Drug Interactions
The following drug interaction has either been reported or are theoretical in humans or animals receiving olsalazine and may be of significance in veterinary patients:

- **WARFARIN**: Olsalazine may increase prothrombin times in patients receiving warfarin

Laboratory Considerations
- Olsalazine may cause increases in **ALT** or **AST**

Doses
- **DOGS:**
  a) For dogs who cannot tolerate sulfasalazine: 10–20 mg/kg PO three times daily (Leib 2000)
  b) When response is poor to initial sulfasalazine therapy: 11 mg/kg PO twice daily (Tams 2000)
  c) 10–15 mg/kg PO q8–12h (Hall 2004)
  d) Initially at 5–10 mg/kg PO three times daily, then reduce gradually. (Allensbach 2005)

Monitoring
- Clinical efficacy
- Adverse effects

Client Information
- Should be given with food in evenly spaced doses (if possible)
- If diarrhea worsens or dogs eyes become dry, contact veterinarian

Chemistry/Synonyms
Olsalazine sodium occurs as a yellow crystalline powder that is soluble in water and stable under physiologic acidic and alkaline conditions. It is basically 2 molecules of mesalamine (5-ASA) connected at the azo bonding site.

Olsalazine sodium may also be known as: azodisal sodium, dimesalamine, CI mordant yellow 5, CI No. 14130, CJ-91B, olsalazinum natricum, sodium azodisalicylate, *Dipentum*® or *Rasal*®.

Storage/Stability
Store capsules at room temperature.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

The ARCI (Racing Commissioners International) has designated this drug as a class 4 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Olsalazine Sodium Capsules: 250 mg; *Dipentum*® (Celltech); (Rx)

OMEPRAZOLE

(oh-*meh*-prah-zahl) Gastrogard®, Prilosec®

PROTON PUMP INHIBITOR

Prescriber Highlights
- Proton pump inhibitor used for GI ulcers & erosions
- Contraindications: Known hypersensitivity; may need to adjust dosage with hepatic or renal disease
- Adverse Effects: HORSES: Unlikely; potential hypersensitivity. SMALL ANIMALS: Appears to be well tolerated. Potentially: GI distress (anorexia, colic, nausea, vomiting, flatulence, diarrhea), hematologic abnormalities, urinary tract infections, proteinuria, or CNS disturbances
- Treatment is relatively expensive, but human generics are now available & costs are decreasing for small animals

Uses/Indications
Omeprazole is potentially useful in treating both gastroduodenal ulcer disease and to prevent or treat gastric erosions caused by ulcerogenic drugs (*e.g.*, aspirin). An oral paste product is labeled for the treatment and prevention of recurrence of gastric ulcers in horses.

Pharmacology/Actions
Omeprazole is a substituted benzimidazole gastric acid (proton) pump inhibitor. In an acidic environment, omeprazole is activated to a sulphenamide derivative that binds irreversibly at the secretory surface of parietal cells to the enzyme, H^+/K^+ ATPase. There it inhibits the transport of hydrogen ions into the stomach. Omeprazole reduces acid secretion during both basal and stimulated conditions. Omeprazole also inhibits the hepatic cytochrome P-450 mixed function oxidase system (see Drug Interactions below).

Pharmacokinetics
Omeprazole is rapidly absorbed from the gut; the human commercial product is in an enteric-coated granule form as the drug is rapidly degraded by acid. The equine paste is not enteric coated. In humans, peak serum levels occur within 0.5–3.5 hours and onset of action within 1 hour. Omeprazole is distributed widely, but primarily in gastric parietal cells. In humans, approximately 95% is bound to albumin and alpha$_1$-acid glycoprotein. It is unknown whether omeprazole enters maternal milk.

Omeprazole is extensively metabolized in the liver to at least six different metabolites. These are excreted principally in the urine, but also via the bile into feces. Significant hepatic dysfunction will reduce the first pass effect of the drug. In humans and dogs with normal hepatic function, serum half-life averages about 1 hour, but the duration of therapeutic effect may persist for 24–72 hours or more. Effects on acid production in horses can last up to 27 hours, depending upon dose.

