprostol is a synthetic prostaglandin. It is a synthetic analogue of prostaglandin $E_1$ ($PGE_1$). It is an agonist for the prostaglandin receptors $E_2$, $E_3$, and $E_4$, and produces a cytoprotective effect on the GI mucosa. It has been shown in dogs and people to decrease injury to GI mucosa caused by NSAIDs, such as aspirin. In studies in dogs, misoprostol was not effective for decreasing adverse effects caused by corticosteroids. Misoprostol also has anti-inflammatory effects and has been used to treat pruritus in dogs. Because it is a synthetic prostaglandin, it has uterotonic and cervical ripening effects. It produces these effects by increasing the activity of collagenases, elastase, glycosaminoglycan, and hyaluronic acid in the cervix and increases the calcium levels in the uterus to induce contractions. It can induce labor, interfere with pregnancy, and has been used to induce abortion (see later).

*Pharmacokinetics:* In horses after a dose of 5 mcg/kg, oral absorption was better in unfed horses compared with fed horses. The half-life was approximately 2.8 hours in the nonfed horses. Rectal administration of misoprostol to horses produced less complete absorption and a shorter half-life compared with oral administration.

## Indications and Clinical Uses

Misoprostol is used to decrease the risk of GI ulceration when administered concurrently with NSAIDs. Efficacy has been established for this indication in trials with aspirin but not with other NSAIDs in animals. There is no evidence to show that it decreases GI bleeding caused by other drugs (e.g., corticosteroids). Clinical trials also are available to show that misoprostol is effective for treating pruritus in patients with atopic dermatitis, although it is less effective than other drugs.



The GI effects in horses have been explored through small observational studies and anecdotal accounts. Misoprostol may be helpful in horses for treating right dorsal colitis. Equine GI experts consider misoprostol a valid first-line option for equine glandular gastric disease at a dose of 5 mcg/kg PO and was superior to omeprazole and sucralfate. However, it should not be used with omeprazole in horses or in pregnant mares. The optimum dose in horses has not been determined, but a dose of 5 mcg/kg oral produces plasma drug concentrations that are similar to effective doses in people.

Misoprostol has been used to induce abortion, but it is much more effective when used with other agents such as aglepristone or mifepristone. In people, it is used with mifepristone. It should not be used alone to induce abortion because high doses are needed, which can increase the risk of adverse effects.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are caused by effects of prostaglandins. The most common adverse effects are GI discomfort, vomiting, and diarrhea. Diarrhea and abdominal discomfort have been reported in horses, but these effects are usually mild and self-limiting. It was tolerated in experimental horses at a dose of 5 mcg/kg oral.

### Contraindications and Precautions

Do not administer to pregnant animals; it may cause abortion. Women should handle this medication carefully because it can induce abortion.

### Drug Interactions

Misoprostol may compromise the acid-suppressing effects of omeprazole, so these drugs should not be used together.

## Instructions for Use

Doses and recommendations are based on clinical trials in which misoprostol was administered to prevent GI mucosal injury caused by aspirin. These effects can likely be extended to other NSAIDs. The effects in horses for treating right dorsal colitis and equine glandular gastric disease are from observations from clinical experts. Careful handling of misoprostol should be observed because of its potential to induce abortion.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Misoprostol is available in 0.1-mg (100-mcg) and 0.2-mg (200-mcg) tablets.

## Stability and Storage

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

## Small Animal Dosage

**Dogs**

- 2–5 mcg/kg q12h PO.
- Atopic dermatitis: 5 mcg/kg q8h PO.

**Cats**

- 2–4 mcg/kg q12h PO
- Induce abortion: 200 mcg per cat q12h PO until abortion begins, administered with aglepristone or mifepristone. Higher doses can induce abortion when administered alone but with more frequent and more severed adverse effects.

## Large Animal Dosage

**Horses**

- 5 mcg/kg q12h PO.

## Regulatory Information

Do not use in animals that produce food.
RCI Classification: 4

# Mitotane

mye′toe-tane

**Trade and other names:** Lysodren and op'-DDD

**Functional classification:** Adrenolytic agent

## Pharmacology and Mechanism of Action

Mitotane is a cytotoxic agent that has specific effects on the adrenal gland. It binds to adrenal proteins and is then converted to a reactive metabolite, which then destroys cells of the zona fasciculata and zona reticularis of the adrenal cortex. The precise mechanism of action is through inhibition of sterol-O-acetyl-transferase. This is an enzyme that converts cholesterol to the active esters. By inhibiting this conversion, cholesterol accumulates in the cells which leads to cell death. Destruction of the adrenal cells is relatively specific and can be complete or partial, depending on the dose used. If only partial destruction of adrenal cortical cells occurs, repeated

### Precautionary Information

**Adverse Reactions and Side Effects**

No adverse effects reported in animals.

**Contraindications and Precautions**

Do not administer to patients sensitive to salicylate compounds.

**Drug Interactions**

No drug interactions have been reported for animals.

### Instructions for Use

Olsalazine is used in patients that cannot tolerate sulfasalazine.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Olsalazine is available in 500-mg tablets.

### Stability and Storage

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

### Small Animal Dosage

- Dosage not established, but 5–10 mg/kg q8h has been used. (The usual human dosage is 500 mg twice daily.)

### Large Animal Dosage

- No doses are reported for large animals.



### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at www.FARAD.org.
Racing Commissioners International (RCI) Classification: 4

## Omeprazole

oh-mep′rah-zole

**Trade and other names:** Prilosec (formerly Losec; human preparation), Zegerid (human formulation), GastroGard, and UlcerGard (equine preparations); outside the United States, Peptizole and Gastrozol are available for horses

**Functional classification:** Antiulcer agent

### Pharmacology and Mechanism of Action

Omeprazole is the most widely used proton pump inhibitor (PPI) in animals. Omeprazole inhibits gastric acid secretion by inhibiting the $K^+/H^+$ pump (potassium pump). Omeprazole is more potent and longer acting than the histamine $H_2$ antagonists and is associated with better efficacy. There are other PPIs, including pantoprazole (Protonix), lansoprazole (Prevacid), and rabeprazole (Aciphex). They all act via similar mechanism and are equally effective. PPIs also have some effect for inhibiting *Helicobacter* organisms in the stomach when administered with antibiotics.

Omeprazole is decomposed in the acid environment of the stomach. Oral absorption is decreased if administered with food. Formulations are designed to protect from degradation by stomach acid, such as by adding a buffering agent or enteric coating, to improve oral absorption. Some human formulations also contain bicarbonate.

An equivalent drug is esomeprazole (Nexium) (see Esomeprazole), which is the S-isomer of omeprazole (the active isomer). It is expected to have equal efficacy at equivalent dosages, but there is some evidence of better efficacy with esomeprazole compared to omeprazole.

*Pharmacokinetics:* When administered orally to horses, maximum serum concentration occurs at 45–60 minutes with effective acid suppression within 1–2 hours. Half-life from oral administration to horses varies from 70 to 100 minutes, depending on the formulation. Pharmacokinetics and acid suppression have also been studied in dogs and cats, with effective acid suppression at the dosages provided in the dosing section.

## Indications and Clinical Uses

Omeprazole, like other PPIs, is used for treatment and prevention of GI ulcers and gastroesophageal reflux. It has been used in dogs, cats, and exotic species, but most efficacy data for animals have been produced in horses, in which it has been shown that omeprazole is effective for treating and preventing gastric ulcers. In foals, 4 mg/kg q24h suppresses acid secretion for 22 hours. By comparison, ranitidine suppresses acid up to 8 hours at a dose of 6.6 mg/kg. In studies performed in horses, omeprazole was more effective than ranitidine for treating gastric ulcers.

For treatment of ulcers in horses, the approved label treatment in the United States is 4 mg/kg PO once per day. However, there is evidence to indicate that a dosage of 1 mg/kg per day is equally effective. For more effective healing of gastric ulcers, consider twice-daily administration instead of once daily.

The equine formulations in the United States (GastroGard and UlcerGard) are buffered formulations. An enteric-coated formulation is available for horses in some countries (Gastrozol). Plasma omeprazole concentrations after single doses are significantly higher with GastroGard than Gastrozol when each is administered at the labeled dose.

These formulations, when combined with environmental changes, promote healing of gastric ulcers in horses. The response to treatment will depend on the type of equine gastric ulcer syndrome being treated. Horses with equine squamous gastric disease (ESGD) respond much more favorably to acid suppression with omeprazole than those with equine glandular gastric disease (EGGD), reflecting the differences in pathogenesis and response between these two distinct forms of equine gastric disease. There was a 25% response rate for EGGD and a 78% response rate for ESGD at a dosage of 4 mg/kg once daily for 28–35 days. Some experts recommend oral omeprazole (4 mg/kg q24h) in combination with oral sucralfate 12 mg/kg q12h) for better healing rates for treating EGGD.

