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.*)

It is not known whether this drug is excreted in maternal milk; exercise caution.

Overdosage/Acute Toxicity

The acute LD_{50} of pralidoxime in dogs is 190 mg/kg and, at high dosages, causes signs associated with its own anticholinesterase activity. Clinical signs of toxicity in dogs may be exhibited as muscle weakness, ataxia, vomiting, hyperventilation, seizures, respiratory arrest, and death.

Drug Interactions

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

- **BARBITURATES**: Anticholinesterases can potentiate the action of barbiturates; use with caution.
- **CIMETIDINE**, **SUCCINYLCHOLINE, THEOPHYLLINE, RESERPINE,** and **RESPIRATORY DEPRESSANT DRUGS** (*e.g.*, **narcotics, phenothiazines**): Use should be avoided in patients with organophosphate toxicity.

Doses

Note: Often used in conjunction with atropine; refer to that monograph and/or the references below for more information.

- **DOGS & CATS:**

  For organophosphate poisoning:

  a) Pralidoxime works best when combined with atropine. Pralidoxime at 20 mg/kg, 2–3 times a day. Initial dose may be given either IM or slow IV. Subsequent doses may be given IM or SC. (Refer to reference for more specific guidelines regarding adjunctive therapy) (Fikes 1990)

  b) 10–15 mg/kg IM or SC q8–12h; 36 hour minimum (Firth 2000)

  c) Give atropine first at 0.1 mg/kg IV, followed by an additional 0.3 mg/kg IM. Then pralidoxime at 50 mg/kg diluted in 10% glucose and administered via slow IV. If a severe poisoning and muscle weakness has not been relieved, may give another dose in one hour. For small dogs or cats, pralidoxime may be administered IM or IP. Reduce dose in presence of renal failure. Recovery should occur gradually over 48 hours. (El Bahri 2002)

  d) Dogs: 50 mg/kg; Cats 20 mg/kg. Give IV slowly or with fluids over a 30-minute period. Repeat in one hour if clinical signs persist and then q8h for 24–48 hours. Author recommends using pralidoxime in animals that are severely depressed, weak, and anorectic one or more days after exposure if not previously treated with pralidoxime. In animals that have clinical signs intensified (*e.g.*, respiratory depression), reduce dose and give as repeated one-hour infusions every 4–8 hours in combination with atropine (0.04–0.4 mg/kg) once or as needed (Mount 1989)

  e) Cats: 20 mg/kg IM or IV within first 24 hours of exposure. May repeat q6–8h and combine with atropine or give separately. Do not use in carbamate toxicity. (Reid and Oehme 1989)

- **CATTLE:**

  Note: When used in food animals, FARAD recommends a 28 day meat and a 6 day milk withdrawal time. (Haskell, Payne et al. 2005)

  For organophosphate poisoning:

  a) 25–50 mg/kg as a 20% solution IV over 6 minutes; or as a maximum of 100 mg/kg/day as an IV drip (Smith 1986)

- **HORSES:**

  For organophosphate poisoning:

  a) 20 mg/kg (may require up to 35 mg/kg) IV and repeat q4–6h (Oehme 1987c)

- **BIRDS:**

  For organophosphate poisoning:

  a) 10–20 mg/kg q8–12h (route not specified) with atropine (0.2–0.5 mg/kg IM q3–4h). (Jones 2007a)

Monitoring

- Pralidoxime therapy is monitored via the clinical signs associated with organophosphate poisoning. For more information, refer to one of the references outlined in the dosage section.

Client Information

- This agent should only be used with close professional supervision.

Chemistry/Synonyms

A quaternary ammonium oxime cholinesterase reactivator, pralidoxime chloride occurs as a white to pale yellow, crystalline powder with a pK_a of 7.8–8. It is freely soluble in water. The commercially available injection has a pH of 3.5–4.5 after reconstitution.

Pralidoxime Chloride may also be known as: 2-Formyl-1-methylpyridinium chloride oxime, 2-PAM, 2-PAM chloride, 2-PAMCl, 2-pyridine aldoxime methochloride and *Protopam*®.

