c) For penicillinosis: With appropriate adjunctive surgical curettage and topical therapy, thiabendazole: 20 mg/kg/day PO for 4–6 weeks (Barsanti 1984)

d) For aspergillosis: Administer 10 mg/kg as nasal flush. Dilute in 10–20 mL of water. Flush twice daily for 10 days.

Orally: 20 mg/kg/day divided twice daily for 6 weeks (Morgan 1988)

e) For treatment of nasal aspergillosis: 20 mg/kg divided q12h PO for 6–8 weeks. If anorexia or nausea develops, may withdraw drug and then gradually reintroduce to the full dosage. Administer with food to enhance absorption and reduce anorexia. May be effective in 40–50% of dogs treated. (Sharp 1989)

■ **RABBITS, RODENTS, SMALL MAMMALS:**

a) Rabbits: For pinworms: 50–100 mg/kg PO for 5 days or 50 mg/kg PO, repeat in 3 weeks (Ivey and Morrisey 2000)

b) Mice, Rats, Gerbils, Hamsters, Guinea pigs: 100 mg/kg, PO for 5 days.

Chinchillas: 50–100 mg/kg PO for 5 days (Adamcak and Otten 2000)

c) For pinworms in Mice, Rats, Hamsters, Gerbils and Rabbits: 50 mg/kg, PO once (Burke 1999)

■ **CATTLE:**

For susceptible parasites:

a) 66 mg/kg PO; 110 mg/kg PO for Cooperia and severe infections of other susceptible nematodes. Retreat treatment in 2–3 weeks if indicated (Paul 1986), (Roberson 1988b)

b) 50–100 mg/kg PO (Brander, Pugh, and Bywater 1982)

■ **HORSES:**

For susceptible parasites:

a) 44 mg/kg, PO (Robinson 1987)

b) 44 mg/kg; 88 mg/kg for ascarids (Roberson 1988b)

c) 50–100 mg/kg PO (Brander, Pugh, and Bywater 1982)

■ **SWINE:**

For susceptible parasites:

a) For baby pigs with *Strongyloides ransomi*: 62–83 mg/kg PO, retreat in 5–7 days if necessary. To prevent Ascaris suum: Feed at 0.05–0.1% per ton of feed for 2 weeks, then 0.005–0.02% per ton for 8–14 weeks (Paul 1986)

b) 75 mg/kg, PO (Roberson 1988b)

c) 50 mg/kg, PO (Brander, Pugh, and Bywater 1982)

■ **SHEEP & GOATS:**

For susceptible parasites:

a) 44 mg/kg PO; 66 mg/kg PO for severe infections in goats (Paul 1986), (Roberson 1988b)

b) 50–100 mg/kg PO (sheep) (Brander, Pugh, and Bywater 1982)

■ **LLAMAS:**

For susceptible parasites:

a) 50–100 mg/kg PO for 1–3 days. Use higher dosage rate over several days when animal is severely parasitized. (Cheney and Allen 1989)

b) 66 mg/kg PO (Fowler 1989)

■ **BIRDS:**

For susceptible parasites:

a) For ascarids: 250–500 mg/kg PO once. Repeat in 10–14 days.

For Syngamus trachea: 100 mg/kg, PO once a day for 7–10 days (Clubb 1986)

b) For ascarids, Capillaria, gapeworms:

Chickens, pheasants, turkeys, and pigeons: Mix 0.5% in feed for 10 days or administer orally at 44 mg/kg as a single dose.

Psittacines: 44 mg/kg PO; do not exceed this dose.

Falcons: 100 mg/kg PO as a single dose (Stunkard 1984)

c) For thorny headed worms in waterfowl and raptors: 250 mg/lb (Stunkard 1984)

Client Information

■ Shake suspension well before using.

■ Follow veterinarian's or label's directions carefully.

Chemistry/Synonyms

The prototypic benzimidazole, thiabendazole occurs as an odorless or nearly odorless, tasteless, white to practically white powder. It has a melting range of 296°–303°C and a pK_a of 4.7. Thiabendazole is practically insoluble in water and slightly soluble in alcohol.