In dogs, 1 mg/kg q24h PO is as effective as pantoprazole (1 mg/kg) and famotidine (0.5 mg/kg q12h) for maintaining stomach pH greater than 3–4, which is the recommended pH range for ulcer healing. Twice-daily administration of omeprazole may be more effective than once daily. Repeated doses may be necessary (two to five doses) for complete inhibition of acid secretion. In dogs and cats, PPIs may be more effective than other drugs (e.g., histamine $H_2$ blockers) because of the long duration of effect.

In cats, the equine formulation and fractionated tablets were equally effective for suppressing acid secretion and were superior to an $H_2$ blocker (famotidine). In

a similar study performed in dogs, omeprazole tablets or equine paste administered once daily provided superior acid suppression compared to famotidine twice daily.

Omeprazole, like other PPIs, may be effective for preventing nonsteroidal anti-inflammatory drug (NSAID)–induced ulcers. Omeprazole has also been used in combination with other drugs (antibiotics) for treatment of *Helicobacter* infections in animals.

## Precautionary Information

### Adverse Reactions and Side Effects

The only reported adverse effect in dogs has been diarrhea in some cases. Otherwise, adverse effects have not been reported in animals. In people, there is concern about hypergastrinemia with chronic use, but this has not been a concern in animals.

Horses have tolerated 20 mg/kg q24h for 91 days and 40 mg/kg q24h PO for 21 days. Dogs and cats also have tolerated the regimens listed in the dosing section. Overgrowth of *Clostridium* bacteria has been a concern from chronic use because of chronic gastric acid suppression, but the clinical importance of this observation in animals has not been established. In people, long-term use of PPIs has been associated with a modest risk of hip fractures because of decreased oral absorption of calcium and increased bone resorption by osteoclasts. This problem has not been reported in animals.

In cats with chronic kidney disease, omeprazole was well tolerated, but treatment increased sodium concentrations. The cause or the significance of this observation is undetermined. Although effects on bone have been a concern in people, when administered for 60 days to cats (1 mg/kg q12h), there was no change in cobalamin, calcium, magnesium, or bone mineral content or density.

### Contraindications and Precautions

One of the human formulations (Zegerid) is a packet to be mixed with water for oral administration. This formulation contains xylitol, which can be toxic to dogs if administered at high doses or with other medications that contain xylitol.

### Drug Interactions

Although omeprazole has not been associated with drug interactions in animals, PPIs may inhibit some drug-metabolizing enzymes (CYP450 enzymes). In people, metabolism of clopidogrel to the active metabolite can be inhibited by omeprazole, but this inhibition was not demonstrated in studies in dogs and has not been studied in horses or cats. Metabolism of other drugs may be inhibited by omeprazole, but this has not been studied in domestic animals.

Because all PPIs decrease stomach acid, do not administer with drugs that depend on stomach acid for absorption (e.g., ketoconazole and itraconazole). In people, there may be an increased risk of intestinal injury when PPIs are administered with NSAIDs, but this has not been studied in animals.

Omeprazole may be administered with sucralfate, which may increase efficacy for some gastric and esophageal diseases. However, in horses and perhaps other animals, the combination is more effective when sucralfate is administered 60–90 minutes after omeprazole.

## Instructions for Use

Omeprazole is the most common drug of this class used in animals. Other PPIs include pantoprazole (Protonix), lansoprazole (Prevacid), rabeprazole (Aciphex), and the S-isomer of omeprazole, esomeprazole. Less experience with these other products

is reported for veterinary medicine. Pantoprazole and rabeprazole have the advantage in that they are available as tablets that can be crushed.

The equine formulations available include GastroGard and UlcerGard, which are buffered formulations to enhance oral absorption. Gastrozol is an enteric-coated formulation for horses available in Australia (see Indications and Clinical Use for comparison). Rectal administration has been studied in horses but has produced low and inconsistent response.

Treatment response varies in horses depending on the type of gastric ulcer syndrome treated. Patients with ESGD respond much more favorably to omeprazole than those with EGGD. In horses, it is recommended that at least 4 weeks of treatment is needed for full healing in addition to other changes in diet and feeding. To achieve the full extent of acid suppression, it is recommended to administer omeprazole to horses 60–90 minutes before feeding so that the peak concentration occurs at the time that the proton pumps in the stomach are maximally activated. This recommendation may also apply to treating other animals, such as dogs and cats. Twice-daily administration produces more consistent acid suppression to maintain the stomach pH above 3–4 than once-daily administration.

Because there are no small animal formulations available, the human forms have been administered to dogs and cats, and the equine formulation has been diluted in oil to 10 and 40 mg/mL (see the Formulations section) for administration to small animals. Studies with the equine formulation compounded in oil have shown that the equine formulation administered orally to dogs can be efficacious.

## Patient Monitoring and Laboratory Tests

Omeprazole and PPIs are generally considered safe. No routine tests for monitoring adverse effects are recommended. If gastrin concentrations are measured, a 7-day withdrawal from omeprazole treatment should be used; otherwise, there is a significant increase in serum gastrin concentrations from omeprazole treatment.

## Formulations

- Human formulations: 20-mg generic capsules. Zegerid is available either as 40- or 20-mg capsules with 1100 mg of sodium bicarbonate. Zegerid is also available either as 40-mg or 20-mg single-dose packets of powder for oral suspension with 1680 mg of sodium bicarbonate.
- Equine paste, GastroGard. The over-the-counter equine paste is UlcerGard. Paste for horses is 370 mg/g of paste in a buffered formulation to prevent degradation in the stomach. Gastrozol is an enteric-coated formulation in a paste for horses available in Australia but is not approved in the United States.

### Compounded Formulations

- Studies using compounded products from non–Food and Drug Administration (FDA) formulations in horses failed to produce therapeutic effects.
- Compounded formulations for dogs and cats have used the approved equine paste. The equine formulation can be diluted in corn oil, cod liver oil, or sesame oil for small animal use because otherwise, it is very concentrated. It has been diluted to 10 and 40 mg/mL by suspending the approved equine oral paste formulation in oil and stored at controlled cold temperature (7°C) and protected from light. The formulation has been stable for 6 months.
- Extemporaneously prepared omeprazole can be prepared from oral capsules. Empty the contents of five 20-mg capsules in 50 mL of 8.4% sodium bicarbonate solution for a final concentration of 2 mg/mL. This solution is stable for up to 14 days at 24°C and for up to 30 days at 5°C and –20°C.
- IV forms of omeprazole have been formulated in sterile water and administered to experimental horses, but these formulations are not commercially available.

## Stability and Storage

Omeprazole should be maintained in the manufacturer's original formulation (capsules or paste) for optimum stability and effectiveness. It is stable at pH 11 but rapidly decomposes at a pH less than 7.8.

## Small Animal Dosage

**Dogs**

- 20 mg per dog q24h PO or 1–2 mg/kg q24h PO. For a more consistent acid-suppressing effect, administer q12h instead of q24h.

**Cats**

- 1 mg/kg q24h PO. For a more consistent acid-suppressing effect, administer q12h instead of q24h.

## Large Animal Dosage

**Horses**

- Treating ulcers: 4 mg/kg once daily for 4 weeks PO. Twice-daily administration may be more effective than once-daily administration for ulcers not responding to once-daily treatment. There is some evidence that 1–2 mg/kg is as effective for treatment as a higher dose.
- Preventing ulcers: 1–2 mg/kg q24h PO. (1 mg/kg was effective for prevention in studies performed in horses.)
- IV use (if a formulation is available): Loading dose of 1 mg/kg followed by 0.5 mg/kg per day for 14–28 days.

**Ruminants**

- Oral absorption may not be high enough for effective therapy.

## Regulatory Information

Not intended for administration to animals that produce food. Oral absorption in ruminants is not established. Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.
RCI Classification: 5



# Ondansetron Hydrochloride

on-dan′sih-tron hye-droe-klor′ide

**Trade and other names:** Zofran

**Functional classification:** Antiemetic

## Pharmacology and Mechanism of Action

Ondansetron is an antiemetic drug from the class of drugs called *serotonin antagonists.* Like other drugs of this class, ondansetron acts by inhibiting serotonin type 3 (5-$HT_3$) receptors. It is effective as an antiemetic during chemotherapy, for which it has been effective by blocking emetic stimuli from the release of serotonin. During chemotherapy or after GI injury, 5-HT is released from the GI tract, which stimulates

## Stability and Storage

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vomiting centrally. This stimulus is blocked by this class of drugs. These drugs also have been used to treat vomiting from gastroenteritis, pancreatitis, and inflammatory bowel disease. The use in dogs and cats is based primarily on anecdotal evidence and recommendations from clinical experts. There have not been well-controlled clinical studies with ondansetron in animals.

