Cromolyn solution is reportedly **compatible** with acetylcysteine, albuterol, epinephrine, isoetherine, isoproterenol, metaproterenol, or terbutaline solutions for up to 60 minutes. It is **not compatible** with bitolterol.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Cromolyn Sodium Solution for Inhalation: 20 mg/2 mL vials or amps; *Intal*® (Aventis), generic; (Rx)

Cromolyn Sodium Aerosol for Inhalation: 800 mcg/actuation in 8.1 g (112 sprays) and 14.2 g (200 sprays) canisters; *Intal*® (Aventis); (Rx)

There is also an OTC nasal solution (*Nasalcrom*®), and an oral concentrate (*Gastrocrom*®) indicated for mastocystosis available, but these dosage forms are unlikely to be of use in veterinary medicine.

CYANOCOBALAMIN (VITAMIN B12)

(sye-***an***-oh-koe-***bal***-ah-min)

VITAMIN/NUTRITIONAL

Prescriber Highlights

- Used for parenteral treatment of vitamin B12 deficiency
- Very safe

Uses/Indications

Cyanocobalamin is used for treating deficiencies of vitamin B12. Malabsorption of the nutrient secondary to gastrointestinal tract disease, or dietary chromium deficiencies (in ruminants) can be associated with dietary deficiencies of vitamin B12. As there appears to be a high percentage of cats with exocrine pancreatic insufficiency or gastrointestinal disease that are deficient in cobalamin, there is considerable interest in evaluating serum cobalamin (vitamin B12) in these patients. Giant schnauzers may have a genetic defect affecting the location of the cobalamin-intrinsic factor, causing cobalamin deficiency. Dogs with inflammatory bowel disease may also develop cobalamin deficiency.

Pharmacology/Actions

Vitamin B12 (cobalamin), a cobalt-containing water-soluble vitamin, serves as an important cofactor for many enzymatic reactions in mammals that are required for normal cell growth, function and reproduction, nucleoprotein and myelin synthesis, amino acid metabolism, and erythropoiesis. Cobalamin is required for folate utilization; B12 deficiency can cause functional folate deficiency. Unlike humans, macrocytic anemias do not appear to be a significant component to cobalamin deficiency in dogs or cats.

Clinical signs associated with cobalamin deficiency in cats may include weight loss, poor haircoat, vomiting, or diarrhea. Increases in serum methionine and methylmalonic acid, and decreased serum cystathionine and cysteine values may be noted. Homocysteine levels do not appear to be affected.

In dogs, cobalamin deficiency may cause or contribute to inappetance, diarrhea, weight loss, leukopenia, or methylmalonylaciduria.

In ruminants, vitamin B12 appears to be synthesized by rumen microflora and requires dietary cobalt to be present for its formation. Clinical signs seen with cobalamin deficiency states associated with cobalt deficiency in cattle and sheep include inappetance, lassitude, poor haircoat/fleece, poor milk production, weight loss, or failure to grow.

Pharmacokinetics

After food is consumed in monogastric mammals, cobalamin in food is bound to a protein (haptocorrin) in the stomach. Haptocorrin/cobalamin is degraded by pancreatic proteases in the duodenum, but cobalamin is then bound by Intrinsic factor (IF), a protein produced in the stomach and pancreas in dogs, in the pancreas (only) in cats, and in the stomach (only) in humans. The cobalamin-IF complex is absorbed in the small intestine where it binds to cubulin, which facilitates its entry into the portal circulation. A protein called transcobalamin 2 (TCII) then binds to cobalamin allowing its entry into target cells. Some cobalamin is rapidly excreted into the bile where entero-hepatic recirculation occurs. Dogs and cats, unlike humans, do not possess cobalamin-binding protein TC1. This means that dogs and cats with B12 dietary deficiency or malabsorption can rapidly deplete their stores of B12 in one to two months, whereas in humans it may require 1–2 years.

In normal cats, circulating half-life of cobalamin is approximately 13 days, but in two cats with inflammatory bowel disease, it was only 5 days (Simpson, Fyfe et al. 2001).

Contraindications/Precautions/Warnings

For injectable use, no contraindications are documented for domestic animals. In humans, cyanocobalamin is contraindicated in patients hypersensitive to it or hydroxocobalamin.

Adverse Effects

Cyanocobalamin appears very well tolerated when used parenterally in animals. In humans, anaphylaxis has been reported rarely after parenteral use. Some human patients complain of pain at the injection site, but this is uncommon.

Reproductive/Nursing Safety

Studies documenting safety during pregnancy have apparently not been done in humans or animals, but it is likely safe to use. Vitamin B12 deficiency states are thought to cause teratogenic effects.

While vitamin B12 can be excreted into milk, it is safe to use while nursing.

Overdosage/Acute Toxicity

No overdose information was located, but an inadvertent overdose of cyanocobalamin given via SC or IM injection is unlikely to cause significant morbidity.

Drug Interactions

No significant drug interactions have been identified when cyanocobalamin is administered parenterally.