Contraindications/Precautions/Warnings
Omeprazole is contraindicated in patients hypersensitive to it. In patients with hepatic or renal disease, the drug's half–life may be prolonged and dosage adjustment may be necessary if the disease is severe.

Adverse Effects

The manufacturer does not note any adverse effects for use in horses at labeled dosages. There is an anecdotal case report of one horse developing urticaria after receiving omeprazole. The drug appears to be quite well tolerated in both dogs and cats at effective dosages. Potentially, GI distress (anorexia, colic, nausea, vomiting, flatulence, diarrhea) could occur, as well as hematologic abnormalities (rare in humans), urinary tract infections, proteinuria, or CNS disturbances. Chronic very high doses in rats caused enterochromaffin-like cell hyperplasia and gastric carcinoid tumors; effects occurred in dose related manner. The clinical significance of these findings for long-term low-dose clinical usage is not known, however, at the current time in humans, dosing for longer than 8 weeks is rarely recommended unless the benefits of therapy outweigh the potential risks. In dogs, omeprazole use is believed safe for at least 4 weeks of therapy. Treatment of horses for up to 90 days is believed safe.

Reproductive/Nursing Safety

Omeprazole's safety during pregnancy has not been established, but a study done in rats at doses of up to 345 times those recommended did not demonstrate any teratogenic effects; however, increased embryo–lethality has been noted in lab animals at very high dosages. In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.*)

It is not known whether these agents are excreted in maternal milk. In rats, omeprazole administration during late gestation and lactation at doses of 35–345 times the human dose resulted in decreased weight gain in pups. In humans, because of the potential for serious adverse reactions in nursing infants, and the potential for tumorigenicity shown in rat carcinogenicity studies, nursing is discouraged if the drug is required.

Overdosage/Acute Toxicity

The LD_{50} in rats after oral administration is reportedly >4 g/kg. Humans have tolerated oral dosages of 360 mg/day without significant toxicity. Should a massive overdose occur, treat symptomatically and supportively.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving omeprazole and may be of significance in veterinary patients:

- **BENZODIAZEPINES**: Omeprazole may potentially alter benzodiazepine metabolism and prolong CNS effects
- **CLARITHROMYCIN**: Increased levels of omeprazole, clarithromycin and 14-hydroxyclarithromycin are possible
- **CYANOCOBALAMIN** (**oral**): Omeprazole may decrease oral absorption
- **CYCLOSPORINE**: Omeprazole may reduce cyclosporine metabolism
- **DRUGS REQUIRING DECREASED GASTRIC PH FOR OPTIMAL ABSORPTION** (*e.g.*, **ketoconazole, itraconazole, iron, ampicillin esters**): Omeprazole may decrease drug absorption
- **SUCRALFATE**: May decrease bioavailability of orally administered omeprazole
- **WARFARIN**: Omeprazole may increase anticoagulant effect

Laboratory Considerations

- Omeprazole may cause increased **liver enzymes**
- Omeprazole will increase **serum gastrin** levels early in therapy

Doses

Dose dependent on formulation, equine paste and human oral forms may not be interchangeable. Be wary of compounded formulations; bioequivalence is not assured.