*Pharmacokinetics:* Most of ondansetron is metabolized by the liver (95%). In cats, the oral absorption rates were 32% from oral administration and 75% from SQ administration. The half-lives in cats are 1.8 hours from IV administration, 1.2 hours from oral administration, and more prolonged (3.2 hours) from SQ administration. Protein binding in cats is 81%–89%. It is not absorbed from transdermal application in cats. In dogs, it is much less bioavailable (less than 10%) after oral administration and has a shorter half-life of 30 minutes, raising questions about the clinical effectiveness of oral ondansetron in dogs.

Other serotonin antagonists used for antiemetic therapy include granisetron, ondansetron, dolasetron, azasetron, and tropisetron.

## Indications and Clinical Uses

Ondansetron, like other serotonin antagonists, is used to treat nausea and prevent vomiting. It can be effective for various types of vomiting that originate from injury to the GI tract. It is effective to prevent vomiting from drug chemotherapy (cancer drugs and dexmedetomidine). Only limited efficacy information is available for ondansetron's effectiveness in animals, but oncologists have found it to be effective for managing vomiting from chemotherapy in animals. It has been effective in cats at blocking vomiting caused by administration of sedative and anesthetic agents.

## Precautionary Information

### Adverse Reactions and Side Effects

Ondansetron's adverse effects have not been reported in animals. These drugs have little affinity for other 5-HT receptors. Because some severe adverse effects can occur from concurrent cancer drugs, it may be difficult to distinguish these from ondansetron effects.

### Contraindications and Precautions

Ondansetron is eliminated via metabolic pathways and relies less on kidneys for elimination. In cats with liver disease, there was increased exposure and decreased clearance; therefore, ondansetron should be administered less frequently if cats have liver disease. Cats with kidney disease have no significant changes in clearance. Do not administer as a transdermal formulation to cats because it is not absorbed. Oral absorption in dogs is low and may not be effective.

### Drug Interactions

If infused through an IV catheter, it may precipitate if mixed with other drugs (e.g., metoclopramide). Other drug interactions have not been reported for animals.

## Instructions for Use

Based on pharmacokinetic studies with ondansetron, it may be unlikely to maintain effective concentrations at a dosage of 0.5 mg/kg q12h orally or IV, but because of a longer SQ half-life, it may be better suited for administration via this route. In dogs, the oral absorption is low (less than 10%) because of high first-pass metabolism and a short-half-life, which raises questions about effectiveness of oral doses that have been recommended but not tested for efficacy. Granisetron is a similar drug that has been substituted for a similar purpose.

### Patient Monitoring and Laboratory Tests
Monitor GI signs in a vomiting patient.

### Formulations
- Ondansetron is available in 4- and 8-mg tablets, 4-mg/5-mL flavored syrup, and 2-mg/mL injection. Ondansetron is not absorbed in cats when administered as a transdermal formulation.

### Stability and Storage
Store in a tightly sealed container, protected from light, and at room temperature. Ondansetron is soluble in water. Solutions are stable, but pH should be less than 6 to prevent precipitation. Oral preparations have been mixed with syrups, juices, and other oral vehicles (e.g., Ora Sweet). It was stable for 42 days as long as pH remained low.

### Small Animal Dosage
**Dogs**
- During cancer chemotherapy: 0.5–1 mg/kg IV or SQ 30 minutes prior to administration of cancer drugs intravenously.
- Vomiting from other causes: 0.1–0.2 mg/kg slow IV injection and repeated q6–12h. If this dosage is initially ineffective, it may be increased to 0.5 mg/kg.
- Oral administration: Although an oral form is available, oral absorption is low in dogs (less than 10%), which may compromise the effectiveness.

**Cats**
- Cat dosages are similar to those for dogs: 0.5 mg/kg q8h SQ, IV, or PO. A dose of 2 mg per cat is common (half a tablet for the oral formulation), administered q8h. Reduce to twice daily in cats with liver disease.
- Constant-rate infusion (CRI): Administer 0.5 mg/kg IV loading dose followed by 0.5 mg/kg/h IV infusion.

### Large Animal Dosage
- No dosing information is available.

### Regulatory Information
No regulatory information is available. Because of a low risk of residues, no withdrawal times are suggested.

## Orbifloxacin
or-bih-floks′ah sin

**Trade and other names:** Orbax

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action
Orbifloxacin is a fluoroquinolone antimicrobial used primarily in cats but occasionally in dogs. Orbifloxacin acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. It is a bactericidal with a broad spectrum of activity. The antimicrobial spectrum includes staphylococci, gram-negative bacilli, and some *Pseudomonas* species.

### Patient Monitoring and Laboratory Tests
Monitor patient's respiration rate, heart rate, and rhythm during use. If possible, monitor the oxygenation status during anesthesia.

### Formulations
- Pancuronium is available in a 1- and 2-mg/mL injection.

### Stability and Storage
Stable if stored in a tightly sealed container, protected from light, and at room temperature for 24 hours.

### Small Animal Dosage
**Dogs and Cats**
- 0.1 mg/kg IV or start with 0.01 mg/kg and additional 0.01-mg/kg doses every 30 minutes.
- Constant-rate infusion (CRI): 0.1 mg/kg IV followed by a 2-mcg/kg/min infusion.

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

### Regulatory Information
Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.
Racing Commissioners International (RCI) Classification: 2

## Pantoprazole
pan-toe-pray′zole

**Trade and other names:** Protonix

**Functional classification:** Antiulcer agent

P

### Pharmacology and Mechanism of Action
Pantoprazole is a PPI with action similar to another popular drug in this class, omeprazole. Pantoprazole inhibits gastric acid secretion by inhibiting the $K^+/H^+$ pump. Pantoprazole, like other PPIs, has potent and long-acting effects and are more effective than histamine $H_2$-blocking drugs. Acid suppression may have a duration of approximately 24 hours in some animals. Pantoprazole is the first PPI that can be administered IV and is useful for treatment in a hospital setting.

### Indications and Clinical Uses
Pantoprazole is used for treatment and prevention of GI ulcers and gastroesophageal reflux. Other PPIs include omeprazole, esomeprazole, lansoprazole (Prevacid), and rabeprazole (AcipHex). All PPIs act via a similar mechanism and are equally effective. However, there has been more experience with omeprazole in animals than the other drugs of this group. In dogs, pantoprazole (1 mg/kg) maintained a stomach pH greater than 3–4 when administered IV, which is the pH necessary for ulcer prevention and healing. Pantoprazole, being the only one in an IV formulation, is often used when an IV drug is preferred for treatment.

## Precautionary Information

### Adverse Reactions and Side Effects

Side effects have not been reported in animals. However, in people, there is concern about hypergastrinemia with chronic use. This has not been a concern in animals. Overgrowth of *Clostridium* bacteria has been a concern from chronic use because of chronic gastric acid suppression, but the clinical importance of this concern in animals has not been established. In people, the PPI may increase the risk of kidney disease, but this problem has not been reported in animals.

### Contraindications and Precautions

No known contraindications.

### Drug Interactions

Do not mix IV solution with other drugs. Do not administer with drugs that depend on stomach acid for absorption (e.g., ketoconazole, itraconazole, iron supplements). PPIs may inhibit some drug-metabolizing enzymes (CYP450 enzymes), although in people, there was a low risk of drug interactions caused by enzyme inhibition. In people, there may be an increased risk of intestinal injury when PPIs are administered with nonsteroidal anti-inflammatory drugs (NSAIDs), but this has not been studied in animals.

## Instructions for Use

For treating GI ulcers, administer once per day for 7–10 days. For gastrin-secreting tumors, use higher dose (1 mg/kg) twice daily. The primary advantage with pantoprazole compared with other PPIs is that it is available in an IV dosage formulation and can be mixed with fluid solutions. For IV use, mix a 40-mg vial with 10 mL of saline and further dilute with saline, lactated Ringer's solution, or 5% dextrose to 0.4 mg/mL. Administer IV infusion over 2 minutes or 15 minutes. Follow directions below for IV infusion. If administering the enteric-coated oral tablets, do not crush. Oral tablets can be administered with or without food. PPIs may be more effective if administered 30 minutes prior to feeding.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. When treating ulcers, monitor hematocrit or CBC to detect bleeding. Monitor for signs of vomiting and diarrhea.

