

Laboratory Considerations

- Serum samples to be analyzed for cobalamin and/or folate should be protected from bright light and excessive heat
- Hemolysis can cause falsely elevated serum concentrations of folate
- Potentially, decreased cobalamin serum levels (B-12) can occur in patients receiving prolonged folic acid supplementation

Doses**■ DOGS/CATS:**

- For severe folate deficiency: 0.5–2 mg (total dose) once daily for 1 month. (Williams 2000)
- For cats with folate deficiency secondary to exocrine pancreatic insufficiency: 400 mcg (0.4 mg) PO once daily. (Steiner and Williams 2005)
- For cats on long-term use of high dose trimethoprim/sulfa (for treating *Nocardia*): 2 mg (total dose) PO once daily. (Wolf 2006a)
- For dogs with folate and cobalamin deficiency secondary to inflammatory bowel disease: folic acid at 5 mg (total dose) PO once daily for 1–6 months and cyanocobalamin 750 mcg (total dose) parenterally once per month. (Hoskins 2005a)

■ HORSES:

- Prolonged therapy with antifolate medications (e.g., trimethoprim, pyrimethamine): Sometimes recommend folic acid at 20–40 mg (total dose) PO per day. Pregnant mares should routinely receive folic acid supplementation during treatment with antifolates. (Granstrom and Saville 1998)

Monitoring

- Small Animals: folate & cobalamin levels (serum); before and after treatment
- Clinical signs associated with deficiency
- CBC, baseline and ongoing if abnormal

Client Information

- When used to treat folate deficiency associated with small intestinal disease or pancreatic insufficiency, lifelong monitoring and periodic replacement therapy may be required

Chemistry/Synonyms

Folic acid occurs as a yellow, yellow-brownish, or yellowish-orange, odorless crystalline powder. It is very slightly soluble in water and insoluble in alcohol. Commercially available folic acid is obtained synthetically.

Folic acid may also be known as: folate, folacin, vitamin B₉, acidum folicum, pteroylglutamic acid, pteroylmonoglutamic acid, *Folvite*® and vitamin B₁₁.

Storage/Stability

Folic acid tablets should be stored in well-closed containers below 40°C (104°F), preferably between 15–30°C; protect from light and moisture. The injection should be stored protected from light below 40°C (104°F), preferably between 15–30°C. Do not allow to freeze.

Dosage Forms/Regulatory Status**VETERINARY-LABELED PRODUCTS:**

None as sole ingredient products. There are many products available that contain folic acid as one of the ingredients. If using one of these products, be certain it has enough folic acid to treat folate deficiency without overdosing fat soluble vitamins A or D.

HUMAN-LABELED PRODUCTS:

Folic Acid Tablets: 400 mcg (0.4 mg), & 800 mcg (0.8 mg); generic; (depending on label either OTC or Rx)

Folic Acid Tablets: 1 mg; generic; (Rx)

Folic Acid Injection: 5 mg/mL in 10 mL vials; *Folvite*® (Lederle), generic; (Rx)

FOMEPIZOLE

4-METHYLPYRAZOLE (4-MP)

(foe-me-pi-zole) Antizol-Vet®

ANTIDOTE**Prescriber Highlights**

- Synthetic alcohol dehydrogenase inhibitor used to treat dogs for ethylene glycol poisoning
- May be efficacious in cats at high dosages, if given within 3 hours of ingestion
- Adverse Effects: Rapid IV infusion may cause vein irritation & phlebosclerosis; anaphylaxis is potentially possible
- Dilute as directed in the commercially available kit
- Monitor & treat acid/base, fluid, electrolyte imbalances
- May inhibit elimination of ethanol (& vice versa)
- Expense & rapid availability may be issues

Uses/Indications

Fomepizole is used for the treatment of known or suspected ethylene glycol toxicity in dogs (and humans). Fomepizole, at high doses, may be efficacious in treating recent (within 3 hours) ingestion of ethylene glycol in cats.

Pharmacology/Actions

Ethylene glycol itself is only mildly toxic in dogs, but when it is metabolized to glycoaldehyde, glycolate, glyoxalic acid, and oxalic acid, the resultant metabolic acidosis and renal tubular necrosis can be fatal. Fomepizole is a competitive inhibitor of alcohol dehydrogenase, the primary enzyme that converts ethylene glycol into glycoaldehyde and other toxic metabolites. This allows ethylene glycol to be excreted primarily unchanged in the urine decreasing the morbidity and mortality associated with ethylene glycol ingestion.

Pharmacokinetics

Fomepizole is excreted primarily by the kidneys and apparently exhibits a dose-dependent accumulation of the drug over time; therefore, a reduction in subsequent doses can safely occur.

Contraindications/Precautions/Warnings

There are no labeled contraindications to fomepizole's use. Fomepizole has been shown to be effective in treating ethylene glycol in cats, but a high dosage is required.