Storage/Stability

Unless otherwise instructed by the manufacturer, pralidoxime chloride powder for injection should be stored at room temperature. After reconstituting with sterile water for injection, the solution should be used within a few hours. Do not use sterile water with preservatives added.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Pralidoxime Chloride Powder for Injection: 1 g in 20 mL single-use vials; *Protopam® Chloride* (Wyeth-Ayerst); (Rx)

PRAZIQUANTEL

(pra-zi-***kwon***-tel) **Droncit®**

ANTICESTODAL ANTIPARASITIC

Prescriber Highlights

- **Anticestodal anthelmintic also may be useful for some other parasites**
- **Contraindications: Puppies less than 4 weeks old or kittens less than 6 weeks old; hypersensitivity to the drug**
- **Adverse Effects: Uncommon after oral use; pain at injection site, anorexia, salivation, vomiting, lethargy, weakness, or diarrhea possible after using injectable**

Uses/Indications

Praziquantel is indicated for (approved labeling) for the treatment of *Dipylidium caninum*, *Taenia pisiformis*, and *Echinococcus granulosis* in dogs, and *Dipylidium caninum* and *Taenia taeniaeformis* in cats. Fasting is not required nor recommended before dosing. A single dose is usually effective, but measures should be taken to prevent reinfection, particularly against *D. caninum*. Praziquantel can also be used for treating *Alaria* spp. in dogs and cats and *Spirometra mansonoides* infections in cats.

Praziquantel has been used in birds and other animals, but it is usually not economically feasible to use in large animals. In humans, praziquantel is used for schistosomiasis, other trematodes (lung, liver, intestinal flukes) and tapeworms. It is not routinely effective in treating *F. hepatica* infections in humans.

Combination products can give a wide spectrum of internal parasite control in a variety of species.

Pharmacology/Actions

Praziquantel's exact mechanism of action against cestodes has not been determined, but it may be the result of interacting with phospholipids in the integument causing ion fluxes of sodium, potassium and calcium. At low concentrations *in vitro*, the drug appears to impair the function of their suckers and stimulates the worm's motility. At higher concentrations *in vitro*, praziquantel increases the contraction (irreversibly at very high concentrations) of the worm's strobilla (chain of proglottids). In addition, praziquantel causes irreversible focal vacuolization with subsequent cestodal disintegration at specific sites of the cestodal integument.

In schistosomes and trematodes, praziquantel directly kills the parasite, possibly by increasing calcium ion flux into the worm. Focal vacuolization of the integument follows and the parasite is phagocytized.

Pharmacokinetics

Praziquantel is rapidly and nearly completely absorbed after oral administration, but there is a significant first-pass effect. Peak serum levels are achieved between 30–120 minutes in dogs.

Praziquantel is distributed throughout the body. It crosses the intestinal wall and across the blood-brain barrier into the CNS.

Praziquantel is metabolized in the liver to metabolites of unknown activity. It is excreted primarily in the urine; elimination half-life is approximately 3 hours in the dog.

Contraindications/Precautions/Warnings

The manufacturer recommends not using praziquantel in puppies less than 4 weeks old or in kittens less than 6 weeks old. However, a combination product containing praziquantel and febantel from the same manufacturer is approved for use in puppies and kittens of all ages. No other contraindications are listed for this compound from the manufacturer. In humans, praziquantel is contraindicated in patients hypersensitive to the drug.

Adverse Effects

When used orally, praziquantel can cause anorexia, vomiting, lethargy, or diarrhea in dogs, but the incidence of these effects is less than 5%. In cats, adverse effects were quite rare (<2%) in field trials using oral praziquantel, with salivation and diarrhea being reported.

A greater incidence of adverse effects has been reported after using the injectable product. In dogs, pain at the injection site, vomiting, drowsiness, and/or a staggering gait were reported from field trials with the drug. Some cats (9.4%) showed clinical signs of diarrhea, weakness, vomiting, salivation, sleepiness, transient anorexia, and/or pain at the injection site.

Reproductive/Nursing Safety

Praziquantel is considered safe to use in pregnant dogs or cats. In humans, the FDA categorizes this drug as category ***B*** for use during pregnancy (*Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but 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.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as class: ***A*** (*Probably safe. Although specific studies may not have proved he safety of all drugs in dogs and cats, there are no reports of adverse effects in laboratory animals or women.*)

Praziquantel appears in maternal milk at a concentration of approximately 25% of that in maternal serum, but is unlikely to pose harm to nursing offspring.

Overdosage/Acute Toxicity

Praziquantel has a wide margin of safety. In rats and mice, the oral LD_{50} is at least 2 g/kg. An oral LD_{50} could not be determined in dogs, as at doses greater than 200 mg/kg, the drug induced vomiting. Parenteral doses of 50–100 mg/kg in cats caused transient ataxia and depression; injected doses at 200 mg/kg were lethal in cats.

There were 51 exposures to praziquantel reported to the ASPCA Animal Poison Control Center (APCC; www.apcc.aspca.org) during 2001–2006. In these cases 24 were dogs and 27 were cats. No clinical signs were reported.