## Formulations

- Pantoprazole is available as 20- and 40-mg delayed-release tablets. There are also granules for oral suspension (40 mg), which have been mixed with apple juice or applesauce for administration in people.
- Pantoprazole for IV use: Available as a 40-mg vial (diluted to 4 mg/mL). For IV infusion, reconstitute the 40-mg/kg vial with 10 mL of normal saline. Further dilute this solution with 100 mL of 5% dextrose, normal saline, or lactated Ringer's solution to a final concentration of 0.4 mg/mL. To prepare a larger dose (80 mg), reconstitute two vials each with 10 mL of normal saline; combine the content of both vials; and further dilute with 80 mL of 5% dextrose, normal saline, or lactated Ringer's solution to a final concentration of 0.8 mg/mL.
- Pantoprazole compounded oral suspension: To prepare a 2-mg/mL pantoprazole oral suspension, mix pantoprazole tablets with sterile water and sodium bicarbonate powder. Crush 40 tablets in a mortar and reduce to a fine powder. Mix in with 340 mL of sterile water. Next, add 16.8 g of sodium bicarbonate powder and

stir (approximately 20 minutes) until the tablets are fully disintegrated. Then add another 16.8 g of sodium bicarbonate powder and stir again for 5 minutes until all the powder has dissolved. Add enough water to bring the final volume to 400 mL. Transfer the entire contents to an amber-colored bottle and store in a refrigerator. Label with a "shake well" label. This may be stable if stored in refrigerator for 62 days and administered at the doses listed.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Keep tablets at room temperature. Once reconstituted, the vials are stable at room temperature for 6 hours. Do not freeze reconstituted solutions. When further diluted for IV use, it is stable for up to 96 hours at room temperature. The diluted (4-mg/mL) solution may be stored in refrigerator for 28 days. The oral compounded form prepared from tablets (see earlier directions) can be stored in a refrigerator for 62 days.

### Small Animal Dosage

**Dogs and Cats**

- 0.5–0.6 mg/kg, up to 1 mg/kg, twice daily PO.
- IV administration (24 hours): 0.5–1 mg/kg IV infusion over 24 hours. This dose may be delivered in 2 or 15 minutes (see next section).
- IV administration (2 or 15 minutes): First flush the IV line. Administer pantoprazole via an IV line with dextrose 5% injection, sodium chloride 0.9% injection, or Ringer's lactate injection. For the 2-minute infusion, mix 40 mg of powder with 10 mL of sodium chloride 0.9% injection for a final concentration of 4 mg/mL. Infuse a 1-mg/kg dose over 2 minutes. For a 15-minute infusion, mix a 40-mg vial with 10 mL of sodium chloride 0.9% injection. Then further admix this solution with 100 mL of dextrose 5% injection, sodium chloride 0.9% injection, or Ringer's lactate injection to a total volume of 110 mL, producing a solution with a final concentration of approximately 0.4 mg/mL. Administer the final dose (1 mg/kg) over 15 minutes.

### Large Animal Dosage

- No dose is reported for large animals. Doses have been extrapolated from human use (0.5 mg/kg q24h IV), and infusion protocols listed previously for small animals have been used.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.
RCI Classification: 5

## Paregoric

pare-eh-gore′ik

**Trade and other names:** Corrective mixture

**Functional classification:** Antidiarrheal

### Pharmacology and Mechanism of Action

Paregoric (opium tincture) is an old and somewhat outdated product used to treat diarrhea. Paregoric contains 2 mg of morphine in every 5 mL of paregoric. The action is via stimulation of intestinal mu-opiate receptors to cause a decrease in intestinal peristalsis.

# Praziquantel

pray-zih-kwon′tel

**Trade and other names:** Droncit and Drontal (combination with febantel)

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Praziquantel is a popular and widely used antiparasitic drug used for many years to eliminate tapeworms in animals. The action on parasites related to neuromuscular toxicity and paralysis via altered permeability to calcium.

## Indications and Clinical Uses

Praziquantel is widely used to treat intestinal infections caused by cestodes (tapeworms) (*Dipylidium caninum, Taenia pisiformis,* and *Echinococcus granulosus*) and removal and control of canine cestode *Echinococcus multilocularis*. In cats, it is used for removal of feline cestodes *D. caninum* and *Taenia taeniaeformis*. In horses, it is used to treat tapeworms (*Anoplocephala perfoliata*).

Although there are no products approved for treatment of *Spirometra* spp. infections in dogs and cats, praziquantel has been used successfully, but a higher dose is needed (25 mg/kg PO) and administered for 2 consecutive days. Likewise, although no products are approved to treat *Diphyllobothrium* spp. in dogs and cats, praziquantel has been used to treat pseudophyllidean tapeworms. A dosage of 25 mg/kg PO for 2 consecutive days is used. A dose of 35 mg/kg once PO also has been used in cats.

## Precautionary Information

### Adverse Reactions and Side Effects

Vomiting occurs at high doses. Anorexia and transient diarrhea have been reported. It is safe in pregnant animals and during lactation.

### Contraindications and Precautions

Avoid use in cats younger than 6 weeks and dogs younger than 4 weeks. Praziquantel has been safe in pregnancy.

### Drug Interactions

No drug interactions have been reported in animals.

## Instructions for Use

Praziquantel is one of the most common drugs used for tapeworm treatment. It has a wide margin of safety. Some formulations of praziquantel are available in combination (e.g., combination of praziquantel and febantel; combination of ivermectin and praziquantel, moxidectin, and praziquantel).

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Praziquantel is available in 23- and 34-mg tablets and 56.8-mg/mL injection and is also available in pastes and gels.

- In combination, it is available as 13.6 mg of praziquantel and 54.3 mg of pyrantel,18.2 mg of praziquantel and 72.6 of mg pyrantel, or 27.2 mg of praziquantel and 108.6 mg of pyrantel. It is combined with emodepside in Profender.
- Praziquantel is available in pastes and gels for horses in combination with other drugs (e.g., ivermectin, moxidectin, febantel).

### Stability and Storage

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

### Small Animal Dosage

**Dogs**

- Dogs weighing less than 6.8 kg: 7.5 mg/kg once PO.
- Dogs weighing more than 6.8 kg: 5 mg/kg once PO.
- Dogs weighing less than 2.3 kg: 7.5 mg/kg once IM or SQ.
- Dogs weighing more than 2.7–4.5 kg: 6.3 mg/kg once IM or SQ.
- Dogs weighing more than 5 kg: 5 mg/kg once IM or SQ.
- Paragonimus in dogs (lung worms): 23 mg/kg PO q8h for 3 days.
- *Spirometra* spp. and *Diphyllobothrium* spp. treatment: 25 mg/kg PO once daily for 2 consecutive days.

**Cats**

All doses are given once.

- Cats weighing less than 1.8 kg: 11.4 mg/cat PO.
- Cats weighing 1.8–2.2 kg: 11.4 mg/cat SQ or IM.
- Cats weighing 2.3–4.5 kg: 22.7 mg/cat SQ or IM.
- Cats weighing 2.3–5 kg: 23 mg/cat PO.
- Cats weighing more than 5 kg: 34.5 mg/cat PO or 34.1 mg/cat SQ or IM.
- *Spirometra* spp. and *Diphyllobothrium* spp. treatment: 25 mg/kg PO once daily for 2 consecutive days.

### Large Animal Dosage

**Horses**

- 1.5–2.5 mg/kg PO.

### Regulatory Information

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

## Prazosin

pray′zoe-sin

**Trade and other names:** Minipress

**Functional classification:** Vasodilator

### Pharmacology and Mechanism of Action

Prazosin is a nonselective alpha$_1$-adrenergic blocker. Prazosin is a vasodilator that is a selective blocker for the alpha$_1$-adrenergic receptor, but it is not selective

### Instructions for Use
This combination should be used with caution, especially if considered for repeated doses, in animals with intestinal disease. It can produce ileus.

### Patient Monitoring and Laboratory Tests
No specific monitoring is necessary.

### Formulations
- Prochlorperazine edisylate + isopropamide iodide is available in 3.33-mg prochlorperazine and 1.67-mg isopropamide capsules, and prochlorperazine maleate + isopropamide iodide is available in 4 mg of prochlorperazine and 0.28 mg of isopropamide per milliliter injection.
- Capsule for dogs (Neo-Darbazine Spansule Capsule) contains prochlorperazine, isopropamide, and neomycin.

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

### Small Animal Dosage
**Cats**
- 0.14–0.2 mL/kg q12h SQ.

**Dogs**
- 0.14–0.2 mL/kg q12h SQ.
- 2–7 kg body weight: 1 capsule q12h PO.
- 7–13 kg body weight: 1–2 capsules q12h PO.

### Large Animal Dosage
No doses have been reported for large animals. The use is discouraged because isopropamide may decrease GI motility.

