Contraindications/Precautions/Warnings

Famciclovir is contraindicated in patients known to be hypersensitive to it or penciclovir.

It should be used with caution (and dosage adjustment) in patients with renal dysfunction. In humans patients with CrCl <40 mL/min, dosage adjustments are recommended.

Adverse Effects

Adverse effects in cats are not well documented, but the drug appears to be tolerated quite well when used for up to 3 weeks.

In humans, famciclovir can cause nausea, vomiting, diarrhea, and headache. Neutropenia has been reported and renal failure can occur, particularly when doses are not adjusted in patients with renal dysfunction.

Reproductive/Nursing Safety

In laboratory animals, doses of up to 1,000 mg/kg/day did not cause any observed effects on developing embryos or fetuses. In humans, the FDA categorizes this drug as category \boldsymbol{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.)

Famciclovir (as penciclovir) is excreted in the milk of rats. It is unclear if there is any clinical significance for nursing offspring.

Overdosage/Acute Toxicity

Little information is available. Supportive treatment has been recommended. Penciclovir can be removed by hemodialysis.

Drug Interactions

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

■ PROBENECID: Can reduce the amount of penciclovir excreted by the kidneys, increase penciclovir plasma levels can occur

Laboratory Considerations

No concerns noted

Doses

■ CATS:

For feline herpes virus (FHV-1):

- a) For adjunctive treatment of FHV-1 rhinotracheitis: 31.25 mg (¼ of one 125 mg tablet) PO q12h for 14 days. Has not been evaluated for long-term therapy. (Lappin 2007)
- b) For chronic, recurrent and/or severe herpes viral infection: Dose range is variable! Kittens: ¼th of one 125 mg tablet PO once daily (q24h) for 2 weeks; adult cats: ¼ of one 250 mg tablet once daily (q24h) for 3 weeks. (Diehl 2007b)
- c) ¼ of one 125 mg tablet PO twice daily (q12h) for 10–14 days; may continue once daily for up to 30 days. (Ramsey 2006)
- d) For adjunctive treatment (with interferon and lysine) of herpes virus-associated ulcerative facial dermatitis & stomatitis: 125 mg PO q12h. (Hillier 2006c)

Monitoring

- **■** Clinical efficacy
- Adverse effects (most likely GI)
- Consider occasional CBC's and creatinine to monitor for neutropenia or renal dysfunction if using the drug chronically

Client Information

- May be administered with food
- There is limited experience with this drug in cats, report any unusual effects to the veterinarian

Chemistry/Synonyms

A prodrug, famciclovir is a purine-derived, synthetic, acyclic purine nucleoside analog.

Famciclovir may also be known as AV 42810, BRL 42810, famciclovirum, or by the trade name *Famvir*[®].

Storage/Stability

Famciclovir tablets should be stored at room temperature (15–30°C).

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Famciclovir Tablets (film-coated) 125 mg, 250 mg, & 500 mg: Fam-vir® (Novartis); generic; (Rx)

FAMOTIDINE

(fa-moe-ti-deen) Pepcid®

H2-RECEPTOR ANTAGONIST

Prescriber Highlights

- ▶ H₂-receptor antagonist used to reduce GI acid production
- ▶ Longer duration of action & fewer drug interactions than cimetidine
- ▶ Contraindications: Hypersensitivity to H2 blockers
- Caution: Patients with cardiac disease, significantly impaired hepatic or renal function; (consider dosage reduction)
- Adverse Effects: Too rapid IV infusion may cause bradycardia. Potentially: GI effects, headache, or dry mouth or skin, intravascular hemolysis when given IV to cats

Uses/Indications

In veterinary medicine, famotidine may be useful for the treatment and/or prophylaxis of gastric, abomasal and duodenal ulcers, uremic gastritis, stress-related or drug-induced erosive gastritis, esophagitis, duodenal gastric reflux, and esophageal reflux.

Famotidine has fewer drug interactions and activity may persist longer than cimetidine.