- **DOGS:**

  For ulcer management:

  a) 0.5–1 mg/kg PO once daily (Davenport 1992); (Haskins 2000)

  b) For adjunctive treatment of uremic gastropathy: 0.5–1 mg/kg PO q24h; dosage may need to be modified in moderate or severe renal failure. (Vaden 2007)

  c) For severe ulceration unresponsive to H_2 blockers; severe esophagitis unresponsive to metoclopramide and H_2 blockers; gastrinoma (Zollinger-Ellison syndrome): 0.75–1 mg/kg PO once daily (q24h) –OR– one 20 mg capsule for animals >20 kg, 10 mg (1/2 capsule) for animals weighing >5 kg but <20 kg, 5 mg (1/4 capsule for animals weighing <5 kg. When using less than a full capsule, repackage granules in a gelatin capsule to avoid gastric acid degradation. (Johnson, Sherding et al. 1994)

  d) 0.7 mg/kg (>20 kg, 20 mg/dog; <20 kg, 10 mg/dog) PO once daily (Matz 1995)

  e) For adjunctive treatment of esophagitis or gastric ulcers: 0.5–1 mg/kg PO q24h (Sellon 2007a), (Sellon 2007b)

  f) For some animals with gastrinomas or esophagitis (often H-2 receptor antagonists are adequate): 0.7–1.5 mg/kg PO q24h, but if severe esophagitis or gastrinomas may use up to 2 mg/kg PO q12h (Willard 2006d)

  g) For eliminating Helicobacter gastritis infections: Using triple therapy: Metronidazole 33 mg/kg once daily, amoxicillin 11 mg/kg q12h and either sucralfate (0.25–0.5 grams q8h) or **omeprazole** 0.66 mg/kg once daily (Hall 2000)

- **CATS:**

  For ulcer management:

  a) 0.7 mg/kg PO once a day (Johnson 1996)

  b) 0.7–1.5 mg/kg PO q12–24h (Willard 2003b)

  c) For adjunctive treatment of esophagitis or gastric ulcers: 0.5–1 mg/kg PO q24h (Sellon 2007a), (Sellon 2007b)

  d) For adjunctive treatment of uremic gastropathy: 0.7 mg/kg PO q24h; dosage may need to be modified in moderate or severe renal failure. (Vaden 2007)

- **HORSES:** (**Note:** ARCI UCGFS Class 5 Drug)

  For gastric ulcers:

  a) For treatment of gastric ulcers: 4 mg/kg PO once daily for 4 weeks; to prevent recurrence treat for at least another 4 weeks at 2 mg/kg PO once daily (Label Directions; *Gastrogard*®)

  b) 4 mg/kg PO once daily for treatment; 2 mg/kg PO once daily to prevent recurrence in Thoroughbreds in race training (Andrews and Nadeau 1999)

  c) For treatment or prophylaxis of gastric ulcers in foals: 4 mg/kg PO once daily for treatment, 1–2 mg/kg PO once daily for prophylaxis (Wilkins 2004b)

- **SWINE:**

  For ulcer management:

  a) 40 mg of PO daily for two days; fasted for 48 hours (DeMint 1999)

Monitoring

- Efficacy
- Adverse effects

Client Information
- Give before meals, preferably in the morning

Chemistry/Synonyms
A substituted benzimidazole proton pump inhibitor, omeprazole has a molecular weight of 345.4 and pK_a's of 4 and 8.8.

Omeprazole may also be known as: H-168/68, or omeprazolum, *Gastrogard®*, *Prilosec®*, *Ulcergard®* and *Zegerid®*.

Storage/Stability
Omeprazole oral paste should be stored below 86°F. Transient exposure to temperatures up to 104°F is permitted. Omeprazole tablets should be stored at room temperature in light-resistant, tight containers. Omeprazole pellets found in the capsules are fragile and should not be crushed. If needed to administer as a slurry, it has been suggested to mix the pellets carefully with fruit juices, not water, milk or saline.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS:

Omeprazole Oral Paste, 2.28g per syringe; *Gastrogard®* (Merial), (Rx); *Ulcergard®* (Merial), (OTC)

The ARCI (Racing Commissioners International) has designated this drug as a class 5 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Omeprazole Oral Delayed-Release Capsules: 10 mg, 20 mg (tablets & capsules) & 40 mg; *Prilosec®* (AstraZeneca); *Prilosec® OTC* (*Losec®* in Canada) (*Procter & Gamble*); generic; (Rx & OTC)

