ETHANOL
ALCOHOL, ETHYL

(*eth*-a-nol) Alcohol

ANTIDOTE

Prescriber Highlights

- Used for treatment of ethylene glycol or methanol toxicity
- Contraindications: None (above are life threatening)
- Adverse Effects: CNS depression, diuresis, pain, & infection at the injection site.
- Avoid extravasation
- Monitor fluid & electrolyte status, alcohol & toxin levels (if possible)

Uses/Indications

The principal use of ethanol in veterinary medicine is for the treatment of ethylene glycol or methanol toxicity. While fomepizole (4-methyl pyrazole) is now the treatment of choice for ethylene glycol poisoning, alcohol is a readily available and an economical alternative when patients present within a few hours after ingestion.

Percutaneous injection of ethanol 95% has been used successfully to treat feline hyperthyroidism.

Ethyl alcohol has also been used in aerosol form as a mucokinetic agent in horses.

Pharmacology/Actions

By competitively inhibiting alcohol dehydrogenase, alcohol can prevent the formation of ethylene glycol to its toxic metabolites (glycoaldehyde, glycolate, glyoxalate, and oxalic acid). This allows the ethylene glycol to be principally excreted in the urine unchanged. A similar scenario exists for the treatment of methanol poisoning. For alcohol to be effective, however, it must be given very early after ingestion; it is seldom useful if started 8 hours after a significant ingestion.

Pharmacokinetics

Alcohol is well absorbed orally, but is administered intravenously for toxicity treatment. It rapidly distributes throughout the body and crosses the blood-brain barrier. Alcohol crosses the placenta.

Contraindications/Precautions/Warnings

Because ethylene glycol and methanol intoxications are life threatening, there are no absolute contraindications to ethanol's use for these indications.

Use of ethanol with fomepizole is usually contraindicated; see drug interactions for more information.

Adverse Effects

The systemic adverse effects of alcohol are quite well known. The CNS depression and respiratory depression associated with the high levels used to treat ethylene glycol and methanol toxicity can confuse the clinical monitoring of these toxicities. Ethanol's affects on antidiuretic hormone may enhance diuresis. As both ethylene glycol and methanol may also cause diuresis, fluid and electrolyte therapy requirements need to be monitored and managed. Hypocalcemia and metabolic acidosis may be noted and pulmonary edema can occur. Other adverse affects include pain and infection at the injection site and phlebitis. Extravasation should be watched for and avoided. When aerosolized in horses, irritation and bronchoconstriction may result.

Reproductive/Nursing Safety

Alcohol's safety during pregnancy has not been established for short-term use. Use only when necessary. 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.*)

Alcohol passes freely into milk in levels that approximate maternal serum levels, but it is unlikely to have negative effects on nursing offspring.

Overdosage/Acute Toxicity

If clinical signs of overdosage occur, either slow the infusion or discontinue temporarily. Alcohol blood levels may be used to monitor both efficacy and toxicity of alcohol.

Drug Interactions

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

- **BROMOCRIPTINE:** Alcohol may increase the severity of side effects seen with bromocriptine
- **CHARCOAL, ACTIVATED:** Will inhibit absorption of orally administered ethanol; do not use activated charcoal if administering ethanol orally for methanol or ethylene glycol intoxication
- **CNS DEPRESSANT DRUGS** (*e.g.*, **barbiturates, benzodiazepines, phenothiazines,** etc.): Alcohol may cause additive CNS depression when used with other CNS depressant drugs
- **FOMEPIZOLE** (**4-MP**): 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.
- **INSULIN** and **other antidiabetic drugs**: Alcohol may affect glucose metabolism and the actions of insulin or oral antidiabetic agents
- A disulfiram reaction (increased acetaldehyde with tachycardia, vomiting, weakness) may occur if alcohol is used concomitantly with the following drugs: **cefoperazone, chlorpropamide, furazolidone, metronidazole**

Doses

- **DOGS:**

  For ethylene glycol poisoning:

  a) As a 20% solution, give 5.5 mL/kg IV q4h for 5 treatments, then q6h for four additional treatments (Forrester and Lees 1994)

  b) Using a 5% solution, give 22 mL/kg IV every 4 hours for 24 hours, then every 6 hours for another 24 hours; alternatively give a constant rate IV infusion to run at 5.5 mL/kg/hr (Firth 2000)

- **CATS:**

  For ethylene glycol poisoning:

  a) As a 20% solution, give 5 mL/kg IV q6h for 5 treatments, then q8h for four additional treatments (Forrester and Lees 1994)

  b) Using a 5% solution, give a constant rate IV infusion to run at 5 mL/kg/hr (Firth 2000)

Monitoring

- Alcohol blood levels (and ethylene glycol or methanol levels). **Note:** In humans, blood ethanol levels should be maintained at 100 to 130 milligrams/deciliter (21.7 to 28.2 milliMoles/liter). It is safer to maintain a blood ethanol concentration greater than

130 milligrams/deciliter than to have it fall below 100 milligrams/deciliter. (*POISINDEX® Managements*, Thompson; MICROMEDEX® Healthcare Series, 2007)

- Degree of CNS effect
- Fluid/electrolyte status

Client Information

- Systemically administered alcohol should be given in a controlled clinical environment.