Pharmacology/Actions

At the H₂ receptors of the parietal cells, famotidine competitively inhibits histamine, thereby reducing gastric acid output both during basal conditions and when stimulated by food, pentagastrin, histamine or insulin. Gastric emptying time, pancreatic or biliary secretion, and lower esophageal pressures are not altered by famotidine. By decreasing the amount of gastric juice produced, H₂-blockers also decreases the amount of pepsin secreted.

Pharmacokinetics

Famotidine is not completely absorbed after oral administration, but undergoes only minimal first-pass metabolism. In humans, systemic bioavailability is about 40-50%. Distribution characteristics are not well described. In rats, the drug concentrates in the liver,

pancreas, kidney and submandibular gland. Only about 15–20% is bound to plasma proteins. In rats, the drug does not cross the blood brain barrier or the placenta. It is distributed into milk. When the drug is administered orally, about ½ is excreted unchanged in the urine and the remainder primarily metabolized in the liver and then excreted in the urine. After intravenous dosing, about 2/3's of a dose is excreted unchanged.

The pharmacokinetics of famotidine, ranitidine, and cimetidine have been investigated in horses. (Duran and Ravis 1993) After a single IV dosage, elimination half-lives of cimetidine, ranitidine, and famotidine all were in the 2–3 hour range and were not significantly different. Of the three drugs tested, famotidine had a larger volume of distribution (4.28 L/kg) than either cimetidine (1.14 L/kg) or ranitidine (2.04 L/kg). Bioavailability of each of the drugs was low; famotidine (13%), ranitidine (13.5%) and cimetidine (30%).

Contraindications/Precautions/Warnings

Famotidine is contraindicated in patients with known hypersensitivity to the drug.

Famotidine should be used cautiously in geriatric patients and patients with significantly impaired hepatic or renal function. Consider dosage reduction in patients with significant renal dysfunction. Famotidine may have negative inotropic effects and have some cardioarrhythmogenic properties. Use with caution in patients with cardiac disease.

Adverse Effects

Too rapid IV infusion may cause bradycardia. Other H_2 -blockers have been demonstrated to be relatively safe and exhibit minimal adverse effects. Potential adverse effects (documented in humans) that could be seen include GI effects (anorexia, vomiting, diarrhea), headache, or dry mouth or skin. Rarely, agranulocytosis may develop particularly when used concomitantly with other drugs that can cause bone marrow depression.

While some clinicians routinely use famotidine intravenously in cats, there have been anecdotal reports of famotidine causing intravascular hemolysis when given intravenously to cats. It is believed this is probably an idiosyncratic reaction that occurs in a small percentage of cats treated.

Reproductive/Nursing Safety

In lab animal studies, famotidine demonstrated no detectable harm to offspring. Large doses could affect the mother's food intake and weight gain during pregnancy that could indirectly be harmful. Use in pregnancy when potential benefits outweigh the risks. In rats, nursing from mothers receiving very high doses of famotidine, transient decreases in weight gain occurred. In humans, the FDA categorizes this drug as category \boldsymbol{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.)

Famotidine is excreted in the milk of rats. It is unclear if there is any clinical significance for nursing offspring with H₂-blockers in milk.

Overdosage/Acute Toxicity

The minimum acute lethal dose in dogs is reported to be >2 grams/kg for oral doses and approximately 300 mg/kg for intravenous doses. IV doses in dogs ranging from 5–200 mg/kg IV caused: vomiting, restlessness, mucous membrane pallor and redness of the mouth and ears. Higher doses caused hypotension, tachycardia and collapse.

Because of this wide margin of safety associated with the drug,

most overdoses should require only monitoring. In massive oral overdoses, gut-emptying protocols should be considered and supportive therapy initiated when warranted.