Adverse Effects

Giving concentrated drug rapidly intravenously may cause vein irritation and phlebosclerosis. Dilute as directed in the commercially available kit.

One dog during clinical trials was reported to develop anaphylaxis.

Use of fomepizole alone without adequate monitoring and adjunctive supportive care (e.g., correction of acid/base, fluid, electrolyte imbalances) may lead to therapeutic failure. If animal presents within 1–2 hours post ingestion, consider inducing vomiting and/or gastric lavage with activated charcoal to prevent further absorption.

Reproductive/Nursing Safety

Fomepizole's safe use during pregnancy, lactation or in breeding animals has not been established. However, because of the morbidity and mortality associated with ethylene glycol toxicity, the benefits of fomepizole should generally outweigh its risks. 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 this drug is excreted in milk.

Overdosage/Acute Toxicity

Overdosage may cause significant CNS depression. No specific treatment is recommended.

Drug Interactions

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

- **ETHANOL:** Fomepizole inhibits alcohol dehydrogenase; ethanol metabolism is reduced significantly and alcohol poisoning (CNS depression, coma, death) can occur. Use together is generally not recommended, but if both drugs are used, monitoring of ethanol blood levels is mandatory.

Doses

■ DOGS:

- a) For treatment of ethylene glycol toxicity: Initially load at 20 mg/kg IV; at 12 hours post initial dose give 15 mg/kg IV; at 24 hours post initial dose give another 15 mg/kg IV and at 36 hours after initial dose give 5 mg/kg; may give additional 5 mg/kg doses as necessary (animal has not recovered or has additional ethylene glycol in blood). (Package Insert; *Antizol-Ver*®)

■ CATS:

- a) For treatment of ethylene glycol toxicity: Initially, 125 mg/kg slow IV; at 12, 24, 36 hours give 31.25 mg/kg IV. In addition, treat supportively with supplemental fluids. Cats must be treated within 3 hours of ingestion. Cats whose treatment began 4 hours post ethylene glycol had 100% mortality with either fomepizole or ETOH therapy. (Connally and Thrall 2002)

Monitoring

- Ethylene glycol blood levels (mostly important to document diagnosis if necessary and to determine if therapy can be discontinued after 36 hours of treatment.)
- Blood gases and serum electrolytes
- Hydration status
- Renal function tests (e.g., Urine output and urinalysis; BUN or serum creatinine)
- Cats: body temperature

Client Information

- Clients should be informed that treatment of serious ethylene glycol toxicity is an “intensive care” admission and that appropriate monitoring and therapy can be quite expensive, particularly when fomepizole is used in large dogs.

- Because time is of the essence in this therapy, clients will need to make an informed decision rapidly. Dogs treated within 8 hours post ingestion have a significantly better prognosis than those treated after 10–12 hours post ingestion. Cats must be treated within 3 hours of ingestion with high dosages.

Chemistry/Synonyms

A synthetic alcohol dehydrogenase inhibitor, fomepizole is commonly called 4-methylpyrazole (4-MP). Its chemical name is 4-methyl-1H-pyrazole. It has a molecular weight of 81; it is soluble in water and very soluble in ethanol.

Fomepizole may also be known as: 4-methylpyrazole, 4-MP, fomezol, fomezolum, and *Antizol*®.

Storage/Stability/Compatibility

Commercially available solutions should be stored at room temperature. The concentrate for injection may solidify at temperatures less than 25°C. Should this occur, resolubilize by running warm water over the vial. Solidification or resolubilization does not affect drug potency or stability. Store reconstituted vial at room temperature and discard after 72 hours. Reconstituted solutions may be further diluted in D5W or normal saline for IV infusion.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Fomepizole 1.5 g Kit for Injection; *Antizol-Ver*® (Jazz); (Rx). Approved for use in dogs. **Note:** At recommended doses 1 kit will treat a 26 kg dog (up to 58 lb.); larger dogs will require additional kits

Preparation: If drug has solidified run warm water over vial; Add entire contents to 30 mL vial of 0.9% NaCl (in kit), mix well. Resultant solution is: 50 mg/mL

HUMAN-LABELED PRODUCTS:

Fomepizole Injection Concentrate (preservative free): 1 g/mL preservative free (must be diluted) in 1.5 mL vials; *Antizol*® (Orphan Medical); (Rx)

FURAZOLIDONE

(fyoor-a-zoe-li-done) Furoxone®

ANTIBACTERIAL/ANTIPROTOZOAL

Prescriber Highlights

- Antibacterial/antiprotozoal nitrofurantoin used primarily in dogs & cats; availability is an issue
- Contraindications: Known hypersensitivity; food animals
- Adverse Effects: GI effects (anorexia, vomiting, cramping & diarrhea) possible
- May innocuously discolor urine to a dark yellow to brown color
- Drug Interactions

Uses/Indications

Furazolidone is usually a drug of second choice in small animals to treat enteric infections caused by the organisms listed below. Because it is no longer commercially available (in the USA), it may be difficult to locate.