Omeprazole/Sodium Bicarbonate Oral Capsules (Immediate Release): 20 mg omeprazole/1,100 mg sodium bicarbonate; 40 mg omeprazole/1,100 mg sodium bicarbonate; *Zegerid®* (Santarus); (Rx)

Omeprazole/Sodium Bicarbonate Powder for Oral Suspension: 20 mg omeprazole/1,680 sodium bicarbonate; 40 mg omeprazole/1,680 sodium bicarbonate; in 30 unit-dose packets; *Zegerid®* (Santarus); (Rx)

ONDANSETRON HCL

(on-***dan***-sah-tron) Zofran®

5-HT_3 RECEPTOR ANTAGONIST

Prescriber Highlights
- 5-HT_3 receptor antagonist for severe vomiting
- Appears to be well tolerated in dogs
- Generic dosage forms now available

Uses/Indications
Used as an antiemetic when conventional antiemetics are ineffective, such as when administering cisplatin or for other causes of intractable vomiting. The use of ondansetron in cats is somewhat controversial and some state it should not be used in this species.

Pharmacology/Actions
Ondansetron is a 5-HT_3 (serotonin type 3) receptor antagonist. 5-HT_3 receptors are found peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone (CTZ). It is not clear if ondansetron's effects are mediated centrally, peripherally or both.

Pharmacokinetics
No veterinary species data was located for ondansetron pharmacokinetics. In humans, ondansetron is well absorbed from the GI tract, but exhibits some first pass hepatic metabolism. Bioavailability is about 50–60%. Peak plasma levels occur about 2 hours after an oral dose. Ondansetron is extensively metabolized in the liver. Elimination half-lives are about 3–4 hours, but are prolonged in elderly patients.

Contraindications/Precautions/Warnings
Ondansetron is contraindicated in patients hypersensitive to it or other agents in this class. Ondansetron may mask ileus or gastric distention; it should not be used in place of nasogastric suction. Use with caution in patients with hepatic dysfunction as half-life may be prolonged.

Because ondansetron is potentially a neurotoxic substrate of P-glycoprotein, it should be used with caution in those herding breeds (*e.g.*, Collies, Shelties, Australian shepherds, etc.) that may have the gene mutation that causes a nonfunctional protein.

Adverse Effects
Ondansetron appears to be well tolerated. Constipation, extrapyramidal clinical signs, arrhythmias and hypotension are possible (incidence in humans <10%).

Reproductive/Nursing Safety
Safety in pregnancy not clearly established, but high dose studies in rodents did not demonstrate overt fetal toxicity or teratogenicity. In humans, the FDA categorizes this drug as category ***B*** for use during pregnancy (*Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*)

Ondansetron is excreted in the maternal milk of rats. Exercise caution when 5-HT_3 antagonists are administered to nursing patients.

Overdosage/Acute Toxicity
Overdoses of up to 10X did not cause significant morbidity in human subjects. If an overdose occurs, treat supportively.

Drug Interactions/Laboratory Considerations
None reported

Doses
- **DOGS:**
  a) As an antiemetic for adjunctive treatment of pancreatitis: 0.1–0.2 mg/kg IV slowly (Webb 2007a)
  b) As an antiemetic when conventional antiemetics are ineffective: 0.1–1 mg/kg PO q12–24h, or 30 minutes prior to and 90 minutes after starting cisplatin infusion (Frimberger 2000)
  c) For intractable vomiting associated with Parvo enteritis: 0.11–0.176 mg/kg IV given as a slow IV push every 6–12 hours (based on patient response) (Tams 2003d)
  d) As an antiemetic: 0.1–0.2 mg/kg IV q6–12h or 0.1–1 mg/kg PO q12–24h (Otto 2005)
  e) As an antiemetic for adjunctive treatment of uremia: 0.6–1 mg/kg PO or IV q12h; usually combined with metoclopramide. (Polzin 2005a)