Storage/Stability/Compatibility

It is recommended to store midazolam injection at room temperature (15°–30°C) and protected from light. After being frozen for 3 days and allowed to thaw at room temperature, the injectable product was physically stable. Midazolam is stable at a pH from 3–3.6.

Midazolam is reportedly physically **compatible** when mixed with the following products: D_5W, normal saline, lactated Ringer's, atropine sulfate, fentanyl citrate, glycopyrrolate, hydroxyzine HCl, ketamine HCl, meperidine HCl, morphine sulfate, nalbuphine HCl, promethazine HCl, sufentanil citrate, and scopolamine HBr. 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: None

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

HUMAN-LABELED PRODUCTS:

Midazolam HCl Injection: 1 mg (as HCl)/mL in 1 mL, 2 mL, 5 mL vials and *Carpuject* vials, 10 mL vials; 5 mg (as HCl)/mL in 1 mL, 2 mL, 5 mL vials and *Carpuject* vials, 10 mL vials, 2 mL syringes; generic; (Rx, C-IV)

Midazolam HCl Syrup: 2 mg/mL in 118 mL; generic; (Roxane); (Rx, C-IV)

MILBEMYCIN OXIME

(mil-beh-*my*-sin) Interceptor®, Sentinel®

MACROLIDE ANTIPARASITIC

For information on the combination product with lufenuron (Sentinel®), see the lufenuron monograph

Prescriber Highlights

- **GABA inhibitor in invertebrates used for heartworm prophylaxis, microfilaricide, & treat demodicosis, etc.**
- **Contraindications: No absolute contraindications**
- **Adverse Effects: Animals with circulating microfilaria may develop a transient shock-like syndrome; at higher doses, neuro signs become more likely**

Uses/Indications

Milbemycin tablets are labeled as a once-a-month heartworm preventative (*Dirofilaria immitis)* and for hookworm control (*Ancylostoma caninum*). It has activity against a variety of other parasites, including adult hookworms (*A. caninum*), adult roundworms (*T. canis, T. leonina*) and whipworms (*Trichuris vulpis*). In cats, milbemycin has been used successfully to prevent larval infection of *Dirofilaria immitis*.

Milbemycin, like ivermectin can be used for treatment of generalized demodicosis in dogs, but treatment can be significantly more expensive. It is likely safer to use in breeds susceptible to mdr1 genetic mutation (Collies, Shelties, Australian shepherds, etc.) at the doses used for this indication, but neuro toxicity is possible. Older dogs, those that have had a long duration of disease prior to treatment, and dogs with pododemodicosis appear have a lower success rate with milbemycin treatment.

Pharmacology/Actions

Milbemycin is thought to act by disrupting the transmission of the neurotransmitter gamma amino butyric acid (GABA) in invertebrates.

Pharmacokinetics

No specific information was located. At labeled doses, milbemycin is considered effective for at least 45 days after infection by *D. immitis* larva.

Contraindications/Precautions/Warnings

Because some dogs with a high number of circulating microfilaria will develop a transient, shock-like syndrome after receiving milbemycin, the manufacturer recommends testing for preexisting heartworm infections.

The manufacturer states to not use the product (*Interceptor*®) in puppies less than 4 weeks of age or less than 2 lbs. of body weight or in kittens less than 6 weeks of age or less than 1.5 lbs. of body weight.

Adverse Effects

At labeled doses, adverse effects appear to be negligible in microfilaria-free dogs, including breeds susceptible to neurologic toxicity (see Overdosage below). At higher dosages (*e.g.*, used for treating demodicosis) neurologic effects may be more likely particularly in dog breeds (Collies, etc.) with the genetic mutation that affects P-glycoprotein.

Eight week old puppies receiving 2.5 mg/kg (5X label) for 3 consecutive days showed no clinical signs after the first day, but after the second or third consecutive dose, showed some ataxia and trembling.

Reproductive/Nursing Safety

The manufacturer states that safety in breeding, pregnant, and lactating queens and breeding toms has not been established.