Drug Interactions

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

- AZOLE ANTIFUNGALS (ketoconazole, itraconazole, fluconazole): By raising gastric pH, famotidine may decrease the absorption of these agents; if both drugs are required, administer the azole one hour prior to famotidine
- **CEFPODOXIME, CEFUROXIME:** Famotidine may decrease the absorption of these cephalosporins; taking with food may alleviate this effect
- **IRON SALTS** (**ORAL**): Famotidine may decrease the absorption of oral iron; administer iron at least one hour prior to famotidine Unlike cimetidine or ranitidine, famotidine does not appear to inhibit hepatic cytochrome P-450 enzyme systems and dosage adjustments of other drugs (*e.g.*, warfarin, theophylline, diazepam, procainamide, phenytoin) that are metabolized by this metabolic pathway should usually not be required.

Laboratory Considerations

- Histamine2-blockers may antagonize the effects of histamine and pentagastrin in the evaluation gastric acid secretion.
- After using allergen extract **skin tests**, histamine₂ antagonists may inhibit histamine responses. It is recommended that histamine₂ blockers be discontinued at least 24 hours before performing either of these tests.

Doses

■ DOGS:

To reduce gastric acid production:

- a) 0.5 mg/kg PO, SC, IM, IV q12-24 hours (Matz 1995)
- b) 0.5-1 mg/kg PO or IV once or twice daily (Johnson, Sherding et al. 1994)
- c) 0.1-0.2 mg/kg PO q8h (Zerbe and Washabau 2000)
- d) 0.55-1.1 mg/kg PO q24h (or every 12 hours if there is severe esophagitis) for 2-3 weeks in dogs with acute reflex esophagitis (Tams 2003a)
- e) For adjunctive treatment (to prevent/treat gastric ulcers) of mast cell tumors: 0.5 mg/kg once daily (route not specified). (Garrett 2006)
- f) For adjunctive treatment of GI effects (anorexia, nausea, vomiting) associated with chronic kidney disease: 0.5 mg/ kg PO once daily (q24h) Effective evidence grade: 3. (Polzin 2005b)

■ CATS:

Note: See the warning (in the adverse effects section) about IV use in cats.

To reduce gastric acid production:

- a) 0.5 mg/kg PO, SC, IM, IV q12-24 hours (Matz 1995)
- b) 0.5 mg/kg PO or parenterally once daily (Trepanier 1999)
- c) 0.55-1.1 mg/kg PO q24h (or every 12 hours if there is severe esophagitis) for 2-3 weeks in cats with acute reflex esophagitis (Tams 2003a)

For adjunctive treatment of GI effects (anorexia, nausea, vomiting) associated with chronic progressive renal disease:

a) 1 mg/kg PO once daily (q24h) (Wolf 2006b)

b) 0.5-1 mg/kg PO once or twice daily (q12-24h) (Zoran 2006a)

FERRETS:

- a) For stress induced ulcers: 0.25-0.5 mg/kg PO, IV once daily (Williams 2000)
- b) In combination with antibiotics for Helicobacter treatment: 0.25–0.5 mg/kg PO, IV q24h (Fisher 2005)

SMALL MAMMALS:

Rabbits: For stress induced ulcer prevention once critically ill animal has stabilized:

- a) 1 mg/kg IV once daily (q24h) (Johnston 2006)
- **HORSES:** (Note: ARCI UCGFS Class 5 Drug)

As an adjunct in ulcer treatment:

a) IV doses: 0.23 mg/kg, IV q8h or 0.35 mg/kg IV q12h.
Oral doses: 1.88 mg/kg, PO q8h or 2.8 mg/kg PO q12h (Duran and Ravis 1993)

Monitoring

- Clinical efficacy (dependent on reason for use); monitored by decrease in symptomatology, endoscopic examination, blood in feces, etc.
- Adverse effects, if noted

Client Information

- To maximize the benefit of this medication, it must be administered as prescribed by the veterinarian
- Clinical signs may reoccur if dosages are missed

Chemistry/Synonyms

An H₂-receptor antagonist, famotidine occurs as a white to pale yellow, crystalline powder. It is odorless, but has a bitter taste. 740 micrograms are soluble in one mL of water.