Laboratory Considerations

- Serum samples to be analyzed for cobalamin and/or folate should be protected from bright light and excessive heat
- If a microbiologic method assay is used to determine cobalamin values, concurrent use of antibiotics can cause falsely low serum or red blood cell values

Doses

- **DOGS:**
  a) Cobalamin deficiency in dogs with severe GI disease: Injectable cyanocobalamin at 25 mcg/kg once per week for 4–6 weeks, then once monthly thereafter to maintain normal serum levels. (Zoran 2006d)

b) Cobalamin deficiency associated with GI disease: Based on body size, 250–800 mcg SC once weekly for 6 weeks, one more dose a month later and a re-check one month after that. Re-evaluation is important to determine if continued cobalamin supplementation is indicated. (Stiener 2005)

c) Cobalamin deficiency associated with exocrine pancreatic insufficiency: 250–500 mcg parenterally; repeat treatment based upon serum levels. (Westermarck, Wiberg et al. 2005)

■ **CATS:**

a) Cobalamin deficiency in cats with IBD: 250–500 mcg (total dose per cat) SC once per week for 6 weeks, then every 1–2 months. (Marks 2003)

b) Cobalamin deficiency associated with GI disease: Based on body size, 150–250 mcg SC once weekly for 6 weeks, one more dose a month later and a re-check one month after that. Re-evaluation is important to determine if continued cobalamin supplementation is indicated. (Stiener 2005)

c) Cobalamin deficiency associated with exocrine pancreatic insufficiency: 100–250 mcg SC once weekly; periodically assess cobalamin and folate levels. (Westermarck, Wiberg et al. 2005)

■ **HORSES:**

a) For vitamin B12 deficiency: 1–2 mL of a 1000 mcg/mL injection (1000–2000 mcg) injected IM or SC; dosage may be repeated once or twice weekly, as indicated by condition or response. (Label information; Amtech Vitamin B12 1000 mcg—IVX)

■ **CATTLE, SHEEP:**

a) For treatment of vitamin B12 deficiency associated with cobalt deficiency: Lambs: 100 mcg injected once weekly. Adult sheep: 300 mcg injected once weekly. (Baxter 1986)

b) For treatment of vitamin B12 deficiency associated with cobalt deficiency: Cattle and sheep: 0.2–0.4 mL of a 5000 mcg/mL injection (1000–2000 mcg) injected IM or SC; dosage may be repeated in weekly intervals if necessary. (Label information; Vitamin B12 5000 mcg—Butler)

■ **SWINE:**

a) For vitamin B12 deficiency: 0.1–0.4 mL of a 5000 mcg/mL injection (500–2000 mcg) injected IM or SC; dosage may be repeated in weekly intervals if necessary. (Label information; Amtech Vitamin B12 5000 mcg—IVX)

Monitoring

- Cobalamin levels
- In small animals: folate status; both before and after treatment with cyanocobalamin
- Clinical signs associated with deficiency
- CBC, baseline and ongoing if abnormal

Client Information

- Several weeks after starting B12 therapy may be required before improvement is seen
- Vitamin B12 deficiency in animals may require life-long treatment
- As cyanocobalamin may be administered SC, clients can be instructed to administer at home, but the importance of ongoing follow-up with the veterinarian must be stressed

Chemistry/Synonyms

Cyanocobalamin occurs as dark red crystals or crystalline powder. It is sparingly soluble in water (1 in 80) and soluble in alcohol. When in the anhydrous form, it is very hygroscopic and can absorb substantial amounts of water from the air.

Vitamin B12 may also be known as cobalamins. Cyanocobalamin may also be known as: cyanocobalamine, cyanocobalaminum, cobamin, cianokobalaminas, cianocobalamina, or cycobemin; many internationally registered trade names.

Storage/Stability/Compatibility

Cyanocobalamin injection should be stored below 40°C; protect from light and freezing. Cyanocobalamin injection is reportedly **compatible** with all commonly used intravenous fluids.

Dosage Forms

VETERINARY-LABELED PRODUCTS:

Cyanocobalamin (Vitamin B_{12}) Injection 1000, 3000 and 5000 mcg/mL in 100 mL, 250 mL and 500 mL multi-dose vials depending on source; generic; (Rx). Products may be labeled as cyanocobalamin or vitamin B12, and be labeled for use in cattle, horses, dogs, cats, sheep, or swine.

There are many combination products, both oral and injectable, containing cyanocobalamin as one of the ingredients. These are not recommended for use when cobalamin deficiency states exist.

HUMAN-LABELED PRODUCTS:

Cyanocobalamin (crystalline, Vitamin B_{12}) Injection 100 mcg (0.1 mg) per mL and 1000 (1 mg) per mL, vial sizes range from 1 mL single-use to 10 and 30 mL multi-dose; generic; (Rx). Besides generically labeled products, there are several products available with a variety of trade names, including *Cyanoject®*, *Rubesol®*, *Crysti®*, or *Crystamine®*.

Oral tablet dosage forms are also available, but are not appropriate for therapy of cobalamin deficient states in small animal medicine. A nasally administered product is marketed, but there is no information on its use in dogs or cats.

CYCLOPHOSPHAMIDE

(sye-kloe-*foss*-fa-mide) Cytoxan®, Neosar®

IMMUNOSUPPRESSIVE/ANTINEOPLASTIC

Prescriber Highlights

- **Antineoplastic/immunosuppressive used in dogs & cats for a variety of conditions**
- **Contraindications: Prior anaphylaxis; caution in patients with leukopenia, thrombocytopenia, previous radiotherapy, impaired hepatic or renal function, or in those for whom immunosuppression may be dangerous (*e.g.,* infection)**
- **Potentially teratogenic, fetotoxic**
- **Primary adverse effects are myelosuppression, GI effects, alopecia (especially Poodles, Old English Sheepdogs, etc.), & hemorrhagic cystitis**
- **Adequate monitoring essential**

Uses/Indications

In veterinary medicine, cyclophosphamide is used primarily in small animals (dogs and cats) in combination with other agents both as an antineoplastic agent (lymphomas, leukemias, carcinomas, and sarcomas) and as an immunosuppressant (SLE, ITP, IMHA, pemphigus, rheumatoid arthritis, proliferative urethritis, etc.). Its use in treating acute immune-mediated hemolytic anemia is controversial;