Studies in pregnant dogs at daily doses 3X those labeled showed no adverse effects to offspring or bitch.

Milbemycin does enter maternal milk; at standard doses, no adverse effects have been noted in nursing puppies.

Overdosage/Acute Toxicity

Beagles have tolerated a single oral dose of 200 mg/kg (200 times monthly rate). Rough-coated collies have tolerated doses of 10 mg/kg (20 times labeled) without adversity. Toxic doses can cause mydriasis, hypersalivation, lethargy, ataxia, pyrexia, seizures, coma and death. There is no specific antidotal treatment and supportive therapy is recommended.

Drug Interactions

The manufacturer states that the drug was used safely during testing in dogs receiving other frequently used veterinary products, including vaccines, anthelmintics, antibiotics, steroids, flea collars, shampoos and dips.

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

- **BENZODIAZEPINES**: Effects may be potentiated by milbemycin; use together not advised in humans

Caution is advised if using other drugs that can inhibit **p-glycoprotein** particularly in those dogs at risk for MDR1-allele mutation (Collies, Australian Shepherds, Shelties, Long-haired Whippet, etc. "white feet"), unless tested "normal": Drugs and drug classes involved include:

- **AMIODARONE**
- **AZOLE ANTIFUNGALS** (*e.g.*, **ketoconazole**)
- **CARVEDILOL**
- **CYCLOSPORINE**
- **DILTIAZEM**
- **ERYTHROMYCIN; CLARITHROMYCIN**
- **QUINIDINE**
- **SPIRONOLACTONE**
- **TAMOXIFEN**
- **VERAPAMIL**

Doses

- **DOGS:**

For prophylaxis and treatment of dirofilariasis it is suggested to review the guidelines published by the American Heartworm Society at www.heartwormsociety.org for more information

As a parasiticide:

a) For heartworm prophylaxis, control of adult hookworms (*A. caninum*), adult roundworms (*T. canis, T. leonina*) and whipworms (*Trichuris vulpis*) in dogs 4 weeks of age or older and at least 2 lbs. body weight: Minimum dosage is 0.5 mg/kg PO once a month. (Label information; *Interceptor*®—Novartis)

b) 0.5–0.99 mg/kg PO once monthly (also controls hookworm, roundworm and whipworm infestations) (Calvert 1994)

c) For control of fleas (prevents egg development), heartworm prophylaxis, control of adult hookworms (*A. caninum*), adult roundworms (*T. canis, T. leonina*) and whipworms (*Trichuris vulpis*) in dogs 4 weeks of age or older and at least 2 lbs. body weight: Minimum dosage is 0.5 mg/kg PO once a month. (Label directions; *Sentinel*®—Novartis) [**Note**: when used with nitenpyram (*Capstar*®) adult fleas are controlled as well]

For microfilaricide chemotherapy:

a) In adulticide-pretreated dogs: Use preventative/prophylaxis dosage; repeat in 2 weeks if necessary. If heartworm transmission season has started, continue monthly prophylaxis. (Knight 1995)

b) In adulticide-pretreated dogs: Approximately one month after melarsomine give milbemycin at 0.5 mg/kg PO. (Legendre and Toal 2000)

For treatment of generalized demodicosis:

a) 0.5–2 mg/kg PO once daily. Higher dose seems to be more effective. (DeManuelle 2000)

b) 2 mg/kg PO daily for 30 days past two consecutive negative skin scrapings obtained 4–6 weeks apart. At doses no higher than 2 mg/kg/day, breeds at high risk for toxicity (Collies, Shelties, Australian shepherds, etc.) are apparently tolerant to milbemycin. (Torres 2007b)

c) 1 mg/kg PO twice daily for at least 3 months (White 2000)

For treatment of cheyletiellosis:

a) 2 mg/kg PO every 7 days for 3 doses (White 2000)

For treatment of scabies:

a) 2 mg/kg PO every 7 days for 3 doses or 0.75 mg/kg once daily for 30 days (White 2000)