Thiabendazole may also be known as: E233, MK-360, tiabendazolum, tiabendazole, *Benzol®*, *Eprofil®*, *Foldan®*, *Folderm®*, *Mintezol®*, *Thiaben®*, *Thianax®*, *Tiabenzol®*, *Tiabiose®*, *Tiaplex®*, *Triasox®*, or *Tutiverm®*.

Storage/Stability

Thiabendazole tablets, boluses and oral suspension should be stored in tight containers.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

None in the USA for systemic use. Thiabendazole is an active ingredient in the topical/otic preparation *Tresaderm®*.

Food residue tolerances: 0.1 ppm in uncooked meat of cattle, pheasants, swine, sheep and goats; 0.05 ppm in milk.

HUMAN-LABELED PRODUCTS:

Thiabendazole Chewable Scored Tablets: 500 mg; *Mintezol®* (Merck); (Rx)

Thiabendazole Oral Suspension: 100 mg/mL in 120 mL; *Mintezol®* (Merck); (Rx)

Thiacetarsamide (no longer available)—See Melarsomine

THIAMINE HCL
VITAMIN B_1

(***thye***-a-min)

NUTRITIONAL; B VITAMIN

Prescriber Highlights

- A "B" vitamin used for treatment or prevention of thiamine deficiency. May be useful for adjunctive treatment of lead poisoning & ethylene glycol toxicity
- Contraindications: hypersensitivity to it
- Adverse Effects: hypersensitivity reactions (rarely); tenderness, or muscle soreness after IM injection
- Drug Interactions; lab interactions

Uses/Indications

Thiamine is indicated in the treatment or prevention of thiamine deficiency states. Clinical signs of thiamine deficiency may be manifested as gastrointestinal (anorexia, salivation), neuromuscular/CNS signs (ataxia, seizures, loss of reflexes), or cardiac effects (brady- or tachyarrhythmias). Deficiency states may be secondary to either a lack of thiamine in the diet or the presence of thiamine destroying compounds in the diet (*e.g.*, bracken fern, raw fish, amprolium, thiaminase-producing bacteria in ruminants).

Thiamine has also been used in the adjunctive treatment of lead poisoning and ethylene glycol toxicity (to facilitate the conversion of glyoxylate to nontoxic metabolites).

Pharmacology/Actions

Thiamine combines with adenosine triphosphate (ATP) to form a compound (thiamine diphosphate/thiamine pyrophosphate) that is employed for carbohydrate metabolism, but does not effect blood glucose concentrations.

Absence of thiamine results in decreased transketolase activity in red blood cells and increased pyruvic acid blood concentrations. Without thiamine triphosphate, pyruvic acid is not converted into acetyl-CoA; diminished NADH results with anaerobic glycolysis producing lactic acid. Lactic acid production is further increased secondary to pyruvic acid conversion; lactic acidosis may occur.

Pharmacokinetics

Thiamine is absorbed from the GI tract and is metabolized by the liver. Elimination is renal, the majority of the drug is eliminated as metabolites.

Contraindications/Precautions/Warnings

Thiamine injection is contraindicated in animals hypersensitive to it or to any component of it.

Adverse Effects

Hypersensitivity reactions have occurred after injecting this agent. Some tenderness or muscle soreness may result after IM injection.

Reproductive/Nursing Safety

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.*) If used in doses greater than the RDA, 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, but it should not be of clinical concern.

Overdosage/Acute Toxicity

Very large doses of thiamine in laboratory animals have been associated with neuromuscular or ganglionic blockade, but the clinical significance is unknown. Hypotension and respiratory depression may also occur with massive doses. A lethal dose of 350 mg/kg has been reported. Generally, no treatment should be required with most overdoses.