Drug Interactions

Reportedly in humans, synergistic activity occurs with praziquantel and oxamniquine in the treatment of schistosomiasis. The clinical implications of this synergism in veterinary patients is not clear.

Doses

■ **DOGS:**

a) For susceptible cestodes:
IM or SC using the 56.8 mg/mL injectable product:
Body weight: Dose
≤5 lbs: 17 mg (0.3 mL)
6–10 lbs: 28.4 mg (0.5 mL)
11–25 lbs: 56.8 mg (1 mL)
≥25 lbs: 0.2 mL/5 lb body weight; maximum 3 mL
Oral: Using the 34 mg canine tablet:
Body weight: Dose
≤5 lbs: 17 mg (1/2 tab)
6–10 lbs: 34 mg (1 tab)
11–15 lbs: 51 mg (1.5 tabs)
16–30 lbs: 68 mg (2 tabs)
31–45 lbs: 102 mg (3 tabs)
46–60 lbs: 136 mg (4 tabs)
≥60 lbs: 170 mg (5 tabs maximum); (Package insert; *Droncit® Injectable* and *Tablets*—Bayer)

b) For *Echinococcus granulosis*: 10 mg/kg (Sherding 1989)

c) For *Diphyllobothrium* spp: 7.5 mg/kg PO once (Kirkpatrick, Knochenhauer, and Jacobsen 1987)

d) For *Spirometra mansonoides* or *Diphyllobothrium erinacei:* 7.5 mg/kg, PO once daily for 2 days (Roberson 1988a)

e) For treatment of Paragonimiasis (*Paragonimus kellicotti*): 23–25 mg/kg PO q8h for 3 days (Reinemeyer 1995), (Hawkins 2000)

f) For treatment of liver flukes (Platynosum or Opisthorchiidae families): 20–40 mg/kg PO once daily for 3–10 days (Taboada 1999)
g) For *Alaria* spp.: 20 mg/kg PO (Ballweber 2004)
h) For giardia using *Drontal Plus®*: Use label dose once daily PO for 3 days. (Lappin 2006b)

■ **CATS:**

a) For susceptible cestodes:
IM or SC using the 56.8 mg/mL injectable product:
Body weight: Dose
<5 lbs: 11.4 mg (0.2 mL)
5–10 lbs: 22.7 mg (0.4 mL)
≥10 lbs: 34.1 mg (0.6 mL maximum)
Oral: Using the 23 mg feline tab
Body weight: Dose
<4 lbs:11.5 mg (1/2 tab)
5–11 lbs: 23 mg (1 tab)
>11 lbs: 34.5 mg (1.5 tabs)
(Package insert; *Droncit® Injectable* and *Tablets*—Bayer)
b) For treatment of Paragonimiasis (*Paragonimus kellicotti*): 23–25 mg/kg PO q8h for 3 days (Reinemeyer 1995); (Hawkins 2000)
c) For treatment of Giardia infections: Give two small dog tablets of *Drontal Plus®* (febantel 113.4 mg; pyrantel 22.7 mg; praziquantel 22.7 mg) once daily PO for 5 days. (Scorza, Radecki et al. 2004)
d) For *Alaria* spp.: 20 mg/kg PO (Ballweber 2004)
e) For *Spirometra mansonoides*: 30–35 mg/kg PO. (Bowman 2006b)

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

a) Chinchillas: 6–10 mg/kg PO (Hayes 2000)
b) For tapeworms in mice, rats, hamsters and gerbils: 30 mg/kg, PO once (note the high dosage required) (Burke 1999)
c) Mice, Rats, Gerbils, Hamsters, Guinea pigs, Chinchillas: For tapeworms: 6–10 mg/kg PO (Adamcak and Otten 2000)

■ **SHEEP & GOATS:**

a) For all species of Moniezia, Stilesia, or Avitellina: 10–15 mg/kg (Roberson 1988a)

■ **HORSES:**

For labeled parasites using the oral gel combination of moxidectin/praziquantel:
a) Dial in the weight of the animal on the syringe. Administer gel by inserting the syringe applicator into the animal's mouth through the interdental space and depositing the gel in the back of the mouth near the base of the tongue. Once the syringe is removed, the animal's head should be raised to insure proper swallowing of the gel. Horses weighing more than 1250 lb require additional gel from a second syringe. (Label Directions; *Quest® Plus*—Fort Dodge)

■ **LLAMAS:**

For susceptible parasites:
a) 5 mg/kg, PO (Fowler 1989)