### Regulatory Information
Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.
RCI Classification: 2

## Prochlorperazine Edisylate, Prochlorperazine Maleate
proe-klor-pare′ah-zeen ed-iss′ih-late and proe-klor-pare′ah-zeen mal′ee-ate

**Trade and other names:** Compazine

**Functional classification:** Antiemetic, phenothiazine

### Pharmacology and Mechanism of Action
Prochlorperazine is a phenothiazine derivative used primarily as an antiemetic. It is a central-acting dopamine ($D_2$) antagonist that can suppress vomiting at the vomiting center. Prochlorperazine is related to other phenothiazine antiemetic agents such as chlorpromazine, but prochlorperazine has higher antiemetic efficacy than chlorpromazine. Although chlorpromazine and prochlorperazine can block histamine $H_1$ and dopamine $D_2$ receptors, prochlorperazine is 10 times more selective for $D_2$ than histamine $H_1$ receptors. By antagonizing dopamine activity in the CNS, prochlorperazine produces sedation and prevents vomiting. Antiemetic action also may be related to alpha$_2$ and muscarinic blocking effects. There are two salt

formulations of prochlorperazine: prochlorperazine edisylate and prochlorperazine maleate. They are therapeutically equivalent. Other phenothiazines include chlorpromazine, perphenazine, promazine, trifluoperazine, and triflupromazine.

## Indications and Clinical Uses

Prochlorperazine has been used for sedation, for tranquilization, and as an antiemetic. The antiemetic use is the most common. In people, it is also used to treat schizophrenia and nonpsychotic anxiety. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

## Precautionary Information

### Adverse Reactions and Side Effects

Prochlorperazine causes sedation and other side effects attributed to other phenothiazines. It also produces extrapyramidal side effects (involuntary muscle movements) in some individuals. Because of the alpha receptor–blocking properties, it can potentially produce vasodilation and hypotension.

### Contraindications and Precautions

Like other phenothiazines, it may be contraindicated in some CNS disorders. It may lower the seizure threshold in susceptible animals.

### Drug Interactions

Prochlorperazine may potentiate other sedatives.

## Instructions for Use

Prochlorperazine is used primarily as an antiemetic in animals. Clinical trials are not available; doses are based primarily on extrapolation and anecdotal experience.



## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Prochlorperazine is available in 5-, 10-, and 25-mg tablets (prochlorperazine maleate); 1-mg/mL oral solution; and 5-mg/mL injection (prochlorperazine edisylate).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Prochlorperazine is slightly soluble in water and soluble in ethanol. However, the maleate form is more insoluble in water. Prochlorperazine edisylate may be mixed with fluids such as water for injection. Some yellow discoloration may not affect potency. However, if milky-white precipitate forms in the vial, do not use.

## Small Animal Dosage

### Dogs and Cats

- 0.1–0.5 mg/kg q6–8h IM, IV, or SQ.
- 0.5–1 mg/kg q6–8h PO.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

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

### Formulations
- Psyllium is available as powder, usually 3.4 g per teaspoon.

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

### Small Animal Dosage
**Dogs and Cats**
- 1 teaspoon/5–10 kg (added to each meal).

### Large Animal Dosage
**Horses**
- Up to 1000 mg/kg per day PO via stomach tube or added to feed. Note precaution above about administering by a stomach tube in horses. It may form a gel when mixed with water and plug the tube.

### Regulatory Information
No withdrawal times are necessary.

## Pyrantel Pamoate and Pyrantel Tartrate
pye ran′ tel

**Trade and other names:** Nemex, Strongid, Priex, Pyran, and Pyr-A-Pam

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action
Pyrantel is one of the oldest antiparasitic drugs but is still used in animal for common intestinal parasites. Pyrantel is in the class of tetrahydropyrimidines. Others in this class include morantel. Pyrantel acts to interfere with ganglionic neurotransmission via blocking with acetylcholine receptors and other sites. This causes paralysis of the parasites. Paralyzed worms are expelled from the intestinal lumen by peristalsis. Pyrantel is poorly water soluble and not absorbed systemically in ruminants, although some absorption occurs in monogastric animals. Most of the activity is confined to the intestinal lumen.

### Indications and Clinical Uses
Pyrantel is indicated for treatment of intestinal nematodes. In horses, it is used for treatment and prevention of nematodes, including pinworms (*Oxyuris equi*), large roundworms (*Parascaris equorum*), large strongyles (*Strongylus edentatus, Strongylus equinus,* and *Strongylus vulgaris*), and small strongyles. When added to medicated feed, it is used to control nematodes, including pinworms (*O. equi*), large roundworms (*P. equorum*), large strongyles (*S. edentatus, S. vulgaris,* and *Triodontophorus* spp.), and small strongyles. In pigs, it is used for prevention of large roundworm (*Ascaris suum*) and prevention of the nodular worm *Oesophagostomum* spp. In dogs and cats, it is used for treatment of nematodes, including hookworms (*Ancylostoma* spp.) and roundworms (*Toxocara cati, Toxocara canis*, and *Toxascaris leonina)*. There is some evidence that it is effective for control of some tapeworms, but ordinarily other drugs should be used for tapeworms (see Praziquantel).

## Precautionary Information

**Adverse Reactions and Side Effects**

Pyrantel has a good safety record. No adverse effects reported with regular use.

**Contraindications and Precautions**

No contraindications in animals. It may be used in all ages and in lactating and pregnant animals.

**Drug Interactions**

Central nervous system toxicity may be more likely when co-administered with levamisole, but this is not reported from clinical use in animals. It can be safely administered with several other antiparasitic agents.

## Instructions for Use

Shake suspension prior to use. Doses listed are for single dose, but they may be repeated as part of a parasite management program. Lower doses may be added to daily feed for prevention of parasites.

## Patient Monitoring and Laboratory Tests

Monitor fecal samples for presence of intestinal parasites.

## Formulations

- Pyrantel is available in 171-, 180-, and 226-mg/mL (base) paste; 22.7- and 113.5-mg (base) tablets; and 2.27-, 4.54-, and 50-mg/mL (base) suspension. Equine paste is 19.31%. It is also available in 10.6-, 12.6-, and 21.1-g/kg of pellets for medicated feed.
- Pyrantel pamoate is a salt and contains 34.7% pyrantel base. Doses are based on the amount of pyrantel base. Pyrantel tartrate contains 57.9% pyrantel base.
- Many of the formulations contain other antiparasitic drugs (e.g., praziquantel). For example, it is available as 13.6 mg of praziquantel and 54.3 of mg pyrantel, 18.2 mg of praziquantel and 72.6 mg of pyrantel, or 27.2 mg of praziquantel and 108.6 mg of pyrantel. The product Simparica Trio contains sarolaner, moxidectin, and pyrantel in a single chewable tablet for dogs for once per month administration.



## Stability and Storage

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

## Small Animal Dosage

**Dogs**

- 5 mg/kg once PO; repeat in 7–10 days. (Combination products may be dosed on a different schedule [e.g., once per month]. Consult specific labeling for dose intervals.)

**Cats**

- 20 mg/kg once PO.
- Doses may be mixed with food.

## Large Animal Dosage

**Horses**

- Nematodes: 6.6 mg/kg PO.
- Cestodes: 13.2 mg/kg.
- Medicated feed: 12.5 mg/kg as a single dose or 2.6 mg/kg/day for prevention.

**Pigs**

- 22 mg/kg administered in feed as a single treatment.

### Regulatory Information

Pigs: 1-day withdrawal (United States); 7 days (Canada).
Withdrawal times for other species are not established. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.

## Pyridostigmine Bromide

peer-id-oh-stig′meen broe′mide

**Trade and other names:** Mestinon and Regonol

**Functional classification:** Anticholinesterase, antimyasthenic

### Pharmacology and Mechanism of Action

Pyridostigmine is a cholinesterase inhibitor and antimyasthenic drug. This drug inhibits the enzyme that breaks down acetylcholine. Therefore it prolongs the action of acetylcholine at the synapse. The major difference between physostigmine and neostigmine or pyridostigmine is that physostigmine crosses the blood–brain barrier, and the others do not. Compared with neostigmine, pyridostigmine has a longer duration of action.

### Indications and Clinical Uses

Pyridostigmine is used as an antidote for anticholinergic intoxication and treatment (antidote) for neuromuscular blockade. It is also used as a treatment of myasthenia gravis, ileus, and retention of urine (e.g., postoperative ileus and urine retention) by increasing tone of bladder smooth muscle and stimulating bowel motility. The most common regular used for pyridostigmine is the first drug of choice for myasthenia gravis. It is preferred over neostigmine. If animals with myasthenia gravis do not respond to pyridostigmine alone, immunosuppressive agents are added.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are caused by the cholinergic action resulting from inhibition of cholinesterase. These effects can be seen in the GI tract as diarrhea and increased secretions. Other adverse effects can include miosis, bradycardia, muscle twitching or weakness, and constriction of bronchi and ureters. Pyridostigmine may be associated with fewer adverse effects than neostigmine, but the effects of pyridostigmine may persist longer. If adverse effects are observed, treat with anticholinergic drugs, such as 0.125 mg of hyoscyamine sulfate. Atropine also may be used as an antagonist to reverse adverse effects or an overdose.