- **CATS:**

For prevention of heartworm; treat adult hookworm and adult roundworms:

a) 2 mg/kg PO once monthly (Label directions; *Interceptor*® *Flavor Tabs for Cats*—Novartis)

- **REPTILES:**

For nematodes:

a) 0.5–1 mg/kg PO; repeat in 2 weeks. If 14 days after second dose, fecal is positive a third dose is given and the cycle continued until parasites are cleared. Milbemycin appears to be safe in chelonians (unlike ivermectin). (de la Navarre 2003b)

Client Information

- Review importance of compliance with therapy and to be certain that the dose was consumed.

Chemistry/Synonyms

Milbemycin oxime consists of approximately 80% of the A_4 derivatives and 20% of the A_3 derivatives of 5-didehydromilbemycin. Milbemycin is considered to be a macrolide antibiotic structurally.

Milbemycin may also be known as CGA-179246, *Interceptor*® and *Sentinel*®.

Storage/Stability

Store milbemycin oxime tablets at room temperature.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Milbemycin Oxime Oral Tablets: 2.3 mg (brown, 2–10 lbs), 5.75 mg (green, 11–25 lbs), 11.5 mg (yellow, 26–50 lbs), 23 mg (white, 51–100 lbs), dogs >100 lbs are provided the appropriate combination of tablets; *Interceptor*® *Flavor Tabs*; (Novartis); (Rx). Approved for use in dogs and puppies >4 weeks of age and 2 lbs or greater.

Milbemycin Oxime Oral Tablets: 5.75 mg (1.5–6 lbs), 11.5 mg (6.1–12 lbs), 23 mg (white, 12.1–25 lbs); *Interceptor*® *Flavor Tabs*; (Novartis); (Rx). Approved for cats and kittens >6 wks old and >1.5 lbs.

Milbemycin/Lufenuron Oral Tablets (with Nitenpyram Oral Tablets in the combination flea management system) for Dogs:

For dogs 2–10 lb: 46 mg milbemycin/lufeneron, (11.4 mg nitenpyram)

For dogs 11–25 lb: 115 mg milbemycin/lufenuron, (11.4 mg nitenpyram)

For dogs 26–50 lb: 230 mg milbemycin/lufenuron, (57 mg nitenpyram)

For dogs 51–100 lb: 460 mg milbemycin/lufenuron, (57 mg nitenpyram)

For dogs 100–125 lb: (appropriate number supplied) milbemycin/lufenuron, (57 mg nitenpyram)

Sentinel® *Flavor Tabs & Sentinel*® *Flavor Tabs with Capstar*® *Flea Management System* (Novartis); (Rx). Approved for use in dogs and puppies 4 weeks of age or older.

There is also a milbemycin 0.1% otic solution (*Milbemite*®) available.

HUMAN-LABELED PRODUCTS: None

Milk Thistle—see Silymarin

MINERAL OIL

White Petrolatum

LUBRICANT LAXATIVE

Prescriber Highlights

- Lubricant laxative
- Cautions: Debilitated or pregnant patients, & patients with hiatal hernia, dysphagia, esophageal or gastric retention
- Use caution when administering by tube to avoid aspiration
- Adverse Effects: Lipid pneumonitis if aspirated; granulomatous reactions in liver etc. if significant amounts are absorbed from gut; oil leakage from the anus; long-term use may lead to decreased absorption of fat-soluble vitamins (A, D, E, & K)
- Drug interactions

Uses/Indications

Mineral oil is commonly used in horses to treat constipation and fecal impactions. It is also employed as a laxative in other species as well, but used less frequently. Mineral oil has been administered after ingesting lipid-soluble toxins (*e.g.*, kerosene, metaldehyde) to retard the absorption of these toxins through its laxative and solubility properties.

Petrolatum containing products (*e.g.*, *Felaxin®*, *Laxatone®*, *Kat-A-Lax®*, etc.) may be used in dogs and cats as a laxative or to prevent/reduce "hair-balls" in cats.