■ **BIRDS:**

For susceptible parasites (tapeworms):
a) 1/4 of one 23 mg tablet/kg PO; repeat in 10–14 days. Add to feed or give by gavage. Injectable form is toxic to finches. (Clubb 1986)
b) For common tapeworms in chickens: 10 mg/kg (Roberson 1988a)
c) For cestodes and some trematodes: Direct dose: 5–10 mg/kg PO or IM as a single dose -*or*- 12 mg of crushed tablets baked into a 9"x9"x2" cake. Finches should have their regular food withheld and be pre-exposed to a non-medicated cake. (Marshall 1993)

■ **REPTILES:**

For cestodes and some trematodes in most species:
a) 7.5 mg/kg PO once; repeat in 2 weeks PO (Gauvin 1993)
For removal of common tapeworms in snakes:
a) 3.5–7 mg/kg (Roberson 1988a)

Monitoring

■ Clinical efficacy

Client Information

■ Fasting is neither required nor recommended before dosing. A single dose is usually effective, but measures should be taken to prevent reinfection, particularly against *D. caninum*.
■ Tablets may be crushed or mixed with food.
■ Because tapeworms are often digested, worm fragments may not be seen in the feces after using.

Chemistry/Synonyms

A prazinoisoquinoline derivative anthelmintic, praziquantel occurs as a white to practically white, hygroscopic, bitter tasting, crystalline powder, either odorless or having a faint odor. It is very slightly soluble in water and freely soluble in alcohol.

Praziquantel may also be known as: EMBAY-8440, praziquantelum, *Biltricide®*, *Bio-Cest®*, *Cercon®*, *Cesol®*, *Cestox®*, *Cisticid®*, *ComboCare®*, *Cysticide®*, *Droncit®*, *Drontal®*, *Ehliten®*, *Equimax®*, *Extiser Q®*, *Mycotricide®*, *Opticide®*, *Quest® Plus*, *Praquantel®*, *Prasikon®*, *Prazite®*, *Prozitel®*, *Sincerck®*, *Teniken®*, *Virbantel®*, *Waycital®*, or *Zifartel®* and *Zimecterin Gold Paste®*.

Storage/Stability/Compatibility

Unless otherwise instructed by the manufacturer, praziquantel tablets should be stored in tight containers at room temperature. Protect from light.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Praziquantel Tablets: 23 mg (feline); 34 mg (canine); *Droncit® Tablets* (Bayer); generic; (Rx; OTC). Approved for use in cats and dogs.

Praziquantel Injection: 56.8 mg/mL in 10 mL and 50 mL vials; *Droncit® Injection* (Bayer); generic; (Rx). Approved for use in cats and dogs.

Combination Products:

Tablets: Praziquantel 18.2 mg/pyrantel pamoate 72.6 mg (as base); *Drontal® Tablets* (Bayer); (OTC). Approved for use in cats and kittens that are 4 weeks of age or older and weigh 1.5 lb. or greater.

Chewable Tablets: Praziquantel 30 mg/pyrantel pamoate 30 mg; & Praziquantel 114 mg/pyrantel pamoate 114 mg chewable tablets; *Virbantel Flavored Chewables®* (Virbac); (OTC). Approved for use in dogs.

Tablets: Praziquantel/pyrantel pamoate plus febantel; *Drontal® Plus Tablets* (Bayer); (Rx); small, medium and large dog sizes. Approved for dogs and puppies 3 weeks of age or older and weighing 2 lb. or greater.

Oral Gel: containing 20 mg/mL moxidectin and 125 mg/mL of praziquantel in 11.6 g syringes (sufficient to treat one 1150 lb horse); *Quest® Plus* (Fort Dodge); *ComboCare® Equine Oral Gel* (Farnam); (OTC). Approved for use in horse or ponies not intended for food purposes.

Oral Paste: containing 1.87% ivermectin and 14.03% of praziquantel in oral syringes (sufficient to treat one 1320 lb horse); *Equimax*® (Pfizer); (OTC). Approved for use in horse or ponies not intended for food purposes.

Oral Paste: containing 1.55% ivermectin and 7.75% of praziquantel in oral syringes (sufficient to treat one 1250 lb horse); *Zimecterin Gold Paste*® (Merial); (OTC). Approved for use in horse or ponies not intended for food purposes.