#### Contraindications and Precautions

Do not use in patients with urinary obstruction, intestinal obstruction, asthma or bronchoconstriction, pneumonia, or cardiac arrhythmias. Do not use in patients sensitive to bromide. Consider the amount of bromide in dose in any patient also receiving bromide for treatment of seizures.

#### Drug Interactions

Bromide concentration in the formulation should be considered for animals also receiving bromide (e.g., potassium bromide) for treatment of epilepsy. (Sodium bromide may be used as an alternative.)

sedation is produced in horses that lasts for approximately 45–60 minutes. Deeper sedation occurs with higher doses. Each dose produced effects for at least 60 minutes, and some are observed for 180 minutes. A duration of 180 minutes is more likely with higher doses.

### Patient Monitoring and Laboratory Tests

Monitor vital signs during anesthesia. Monitor heart rate, blood pressure, and ECG if possible during anesthesia.

### Formulations

- Romifidine is available in a 1% injection (10 mg/mL).

### Stability and Storage

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

### Small Animal Dosage

**Dogs and Cats**

- Doses not established for small animals.

### Large Animal Dosage

**Horses**

- Sedation and analgesia: 40–120 mcg/kg IV. (A dose-dependent degree of sedation is observed.)
- Preanesthetic: 100 mcg/kg IV.

### Regulatory Information

Do not administer in animals intended for food.

## Ronidazole

roe-nid′ah-zole

**Trade and other names:** Generic

**Functional classification:** Antibacterial, antiparasitic

### Pharmacology and Mechanism of Action

Ronidazole is an antibacterial and antiprotozoal drug. It is a nitroimidazole in which the activity involves generation of free nitroradicals via metabolism within protozoa and bacteria. Ronidazole disrupts DNA in an organism via reaction with intracellular metabolites. Its action is specific for anaerobic bacteria and protozoa. Like other nitroimidazoles, it is active against some protozoa, including *Trichomonas* spp., *Giardia* spp., and intestinal protozoal parasites.

*Pharmacokinetics:* After oral administration in cats, it is rapidly and completely absorbed. The half-life in cats is approximately 10 hours.

### Indications and Clinical Uses

Ronidazole is currently not an FDA-approved drug, but it has been used in cats to treat intestinal protozoal parasites. Studies for treatment of other organisms are not available. For treatment of feline *Tritrichomonas foetus* intestinal infections, it has been administered orally at a dosage of 30 mg/kg twice daily for 2 weeks. However, twice-daily administration is more likely to produce CNS adverse reactions, and pharmacokinetic data indicate that 30 mg/kg once daily may be equally effective.

Efficacy for long-term remission has not been established, but temporary resolution of feline *T. foetus* intestinal infections has been observed.

## Precautionary Information

### Adverse Reactions and Side Effects

Like other nitroimidazoles, the most severe adverse effect is caused by toxicity to the CNS. High doses may cause lethargy, CNS depression, ataxia, tremors, hyperesthesia, seizures, vomiting, and weakness. The CNS signs are related to inhibition of action of gamma-aminobutyric acid (GABA) and are responsive to benzodiazepines (diazepam). Dogs show neurotoxicity at doses of 50–200 mg/kg (seizures, tremors, and ataxia). Avoid dosages that exceed 60 mg/kg per day in cats. Like other nitroimidazoles, it has the potential to produce mutagenic changes in cells, but this has not been demonstrated in animals. Like other nitroimidazoles, it has a bitter taste and can cause vomiting and anorexia.

### Contraindications and Precautions

Fetal abnormalities have not been demonstrated in animals with recommended doses, but use cautiously during pregnancy.

### Drug Interactions

Like other nitroimidazoles, it may potentiate the effects of warfarin and cyclosporine via inhibition of drug metabolism.

## Instructions for Use

Ronidazole is currently not a marketed drug but has been prepared from bulk powder in compounding pharmacies.

## Patient Monitoring and Laboratory Tests

Monitor for neurologic adverse effects.

## Formulations

- No available formulation exists; it is compounded from bulk chemicals. IV formulations have been prepared by dissolving ronidazole pure powder in 5% dextrose in water (D5W) to a concentration of 3.2 mg/mL. This formulation has been safely administered to research animals.

## Stability and Storage

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

## Small Animal Dosage

### Dogs

- No dose has been reported.

### Cats

- 30 mg/kg q24h PO for 2 weeks. Early clinical studies were performed with 30 mg/kg q12h, but twice-daily administration is more likely to produce CNS toxicity, and an interval of q24h may be equally effective.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Do not administer to animals that produce food. Administration of nitroimidazoles to animals intended for food is prohibited. Treated cattle must not be slaughtered for food.

the preferred drug for initial treatment. The advantages of succimer over other chelators are that it is better tolerated with fewer GI adverse effects, and it is not associated with nephrotoxicosis. It also does not bind other minerals such as copper, zinc, calcium, and iron.

### Precautionary Information

**Adverse Reactions and Side Effects**

No adverse effects have been reported in dogs. However, kidney injury has been associated with succimer treatment in cats. Succimer should not be used as a phosphate binder in cats. When administered to cats, it did not decrease phosphorous, and caused vomiting and clinical decompensation.

**Contraindications and Precautions**

Do not use in cats with kidney disease. (See Adverse Effects and Side Effects.)

**Drug Interactions**

No drug interactions have been reported in animals.

### Instructions for Use

Doses cited are based on studies in dogs. In cats, succimer has been used at 10 mg/kg q8h PO for 2 weeks. Treatment response and duration of treatment is monitored by measuring the blood levels of the toxin (e.g., lead). A poison control center may be contacted for specific protocols to treat toxicity in animals.

### Patient Monitoring and Laboratory Tests

Monitor the patient's blood lead levels during treatment. Monitor renal function during treatment because renal failure has been associated with succimer administration in cats.

### Formulations

- Succimer is available in 100-mg capsules.

### Stability and Storage

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

### Small Animal Dosage

**Dogs**

- 10 mg/kg q8h PO for 5 days; then 10 mg/kg q12h PO for 2 more weeks. It has also been administered rectally in vomiting dogs.

**Cats**

- 10 mg/kg q8h PO for 2 weeks.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

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

## Sucralfate

soo-krahl′fate

**Trade and other names:** Carafate and Sulcrate (in Canada)

**Functional classification:** Antiulcer agent

## Pharmacology and Mechanism of Action

Sucralfate is a gastric mucosa protectant that has both antiulcer effects and some esophageal protectant effects. Sucralfate dissociates in the stomach to form sucrose octasulfate and aluminum hydroxide. Sucrose octasulfate polymerizes to a viscous, sticky substance that creates a protective effect by binding to ulcerated mucosa in the upper GI tract. It has an affinity for negatively charged injured tissue. It protects the stomach mucosa by preventing back-diffusion of hydrogen ions and inactivates pepsin and adsorbs bile acid. The aluminum hydroxide released from sucralfate acts as a buffering agent to reduce injury to the stomach and esophagus from stomach acid. There is some evidence that sucralfate may act as a cytoprotectant by increasing prostaglandin synthesis in the gastric epithelium. This property may enhance the protective effect of prostaglandins in the mucosa and prevent stomach and esophageal injury.

## Indications and Clinical Uses

Sucralfate is used to prevent and treat gastric ulcers and prevent injury from gastroesophageal reflux. Sucralfate is administered orally and may protect ulcerated tissue and promote healing. There is little evidence that it prevents ulcers from NSAIDs in small animals, but experimental evidence demonstrates protective effects in horses. Prevention of esophageal injury from acid reflux is based on studies in people and laboratory animals. Dosage regimens for sucralfate have been extrapolated from human dosages but have been examined in observational studies in small animals and horses.

## Precautionary Information

### Adverse Reactions and Side Effects

Because sucralfate is not absorbed, it is virtually free of systemic adverse effects. The most common side effect associated with its use in people has been constipation.

### Contraindications and Precautions

No contraindications have been listed for animals. Administration of intact tablets may not be effective (see Instructions for Use).

### Drug Interactions

Sucralfate may decrease absorption of other drugs administered orally via chelation with aluminum (e.g., fluoroquinolones, digoxin, theophylline, and tetracyclines). Administer these other drugs at least 30 minutes to 2 hours before sucralfate.

## Instructions for Use

Dosing recommendations are based largely on empiricism and extrapolation from the human dose. There are no studies to demonstrate clinical efficacy of sucralfate in animals, but some evidence is available from studies in research animals. Sucralfate may be administered concurrently with histamine type 2 inhibitors ($H_2$ blockers) without causing an interaction, but this combination is rarely necessary. There is evidence that when intact sucralfate tablets are administered to animals, they may not undergo dissolution in the stomach and pass through the intestine intact. Therefore it is recommended to crush up tablets and prepare a liquid suspension prior to administration to small animals.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Sucralfate is available in 1-g tablets and a 200-mg/mL oral suspension.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Sucralfate is insoluble in water unless it is exposed to strong acid or alkaline conditions.