Pharmacology/Actions

Mineral oil and petrolatum act as laxatives by lubricating fecal material and the intestinal mucosa. They also reduce reabsorption of water from the GI tract, thereby increasing fecal bulk and decreasing intestinal transit time.

Pharmacokinetics

It has been reported that after oral administration, emulsions of mineral oil may be up to 60% absorbed, but most reports state that mineral oil preparations are only minimally absorbed from the gut.

Contraindications/Precautions/Warnings

No specific contraindications were noted with regard to veterinary patients. In humans, mineral oil (orally administered) is considered contraindicated in patients less than 6 yrs. old, debilitated or pregnant patients, and patients with hiatal hernia, dysphagia, esophageal or gastric retention. Use caution when administering by tube to avoid aspiration, especially in debilitated or recalcitrant animals. To avoid aspiration in small animals, orally administered mineral oil should not be attempted when there is an increased risk of vomiting, regurgitation, or other preexisting swallowing difficulty. Many clinicians believe that mineral oil should not be administered orally to small animals due to the risk for aspiration and, if used as a laxative, should be administered rectally.

Adverse Effects

When used on a short-term basis and at recommended doses, mineral oil or petrolatum should cause minimal adverse effects. The most serious effect that could be encountered is aspiration of the oil with resultant lipid pneumonitis; prevent this by using the drug only in appropriate cases, when "tubing", ascertain that the tube is in the stomach, and administrate the oil at a reasonable rate.

Granulomatous reactions have occurred in the liver, spleen and mesenteric lymph nodes when significant quantities of mineral oil are absorbed from the gut. Oil leakage from the anus may occur and be of concern in animals with rectal lesions or in house pets. Long-term administration of mineral oil/petrolatum may lead to decreased absorption of fat-soluble vitamins (A, D, E, and K). No reports were found documenting clinically significant hypovitaminosis in cats receiving long-term petrolatum therapy, however.

Reproductive/Nursing Safety

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.*)

Oral mineral oil should be safe to use during nursing.

Overdosage/Acute Toxicity

No specific information was located regarding overdoses of mineral oil; but it would be expected that with the exception of aspiration, the effects would be self-limiting. See adverse effects section for more information.

Drug Interactions

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

- **DOCUSATE**: Theoretically, mineral oil should not be given with docusate (DSS) as enhanced absorption of the mineral oil could occur. However, this does not appear to be of significant clinical concern with large animals.
- **VITAMINS A, D, E, K**: Chronic administration of mineral oil may affect Vitamin K and other fat-soluble vitamin absorption. It has been recommended to administer mineral oil products between meals to minimize this problem.

Doses

- **DOGS:**

  As a laxative:
  a) 2–60 mL PO (Jenkins 1988), (Kirk 1989)
  b) 5–30 mL PO (Davis 1985a)
  c) 5–25 mL PO (Burrows 1986)

- **CATS:**

  As a laxative (See specific label directions for "Cat Laxative" Products):
  a) 2–10 mL PO (Jenkins 1988), (Kirk 1989)
  b) 2–6 mL PO (Davis 1985a)
  c) 5 mL per day with food (Sherding 1989)

- **RABBITS, RODENTS, SMALL MAMMALS:**

  a) Rabbits: As a laxative/remove hairballs: Using feline laxative product: 1–2 mL/day for 3–5 days (Ivey and Morrisey 2000)

- **CATTLE:**

  Note: Administer via stomach tube.
  As a laxative:
  a) 1–4 liters (Howard 1986)
  b) Adults: 0.5–2 liters; Calves: 60–120 mL (Jenkins 1988)

  For adjunctive treatment of metaldehyde poisoning:
  a) 8 mL/kg; may be used with a saline cathartic (Smith 1986)

  For adjunctive treatment of nitrate poisoning:
  a) 1 liter per 400 kg body weight (Ruhr and Osweiler 1986)