HUMAN-LABELED PRODUCTS:

Praziquantel Tablets (Film-coated): 600 mg; *Biltricide*® (Bayer); (Rx)

PRAZOSIN HCL

(pra-zoe-***sin***) Minipress®

ALPHA-1 ADRENERGIC BLOCKER

Prescriber Highlights

- Alpha$_1$-blocker that may be useful for adjunctive treatment of CHF, systemic hypertension, or pulmonary hypertension in dogs
- Also used to reduce sympathetic tone to treat functional urethral obstruction in dogs & cats
- Caution: Chronic renal failure or preexisting hypotensive conditions
- Adverse Effects: Potentially hypotension, CNS effects (lethargy, dizziness, etc.), & GI effects

Uses/Indications

Prazosin is less well studied in dogs than hydralazine, and its capsule dosage form makes it less convenient for dosing. Prazosin, however, appears to have fewer problems with causing tachycardia, and its venous dilation effects may be an advantage over hydralazine when preload reduction is desired. It could be considered for therapy for the adjunctive treatment of CHF, particularly when secondary to mitral or aortic valve insufficiency when hydralazine is ineffective or not tolerated. Prazosin may also be used for the treatment of systemic hypertension or pulmonary hypertension in dogs.

Pharmacology/Actions

Prazosin's effects are a result of its selective, competitive inhibition of alpha$_1$-adrenergic receptors. It reduces blood pressure and peripheral vascular resistance and, unlike hydralazine, has dilatory effects on both the arterial and venous side.

Prazosin significantly reduces systemic arterial and venous blood pressures, and right atrial pressure; cardiac output is increased in patients with CHF. Moderate reductions in blood pressure, pulmonary vascular resistance, and systemic vascular resistance are seen in these patients. Heart rates can be moderately decreased or unchanged. Unlike hydralazine, prazosin does not seem to increase renin release so diuretic therapy is not mandatory with this agent (but is usually beneficial in CHF).

Pharmacokinetics

The pharmacokinetic parameters for this agent were not located for veterinary species. In humans, prazosin is variably absorbed after oral administration. Peak levels occur in 2–3 hours.

Prazosin is widely distributed throughout the body and is approximately 97% bound to plasma proteins. Prazosin is minimally distributed into milk. It is unknown if it crosses the placenta.

Prazosin is metabolized in the liver and some metabolites have activity. Metabolites and some unchanged drug (5–10%) are primarily eliminated in feces via the bile.

Contraindications/Precautions/Warnings

Prazosin should be used with caution in patients with chronic renal failure or preexisting hypotensive conditions.

Adverse Effects

Syncope secondary to orthostatic hypotension has been reported in people after the first dose of the drug. This effect may persist if the dosage is too high for the patient. CNS effects (lethargy, dizziness, etc.) may occur, but are usually transient in nature. GI effects (nausea, vomiting, diarrhea, constipation, etc.) have been reported. Tachyphylaxis (drug tolerance) has been reported in humans, but dosage adjustment, temporarily withdrawing the drug, &/or adding an aldosterone antagonist (*e.g.*, spironolactone) usually corrects this.

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.*)

Prazosin is excreted in small amounts in maternal milk and unlikely to pose much risk to nursing offspring.

Overdosage/Acute Toxicity

There were 7 exposures to prazosin reported to the ASPCA Animal Poison Control Center (APCC; www.apcc.aspca.org) during 2005–2006. In these cases 6 were dogs with 1 showing clinical signs and 1 reported cat case that showed clinical signs. Clinical signs in that dog in decreasing frequency included hyperactivity. Tachycardia was seen in the cat.

Evacuate gastric contents and administer activated charcoal using standard precautionary measures if the ingestion was recent and if cardiovascular status has been stabilized. Treat shock using volume expanders and pressor agents if necessary. Monitor and support renal function.

Drug Interactions

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

- **BETA-BLOCKING AGENTS** (*e.g.*, **propranolol**): May enhance the postural hypotensive effects seen after the first dose of prazosin
- **CLONIDINE:** May decrease prazosin antihypertensive effects
- **SILDENAFIL** (and other **PDE INHIBITORS**): May increase risk for hypotension
- **VERAPAMIL** or **NIFEDIPINE:** May cause synergistic hypotensive effects when used concomitantly with prazosin

Doses

- **DOGS:**
  a) For adjunctive treatment of heart failure: 1 mg PO three times daily for dogs weighing less than 15 kg; 2 mg three times daily PO for dogs weighing more than 15 kg (Kittleson 1985b), (Atkins 2007a)
  b) For hypertension: 1–4 mg (total dose) PO q12–24 hours (Brown and Henik 2000)
  c) For hypertension in a large dog: 1 mg (total dose) PO q8–12h (Ware 2003)
  d) To decrease urethral resistance: 1 mg per 15 kg of body weight PO q8h (Lane 2000)