The tablets may be crushed and suspended in water to a concentration of 200 mg/mL and stored in the refrigerator for 14 days. Shake this suspension before using.

### Small Animal Dosage

**Dogs**

- 0.5–1 g q8–12h PO.
- If tablets are used in dogs, it is advised to crush up tablets to form a liquid suspension prior to administration.

**Cats**

- 0.25 g (one-fourth tablet) q8–12h PO.

### Large Animal Dosage

**Foals**

- 1 g q8h PO.

### Regulatory Information

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

## Sufentanil Citrate

soo-fen′tah-nil sih′trate

**Trade and other names:** Sufenta

**Functional classification:** Analgesic, opioid

### Pharmacology and Mechanism of Action

Sufentanil is a synthetic opioid agonist related to fentanyl. The action of fentanyl derivatives is via mu-opiate receptor. Sufentanil is 5–7 times more potent than fentanyl, and in some studies, it is as much as 10 times more potent than fentanyl. Doses of 13–20 mcg of sufentanil produce analgesia equal to 10 mg of morphine.

### Indications and Clinical Uses

Sufentanil, like other opiate derivatives, is used for sedation, general anesthesia, and analgesia. It can be used as part of a regimen for balanced general anesthesia. It can be used with other agents or as a primary agent in patients intubated and delivered oxygen. Sufentanil has a rapid onset of effect and rapid recovery. It does not accumulate in tissues; therefore recovery is rapid after an anesthetic procedure. It can also be administered by the epidural route. Compared with other opioids, such as fentanyl, the use of sufentanil has been uncommon in animals. The use is derived from limited clinical observations and extrapolation of the uses from human medicine.



### Precautionary Information

**Adverse Reactions and Side Effects**

Adverse effects are similar to those of morphine. Like all opiates, side effects are predictable and unavoidable. Side effects include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses.

**Contraindications and Precautions**

Use cautiously in animals with respiratory disease. Because of its high potency compared with morphine and other opiates, calculate dose carefully.

**Drug Interactions**

Like other opiates, sufentanil may potentiate other sedatives and anesthetics.

### Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease $T_4$ concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI breakpoint for susceptible organisms is ≤256 mcg/mL, but according to CLSI, susceptibility tests for sulfonamides should only be used to interpret urinary bacteria isolates.

### Formulations

- Sulfadiazine is available in 500-mg tablets. See Trimethoprim–Sulfadiazine for information on those formulations.

### Stability and Storage

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

### Small Animal Dosage

**Dogs and Cats**

- 100 mg/kg IV PO (loading dose) followed by 50 mg/kg q12h IV or PO. In the combination with trimethoprim, it is administered at a dose of 25 mg/kg (see Trimethoprim for more information).

### Large Animal Dosage

- For horses, see dosing for trimethoprim combinations. In the combination, it is administered at a dose of 25 mg/kg.

### Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age. No withdrawal times are established. However, for extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.

## Sulfadimethoxine

sul-fah-dye-meth-oks′een

**Trade and other names:** Albon, Bactrovet, and generic brands

**Functional classification:** Antibacterial



### Pharmacology and Mechanism of Action

Sulfadimethoxine is a sulfonamide antibacterial. Sulfonamides compete with PABA for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic with ormetoprim and used in combination in formulations for small animals. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

### Indications and Clinical Uses

Sulfadimethoxine is used as a broad-spectrum antimicrobial to treat or prevent infections caused by susceptible organisms, usually in livestock. Infections treated may include pneumonia, intestinal infections (especially coccidia), soft tissue infections, and UTIs. It is also approved for treatment of calf diphtheria and foot rot associated with *Fusobacterium necrophorum* susceptible to sulfadimethoxine. However, resistance is common unless combined with ormetoprim (see Primor).

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides include allergic reactions, type II and III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), KCS, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other more toxic metabolites may persist.

### Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed.

### Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides increase the metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde, which may form a complex and precipitate with sulfonamides. When sulfonamides are administered to horses that are receiving detomidine, these horses may develop cardiac arrhythmias. This precaution is only listed for IV forms of trimethoprim–sulfonamides.

## Instructions for Use

Usually, sulfonamides such as sulfadimethoxine are rarely used alone in small animals and horses. There is no clinical evidence that one sulfonamide is more or less toxic or efficacious than another sulfonamide. Sulfadimethoxine has been combined with ormetoprim in Primor.

## Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease $T_4$ concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI breakpoint for susceptible organisms is ≤256 mcg/mL, but according to CLSI, susceptibility tests for sulfonamides should only be used to interpret urinary bacteria isolates.

## Formulations

- Sulfadimethoxine is available in 125-, 250-, and 500-mg tablets; 400-mg/mL injection; and 50-mg/mL suspension.

## Stability and Storage

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

## Small Animal Dosage

**Dogs and Cats**

- 55 mg/kg PO (loading dose) followed by 27.5 mg/kg q12h PO. (For doses of combination with ormetoprim, see Primor.)

## Large Animal Dosage

**Cattle**

- Treatment of pneumonia and other infections: 55 mg/kg as the initial dose followed by 27 mg/kg q24h PO for 5 days.
- Sustained-release bolus (Albon-SR): 137.5 mg/kg PO as a single dose.

### Regulatory Information

Cattle withdrawal time for meat: 7 days.
Cattle withdrawal time for milk: 60 hours.
Withdrawal time for sustained-released bolus: 21 days.
Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age. Currently, sulfadimethoxine is the only sulfonamide with approved indications in dairy cattle.

## Sulfamethazine

sul-fah-meth′ah-zeen

**Trade and other names:** Sulmet and generic brands

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Sulfamethazine is a sulfonamide antibacterial. Sulfonamides compete with PABA for an enzyme that synthesizes dihydrofolic acid in bacteria. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

*Pharmacokinetics:* There have been several pharmacokinetic studies, mostly in food animals and horses. In cattle, the half-life is approximately 3.5–6.5 hours, depending on the study. In pigs, it is longer at 10–16 hours. In horses, the half-life has varied, depending on the study, between 6 and 14 hours.

### Indications and Clinical Uses

Sulfamethazine is used as a broad-spectrum antimicrobial to treat or prevent infections caused by susceptible organisms. Infections treated may include pneumonia, intestinal infections (especially coccidia caused by *Eimeria bovis* and *Eimeria zuernii*), soft tissue infections, calf diptheria, foot rot, and UTIs. However, resistance is common, and this agent should not be considered a first-line agent for these infections.

### Precautionary Information

**Adverse Reactions and Side Effects**

Adverse effects associated with sulfonamides include allergic reactions, type II and III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), KCS, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other more toxic metabolites may persist.

**Contraindications and Precautions**

Do not administer in animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed.

**Drug Interactions**

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde, which may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for IV forms of trimethoprim–sulfonamides.

### Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease $T_4$ concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI breakpoint for sensitive organisms is ≤256 mcg/mL, but according to CLSI, susceptibility tests for sulfonamides should only be used to interpret urinary bacteria isolates.

### Formulations

- Sulfaquinoxaline is available in 34.4-, 128.5-, 192-, 200-, 286.2-, and 340-mg/mL solution. Some formulations have been voluntarily withdrawn by the sponsor.

### Stability and Storage

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

### Small Animal Dosage

- No doses reported for dogs and cats.

### Large Animal Dosage

**Calves**

- 13.2 mg/kg/day PO (usually administered in the drinking water as a 0.015% solution for 5 days).

### Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age.
Cattle withdrawal time: 10 days.
Sheep withdrawal time: 10 days.
Poultry withdrawal time: 10 days.
Rabbit withdrawal time: 10 days.

## Sulfasalazine

sul-fah-sal′ah-zeen

**Trade and other names:** Azulfidine and Salazopyrin (in Canada)

**Functional classification:** Antibacterial, antidiarrheal

### Pharmacology and Mechanism of Action

Sulfasalazine is a sulfonamide combined with an anti-inflammatory drug for oral treatment of intestinal diseases. Sulfasalazine has little effect on its own, and salicylic acid (mesalamine) has anti-inflammatory effects. (See Mesalamine for more details on its use.) When administered as the combination of salicylic acid and the sulfonamide sulfapyridine, the salicylic acid is released by colonic bacteria to produce an anti-inflammatory effect in the intestinal epithelium. The anti-inflammatory effect is believed to be through antiprostaglandin action, antileukotriene activity, or both.

