Chemistry/Synonyms
A selective serotonin-reuptake inhibitor (SSRI), fluvoxamine maleate occurs as a white to almost white crystalline powder. It is freely soluble in alcohol and sparingly soluble in water.

Fluvoxamine may also be known as DU-23000, desifluvoxamin, *Dumirox®, Dumyrox®, Faverin®, Favoxil®, Felixsan®, Fevarin®, Floxex®, Floxyfral®, Fluvohexal®, Fluvosol®, Fluvoxadura®, Fluvoxin®, Luvox®*, and *Maveral®*.

Storage/Stability/Compatibility
The commercially available tablets should be stored in tight containers at room temperatures of 15–30° C (59–86° F) and protected from high humidity.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

The ARCI (Racing Commissioners International) has designated this drug as a class 2 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Fluvoxamine Tablets: 25 mg, 50 mg, & 100 mg; generic, (Rx)

FOLIC ACID

(***foe***-lik ***ass***-id) Folate, Folacin

WATER-SOLUBLE "B" VITAMIN

Prescriber Highlights
- "B" Vitamin necessary for nucleoprotein synthesis & normal erythropoiesis
- Injectable or oral dosage forms
- Folic acid deficiency may be seen in animals (especially cats) with proximal or diffuse small intestinal inflammatory disease
- May be used when dihydrofolate reductase inhibitor drugs (*e.g.*, trimethoprim, ormetoprim, pyrimethamine) are used for a prolonged period
- Very safe

Uses/Indications
Folic acid is used to treat folic acid deficiency in dogs, cats, and horses (theoretically in other animal species as well) often due to small intestinal disease. Cats with exocrine pancreatic insufficiency appear to be most at risk for folate and cobalamin deficiencies secondary to malabsorption of folic acid in the diet. Dogs with exocrine pancreatic insufficiency often are noted to have increased folate levels secondary to overgrowths of folate-synthesizing bacteria in the proximal small intestine. Chronic administration of dihydrofolate reductase inhibiting drugs such as pyrimethamine, ormetoprim or trimethoprim can potentially lead to reduced activated folic acid (tetrahydrofolic acid); folic acid supplementation is sometimes prescribed in an attempt to alleviate this situation.

Pharmacology/Actions
Folic acid is required for several metabolic processes. It is reduced via dihydrofolate reductase in the body to tetrahydrofolate (5-methyltetrahydrofolate) which acts as a coenzyme in the synthesis of purine and pyrimidine nucleotides that are necessary for DNA synthesis. Folic acid is also required for maintenance of normal erythropoiesis.

Pharmacokinetics
Therapeutically administered folic acid is primarily absorbed in the proximal small intestine via carrier-mediated diffusion. In humans, synthetic folic acid is nearly completely absorbed after oral administration while folate in foodstuffs is about 50% bioavailable. Folic acid is converted to its active form, tetrahydrofolic acid, principally in the liver and plasma. Folate is distributed widely throughout the body and is stored in the liver. Erythrocyte and CSF levels can be significantly higher than those found in serum. It can undergo enterohepatic recirculation and is excreted primarily in the urine either as metabolites or unchanged drug (when administered in excess of body requirements).

Contraindications/Precautions/Warnings
Folic acid treatment is contraindicated only when known intolerance to the drug is documented. In humans, cobalamin (B-12) levels may be reduced with megaloblastic anemias; folic acid therapy may mask the signs associated with it. Folic acid doses in people above 0.4 mg/day (except during pregnancy and lactation) are not to be used until pernicious anemia has been ruled out.

As dogs may have increased, normal, or decreased folate levels associated with enteropathies, do not administer therapeutic doses until folate and cobalamin levels have been determined.

Adverse Effects
Folic acid is quite non-toxic and should not cause significant adverse effects. Rarely in humans, folic acid tablets or injection have reportedly caused hypersensitivity reactions or gastrointestinal effects. Very high oral doses in humans (15 mg/day) have occasionally caused CNS effects (*e.g.*, difficulty sleeping, excitement, confusion, etc.).

Reproductive/Nursing Safety
Folic acid is safe to use during pregnancy and in humans it is routinely prescribed as part of prenatal vitamin supplementation as folate deficiency can increase the risk for fetal neural tube defects. In humans, the FDA categorizes this drug as category **A** for use during pregnancy *(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.)*

Folic acid is distributed into milk, but is safe. Folic acid requirements may be increased in lactating animals.

Overdosage/Acute Toxicity
Folic acid is relatively non-toxic and no treatment should be required if an inadvertent overdose occurs. Excess drug is metabolized or rapidly excreted unchanged in the urine.

Drug Interactions
The following drug interactions or have been reported in humans and may be of significance in veterinary patients receiving folic acid or may alter patient folic acid requirements:
- **CHLORAMPHENICOL:** May delay response to folic acid
- **METHOTREXATE, TRIMETHOPRIM, PYRIMETHAMINE (drugs that inhibit dihydrofolate reductase):** May interfere with folic acid utilization
- **PHENYTOIN:** May decrease serum folate levels, and phenytoin dosage may need to be increased; increased frequency in seizures can occur
- **SULFASALAZINE, BARBITURATES, NITROFURANTOIN, PRIMIDONE:** May increase risk for folate deficiency

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:**
  a) For severe folate deficiency: 0.5–2 mg (total dose) once daily for 1 month. (Williams 2000)
  b) For cats with folate deficiency secondary to exocrine pancreatic insufficiency: 400 mcg (0.4 mg) PO once daily. (Steiner and Williams 2005)
  c) For cats on long-term use of high dose trimethoprim/sulfa (for treating *Nocardia*): 2 mg (total dose) PO once daily. (Wolf 2006a)
  d) 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:**
  a) 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.