Drug Interactions

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

- **NEUROMUSCULAR BLOCKING AGENTS:** Thiamine may enhance the activity of neuromuscular blocking agents; clinical significance is unknown

Laboratory Considerations

- Thiamine may cause false-positive **serum uric acid** results when using the phosphotungstate method of determination or urobilinogen urine spot tests using Ehrlich's reagent
- The Schack and Wexler method of determining **theophylline concentrations** may be interfered with by large doses of thiamine

Doses

- **DOGS:**

  For thiamine deficiency:
  a) 5–50 mg IM, SC, or IV (depending on formulation) (Phillips 1988b)
  b) 1–2 mg IM (Greene and Braund 1989)
  c) 2 mg/kg, PO once daily (Davis 1985)
  d) 100–250 mg SC twice daily for several days until regression of symptoms with complete recovery (Hoskins 1988)

  For adjunctive treatment for ethylene glycol toxicity:
  a) 100 mg/day PO (Morgan 1988)

- **CATS:**

  For thiamine deficiency:
  a) 100–250 mg parenterally twice a day (experimentally, as little as 1 mg is effective) (Armstrong and Hand 1989)
  b) 1–2 mg IM (Greene and Braund 1989)
  c) 4 mg/kg, PO once daily (Davis 1985)
  d) 100–250 mg SC twice daily for several days until regression of symptoms with complete recovery (Hoskins 1988)
  e) 10–20 mg/kg IM or SC two to three times daily until signs abate, then 10 mg/kg PO once daily for 21 days (Morgan 1988)

- **CATTLE:**

  For thiamine deficiency:
  a) For polioencephalomalacia: Initially, 10 mg/kg IV; then, 10 mg/kg IM twice daily for 2–3 days. If no improvement within 4 days, may be advisable to recommend slaughter. (Dill 1986)
  b) 10–20 mg/kg IM or SC 3 times daily; if giving IV dilute in isotonic saline or isotonic dextrose. (Walz 2006a)
  c) 10 mg/kg up to 4 times a day; first dose may be given via slow IV and subsequent doses IM. Less severely affected animals may respond to lower or less frequent dosing. Severely affected animals may benefit from corticosteroids (dexamethasone 1–2 mg/kg) and mannitol (1 g/kg in a 20% solution IV through a filtered IV set). (Cebra 2005)

  For adjunctive therapy of lead poisoning:
  a) 2 mg/kg IM (at same time as CaEDTA therapy); total daily dose 8 mg/kg (Brattan and Kowalczyk 1989)

- **HORSES:**

  For thiamine deficiency:
  a) 0.5–5 mg/kg IV, IM or PO (Robinson 1987)
  b) 100–1000 mg IM, SC, or IV (depending on formulation) (Phillips 1988b)

  For adjunctive treatment of perinatal asphyxia syndrome (hypoxic ischemic encephalopathy):
  a) Foals: 1 gram in one liter of fluids IV once a day (Slovis 2003b)

- **SWINE:**

  For thiamine deficiency:
  a) 5–100 mg IM, SC, or IV (depending on formulation) (Phillips 1988b)

■ **SHEEP & GOATS:**

For thiamine deficiency:

a) For polioencephalomalacia: Initially, 10 mg/kg IV; then, 10 mg/kg IM twice daily for 2–3 days. If no improvement within 4 days, may be advisable to recommend slaughter. (Dill 1986)

b) Sheep: 20–200 mg IM, SC, or IV (depending on formulation) (Phillips 1988b)

Monitoring

■ Efficacy

Client Information

■ Epidemiologic investigation as to the cause of thiamine deficiency (diet, plants, raw fish, etc.) should be performed with necessary changes made to prevent recurrence

Chemistry/Synonyms

A water-soluble "B" vitamin, thiamine HCl occurs as bitter-tasting, white, small hygroscopic crystals, or crystalline powder that has a characteristic yeast-like odor. Thiamine HCl is freely soluble in water, slightly soluble in alcohol and has pK_as of 4.8 and 9.0. The commercially available injection has a pH of 2.5–4.5.

Thiamine HCl may also be known as: aneurine hydrochloride, thiamin hydrochloride, thiamine chloride, thiamini hydrochloridum, thiaminii chloridum, vitamin B-1; many trade names available.

Storage/Stability/Compatibility

Thiamine HCl for injection should be protected from light and stored at temperatures less than 40°C and preferably between 15–30°C; avoid freezing.

Thiamine HCl is unstable in alkaline or neutral solutions or with oxidizing or reducing agents. It is most stable at a pH of 2.