Chemistry/Synonyms

A transparent, colorless, volatile liquid having a characteristic odor and a burning taste, ethyl alcohol is miscible with water and many other solvents.

Ethanol may also be known as aethanolum, alcool, grain alcohol, ethanolum, and ethyl alcohol.

Storage/Stability/Compatibility/Preparation

Alcohol should be protected from extreme heat or freezing. Do not use unless the solution is clear. Alcohol may precipitate many drugs; do not administer other medications in the alcohol infusion solution unless compatibility is documented (consult specialized references or a hospital pharmacist for more specific information).

Note: Since alcohol infusions are generally only used in veterinary medicine for the treatment of ethylene glycol/methanol toxicity and obtaining medical or laboratory grade alcohol or pharmaceutical grade products can be very difficult in an emergency, veterinarians have often had to improvise. One method that has been successful, albeit not pharmaceutically elegant, is to use commercially available vodka (40%, 80 proof) diluted in an appropriate IV solution.

- To make a 20% ethanol solution using 80 proof (40%) vodka: dilute with an equal volume (500 mL with 500 mL) of IV fluids (*e.g.*; LRS, Normosol-R).
- To make a 5% solution using 80 proof (40%) vodka: add 125 mL of 80 proof (40%) vodka to 875 mL of IV fluid (remove about 125 mL of fluid from the bag).

100 proof (50%) vodka or 190 proof (95%) grain alcohol ("Everclear") can also be used. Dilute as appropriate to make a 5–20% solution. Regardless of the product used, it is recommended that an in-line filter be used for the IV.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Alcohol (Ethanol) in Dextrose Infusions:

5% Alcohol and 5% Dextrose in Water (450 Cal/L, 1114 mOsm/L) in 1000 mL; generic; (Rx)

5% Alcohol and 5% Dextrose in Water (450 Cal/L, 1125 mOsm/L) in 1000 mL; (McGaw); (Rx)

10% Alcohol and 5% Dextrose in Water (720 Cal/L, 1995 mOsm/L) in 1000 mL; (McGaw) (Rx)

For information on obtaining tax-free alcohol for medicinal purposes, contact a regional office of the Bureau of Alcohol, Tobacco, and Firearms.

ETIDRONATE DISODIUM

(e-*ti*-droe-nate) Didronel®

ORAL BISPHOSPHONATE BONE RESORPTION INHIBITOR

Prescriber Highlights

- Biphosphonate that reduces calcium resorption from bone; used primarily to treat hypercalcemia associated with malignancy
- Contraindications: Treatment of hypercalcemia in patients with severe renal function impairment
- Caution in patients with bone fractures, enterocolitis, cardiac failure, or moderate renal function impairment
- Adverse Effects: Potentially, diarrhea, nausea, or bone pain/tenderness
- Do not confuse etidronate with etretinate or etomidate
- Expense may be an issue

Uses/Indications

Etidronate is a first generation bisphosphonate that may be useful for the treatment of severe hypercalcemia associated with neoplastic disease. Its use in human medicine has been largely replaced with newer, more potent bisphosphonates that can be dosed less often or have fewer adverse effects. Etidronate is also indicated in humans for the treatment of Paget's disease and heterotopic ossification (*e.g.*, after total hip replacement).

Pharmacology/Actions

Etidronate's primary site of action is bone. It reduces normal and abnormal bone resorption. This effect can reduce hypercalcemia associated with malignant neoplasms. Etidronate can also increase serum phosphate concentrations, presumably by increasing the renal tubular reabsorption of phosphate. Some early studies in lab animals suggest that etidronate may inhibit the formation of bone metastases with some tumor types.

Pharmacokinetics

Oral absorption is poor and dose dependent. As little as 1% of a dose (smaller doses) may be absorbed; with higher doses, 6–10% may be absorbed. After oral dosing, the drug is rapidly cleared from blood and 50% of the drug absorbed goes into bone. At usual doses, it appears that etidronate does not cross the placenta. Duration of effect may be very prolonged. In humans, effects have persisted for up to one year after discontinuation in patients with Paget's disease. Effects for hypercalcemia may last for 11 days. Absorbed etidronate is excreted unchanged by the kidneys. Approximately 50% of the absorbed dose is excreted within 24 hours; the remainder is chemisorbed to bone and then slowly eliminated.

Contraindications/Precautions/Warnings

Etidronate is considered contraindicated for the treatment of hypercalcemia in patients with renal function impairment (serum creatinines >5 mg/dL). Risk vs. benefit should be carefully considered in patients with bone fractures (delays healing), enterocolitis (higher risk of diarrhea), cardiac failure (especially with parenteral etidronate as patients may not tolerate the extra fluid load), or those with renal function impairment (serum creatinines 2.5–5 mg/dL).

Do not confuse etidronate with etretinate or etomidate.