### Indications and Clinical Uses

Sulfasalazine is used in small animals for the treatment of idiopathic colitis and other inflammatory intestinal diseases. It is often used for treatment when dietary therapy has been unsuccessful. Although sulfasalazine has been commonly used in small animals, use in animals has been primarily derived from empirical use and opinions

from gastroenterologist specialists. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. The section on mesalamine has additional information on clinical use.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are attributed to the sulfonamide component. Adverse effects are associated with sulfonamides and include allergic reactions, type II and III hypersensitivity, hypothyroidism (with prolonged therapy), KCS, and skin reactions. KCS has been reported in dogs that received sulfasalazine for chronic treatment. The amount of salicylate absorbed appears to be small in cats; therefore, adverse effects from salicylate in cats are unlikely.

### Contraindications and Precautions

Do not administer to animals that are sensitive to sulfonamides. Drug interactions are possible but have not been reported in animals, probably because low systemic drug concentrations are achieved. Mesalamine can potentially interfere with thiopurine methyltransferase and therefore increase the risk of toxicity from azathioprine.

### Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides increase metabolism of cyclosporine, resulting in decreased plasma concentrations.

## Instructions for Use

Sulfasalazine is usually used for treatment of idiopathic colitis, often in combination with dietary therapy. For animals sensitive to sulfonamides, consider other forms of mesalamine (see Mesalamine for more details).

## Patient Monitoring and Laboratory Tests

Monitor tear production in dogs that receive chronic therapy.

## Formulations

- Sulfasalazine is available in 500-mg tablets and has been compounded as an oral suspension for smaller animals.



## Stability and Storage

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

## Small Animal Dosage

### Dogs

- 10–30 mg/kg q8–12h PO.

### Cats

- 20 mg/kg q12h PO.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age.
RCI Classification: 4

# Xylazine Hydrochloride

zye′lah-zeen hye-droe-klor′ide

**Trade and other names:** Rompun and generic brands

**Functional classification:** Alpha$_2$-adrenergic agonist, analgesic, sedative

## Pharmacology and Mechanism of Action

Xylazine is the oldest alpha$_2$-adrenergic agonists used in veterinary medicine. Alpha$_2$ agonists decrease release of neurotransmitters from the neuron. They decrease transmission via binding to presynaptic alpha$_2$ receptors (negative-feedback receptors). The results are decreased sympathetic outflow, analgesia, sedation, and anesthesia. Other drugs in this class include medetomidine, dexmedetomidine, romifidine, detomidine, and clonidine. Xylazine is not as specific as other drugs in this group. The alpha$_2$-specific effects are measured by comparing the alpha$_1$/alpha$_2$-receptor affinity ratio. The ratios are 1:160 for xylazine, 1:260 for detomidine; 1:360 for romifidine, and 1:1620 for dexmedetomidine (medetomidine). Thus, receptor-binding studies indicate that xylazine is the least specific of this class.

*Pharmacokinetics:* The pharmacokinetics have been studied in all domestic species. The pharmacokinetics are characterized by rapid (within minutes) distribution to the central nervous system and elimination half-life of 20–40 minutes from a bolus injection. In horses, after a constant rate infusion (CRI), the terminal half-life is approximately 2 hours.

## Indications and Clinical Uses

Xylazine has been used for many years for short-term sedation, anesthesia, and analgesia in horses, dogs, cats, cattle, and exotic animals. Like other alpha$_2$ agonists, it is used as an anesthetic adjunct and analgesic. The duration of effect is approximately 30 minutes after a bolus injection, but it also may be administered by a CRI for up to 6 hours. Compared with xylazine, dexmedetomidine and medetomidine produce better sedation and analgesia in dogs. Xylazine is used more commonly in large animals for sedation and analgesia than in small animals. Usually, dexmedetomidine is preferred in dogs and cats. Romifidine produces the longest duration of sedative effects followed by detomidine, medetomidine (dexmedetomidine), and xylazine.

## Precautionary Information

### Adverse Reactions and Side Effects

In small animals, vomiting is the most common acute effect, which is more prominent in cats than dogs. Xylazine produces sedation and ataxia, which is expected from all alpha$_2$ agonists. Xylazine, like other alpha$_2$ agonists, decreases sympathetic output. Cardiovascular depression may occur. Xylazine produces an initial hypertensive phase, followed by a hypotensive phase. Cardiac effects can include sinoatrial block, first- and second-degree atrioventricular block, bradycardia, and sinus arrhythmia. Like other alpha$_2$ agonists, xylazine produces transient hyperglycemia, which may increase urine flow.

In ruminants, use of xylazine may decrease gastrointestinal motility and cause bloating, salivation, and regurgitation. Note that cattle, sheep, and goats are much more sensitive to xylazine than other animals; therefore doses need to be lower than those in other animals. Among horses, draft horses are more sensitive to the effects than thoroughbred and Arab horses.

**Contraindications and Precautions**

Ruminants are much more sensitive to xylazine than other species, and lower doses must be used compared with other animals. Use cautiously in animals that are pregnant. Xylazine impairs blood flow to the uterus during gestation in cows and may decrease oxygen delivery to the fetus, especially in late gestation. Use caution when using xylazine to sedate pregnant cows. It also may induce labor. Use cautiously, if at all, in patients with cardiac disease. Because of cardiac depression, it should not ordinarily be used with tranquilizers such as phenothiazines that can produce vasodilation.

**Drug Interactions**

Use with opioid analgesic drugs greatly enhances the central nervous system depression. Consider lowering doses if administered with opioids. Do not administer with other drugs that cause significant cardiac depression.

## Instructions for Use

Xylazine is often used in combination with other drugs (e.g., ketamine, opioids, or butorphanol). It is combined with guaifenesin and ketamine in the equine "triple drip" combination (see dosing section, below).

Although low heart rates are anticipated with xylazine, it is not necessary to premedicate animals with atropine. For large animals, if sedation is needed without recumbency, use the lower end of the dose range. Reverse effects of xylazine with an alpha$_2$ antagonist (e.g., yohimbine, tolazoline, or atipamezole) if adverse effects are serious enough to warrant reversal. Xylazine also may be administered intraosseously to horses when it is not possible to give an IV injection. It is equally bioavailable from the intraosseous route as IV.

## Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during anesthesia with xylazine. It may cause increased plasma glucose concentrations in animals.

## Formulations Available

- Xylazine is available in 20- and 100-mg/mL injections.

## Stability and Storage

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

## Small Animal Dosage

**Dogs**

- 1.1 mg/kg IV.
- 2.2 mg/kg IM.
- Short-term treatment of pain: 0.1–0.5 mg/kg IM, IV, or SQ.

**Cats**

- 1.1 mg/kg IM.
- Emetic dosage: 0.4–0.5 mg/kg IM or IV.
- Short-term treatment of pain: 0.1–0.5 mg/kg IM, IV, or SQ.

## Large Animal Dosage

**Horses**

- 1–2 mg/kg IM.
- Standing chemical restraint: 0.5–1.0 mg/kg IV bolus. (The IV dose also can be administered intraosseously with equal bioavailability.)

- 0.5–1.1 mg/kg IV followed by (if necessary) a 0.72–1 mg/kg/h CRI.
- For colic pain: 0.3–0.5 mg/kg IV (150–250 mg IV for an average-size horse).
- For anesthesia purposes, it is sometimes combined with other agents such as ketamine and guaifenesin in the equine "triple-drip" combination. This combination consists of 500 mg of xylazine and 2 g of ketamine added to 1 L of 5% of guaifenesin in dextrose. It is administered at a rate of 1.1 mL/kg for induction followed by 2–4 mL/kg/h for maintenance. Recovery usually occurs in 25–30 minutes or administer 0.125 mg/kg yohimbine to speed up recovery.

**Pigs**

- 0.5–3 mg/kg IM. Xylazine in pigs is best used in combination with other drugs (e.g., 2 mg/kg xylazine mixed in a syringe with 10 mg/kg of ketamine). It is unreliable used alone.

**Cattle**

- 0.1–0.2 mg/kg IM.
- 0.03–0.1 mg/kg IV.

**Sheep**

- 0.1–0.3 mg/kg IM.
- 0.05–0.1 mg/kg IV.

**Goats**

- 0.05–0.5 mg/kg IM.
- 0.01–0.5 mg/kg IV.

## Regulatory Information

Withdrawal time for cattle: At a dosage of 0.016–0.1 mg/kg, 5 days for meat and 72 hours for milk. At a dosage of 0.05–0.3 mg/kg, 10 days for meat and 120 hours for milk. Whereas in Canada, it is listed as 3 days for meat and 48 hours for milk, in the United Kingdom, it is listed as 14 days for meat and 48 hours for milk. If yohimbine is used as a reversal agent, use a withdrawal time of 7 days for meat and 72 hours for milk.

Racing Commissioners International Classification: 3