Famotidine may also be known as: famotidinum, L-643341, MK-208, and YM-11170; many trade names are available.

Storage/Stability/Compatibility

Tablets should be stored in well-closed, light-resistant containers at room temperature. Tablets are assigned an expiration date of 30 months after date of manufacture.

The powder for oral suspension should be stored in tight containers at temperatures less than 40°C. After reconstitution, the resultant suspension is stable for 30 days when stored at temperatures less than 30°C.; do not freeze.

Famotidine injection should be stored in the refrigerator $(2-8^{\circ}\text{C})$. It is physically **compatible** with most commonly used IV infusion solutions and is stable for 48 hours at room temperature when diluted in these solutions.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

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

HUMAN-LABELED PRODUCTS:

Famotidine Tablets (plain, film-coated & orally disintegrating) & Gelcaps: 10 mg (regular & chewable), (OTC), 20 mg, & 40 mg; *Pepcid®*, *Pepcid®*, *Pepcid AC® Maximum Strength* and *Pepcid RPD®* (Merck); (Rx); *Pepcid AC®* (J & J Merck); generic; (Rx & OTC))

Famotidine Powder for Oral Suspension: 8 mg/mL when reconstituted in 400 mg bottles; *Pepcid*® (Merck); (Rx)

Famotidine Injection: 10 mg/mL in 1 and 2 mL single dose vials and 4 mL, 20 mL and 50 mL multidose vials (may contain mannitol or benzyl alcohol); 20 mg/50 mL premixed (regular & preservative free) in 50 mL single-dose *Galaxy* containers; *Pepcid*® (Merck); generic; (Rx)

FATTY ACIDS, ESSENTIAL/ OMEGA FISH OIL/ VEGETABLE OIL

NUTRITIONAL

Prescriber Highlights

- Used for treatment of dogs with pruritus associated with atopy, idiopathic seborrhea; in cats for pruritus associated with miliary dermatitis & eosinophilic granuloma complex
- May also be useful in other species & for other disease states
- ➤ Safety in pregnancy not established; use <u>caution</u> in patients with coagulopathies
- Adverse Effects: High doses may cause GI distress; rarely some dogs may become lethargic or more pruritic

Uses/Indications

These products are generally indicated for the treatment of pruritus associated with atopy and idiopathic seborrhea. In cats, they can be used for treating pruritus in the adjunctive treatment of miliary dermatitis and eosinophilic granuloma complex. Fatty acids may improve coat quality and be helpful for adjunctive therapy for arthropathies such as hip dysplasia.

When used for pruritus, significant therapeutic effects may be noted in only 25–50% of patients treated and require 2–3 months of treatment before evaluating efficacy. Antihistamine and fatty acid therapy may be synergistic for treatment of pruritus.

Polyunsaturated fatty acids, particularly the omega-3's may prove to be useful for a variety of conditions, including renal failure, arthritis (both degenerative and autoimmune), cardiovascular disease (hypercoagulable states), and some neoplastic diseases. Further studies are required to document any clinical benefits for veterinary use, however.

Pharmacology/Actions

The exact pharmacologic actions of these products are not well described; particularly in light of the combination nature of the commercial products being marketed, it is difficult to ascertain which compounds may be responsible for their proposed efficacy. The particular therapeutic benefits and ratios of omega-3 versus omega-6 fatty acids are still being debated.

Fish oils affect arachidonic acid levels in plasma lipids and platelet membranes. They may affect production of inflammatory prostaglandins in the body, thereby reducing inflammation and pruritus. Linolenic or linoleic acids may be used as essential fatty acid sources which are necessary for normal skin and haircoats.

Contraindications/Precautions/Warnings

Because of potential affects on bleeding times, use with caution in patients with coagulation disorders or those receiving anticoagulant medications. Use with caution in patients with non-insulin dependent diabetes as omega-3 fatty acids have impaired insulin secretion with resultant increased glucose levels in humans with type-2