Thiamine HCl is reportedly physically **compatible** with all commonly used intravenous replacement fluids. Compatibility is dependent upon factors such as pH, concentration, temperature, and diluent used; consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Thiamine HCl for Injection: 200 mg/mL in 100 mL and 250 mL vials; *Amtech® Thiamine Hydrochloride Injection* (Phoenix Scientific), *Am-Vet® Thiamine Hydrochloride 200 Mg*, (Neogen), generic, (Vet Tek, IVX, Vedco), *Vita-Jec® Thiamine HCl* (RXV); (Rx)

Thiamine HCl for Injection: 500 mg/mL in 100 mL vials; *Am-Vet® Thiamine Hydrochloride 500 mg* (Neogen), generic, (Butler, IVX, Vedco); (Rx). Labeled for use in horses, dogs and cats.

Thiamine HCl Dietary Supplement: 8,200 mg/lb.; *Horse Care Durvit B-1 Crumbles®* (Durvet); (OTC), Labeled for use in horses.

Thiamine HCl Supplement: 500 mg/oz in 1.5 lb, 4 lb and 20 lb containers; *Thia-Dex®* (Neogen), *Vitamin B-1 Powder®* (AHC); (OTC). Labeled for use in dogs & horses.

There are several B-complex vitamin preparations available that may also have thiamine included.

HUMAN-LABELED PRODUCTS:

Thiamine Tablets: 50 mg, 100 mg, and 250 mg; generic; (OTC)

Thiamine Enteric Coated Tablets: 20 mg; *Thiamilate®* (Tyson); (OTC)

Thiamine HCl Injection: 100 mg/mL in 1 mL, 2 mL multi-dose vials and 2 mL *Tubex*; generic; (Rx)

THIOGUANINE

(thye-oh-*gwah*-neen)

ANTINEOPLASTIC

Prescriber Highlights

- Oral purine analog antineoplastic that may be useful as adjunctive treatment for acute lymphocytic or granulocytic leukemia in dogs or cats
- Contraindications: Hypersensitivity to thioguanine
- Caution: Hepatic dysfunction, bone marrow depression, infection, renal function impairment (adjust dosage), or history of urate urinary stones
- Potentially mutagenic & teratogenic; use milk replacer if nursing
- Adverse Effects: GI effects, bone marrow suppression, hepatotoxicity, pancreatitis, GI (including oral) ulceration, & dermatologic reactions
- Cats may be more susceptible than dogs to adverse effects
- Low therapeutic index; monitoring mandatory

Uses/Indications

Thioguanine may be useful as adjunctive therapy for acute lymphocytic or granulocytic leukemia in dogs or cats.

Pharmacology/Actions

Intracellularly, thioguanine is converted to ribonucleotides that cause the synthesis and utilization of purine nucleotides to be blocked. The drug's cytotoxic effects are believed to occur when these substituted nucleotides are inserted into RNA and DNA. Thioguanine has limited immunosuppressive activity. Extensive cross-resistance usually occurs between thioguanine and mercaptopurine.

Pharmacokinetics

Thioguanine is administered orally, but absorption is variable. In humans, only about 30% of a dose is absorbed. Thioguanine is distributed into the DNA and RNA of bone marrow, but several doses may be necessary for this to occur. It does not apparently enter the CNS, but does cross the placenta. It is unknown whether it enters maternal milk.

Thioguanine is rapidly metabolized primarily in the liver to a methylate derivative that is less active (and toxic) than the parent compound. This and other metabolites are eliminated in the urine.

Contraindications/Precautions/Warnings

Thioguanine is contraindicated in patients hypersensitive to it. The drug should be used cautiously (risk versus benefit) in patients with hepatic dysfunction, bone marrow depression, infection, renal function impairment (adjust dosage) or with a history of urate urinary stones. Thioguanine has a very low therapeutic index and should only be used by clinicians with experience in the use of cytotoxic agents and able to monitor therapy appropriately.

Adverse Effects

At usual doses, GI effects (nausea, anorexia, vomiting, diarrhea) may occur in small animals. However, bone marrow suppression, hepatotoxicity, pancreatitis, GI (including oral) ulceration, and dermatologic reactions are potentially possible. Cats may be particularly susceptible to the hematologic effects of thioguanine.