Comments? Questions?
Email: compendium@medimedia.com
Web: VetLearn.com • Fax: 267-685-1221

PHARM PROFILE

FENBENDAZOLE

- **Used as a benzimidazole anthelmintic and antiprotozoal agent**

Matthew Panarella, DVM
Barton's West End Farm, Inc.
Oxford, New Jersey

Fenbendazole (FBZ) is a benzimidazole anthelmintic and antiprotozoal agent that is poorly soluble in water but soluble in dimethyl sulfoxide. As a chemical compound, FBZ is a white crystalline powder.[1]

PHARMACOLOGY

Fenbendazole (methyl 5-phenylthiol-2 benzimidazole carbamate) reportedly has limited absorption from the gastrointestinal (GI) tract, with plasma levels that are typically less than 1% of the administered dose.[1] Absorption typically occurs over 6 to 30 hours after dosing, and better absorption occurs when the drug is given with food, regardless of preparation.[1] Administering FBZ with food enhances bioavailability.[2,3] In sheep, cattle, and pigs, approximately 50% of the drug is excreted unchanged in the feces and up to 1% is excreted unchanged in the urine.[1]

The mode of action of FBZ is via reversible binding to parasite β-tubulin (a protein), which hinders polymerization of microtubules within organelles of cells. This binding inhibits the parasite's ability (at a cellular level) to generate energy and ultimately causes death.[1] FBZ preferentially binds to parasite tubulin due to the temperature differential between host and parasite.[1] Ruminants and horses have delayed passage of FBZ due to the presence of a rumen and cecum, respectively.[4] Greater retention of drug occurs in the rumen, which acts as a depot and increases drug absorption.

Fenbendazole is metabolized in the liver to the two active compounds oxfendazole sulfoxide and oxfendazole sulfone. In swine, FBZ is metabolized by hepatic microsomal oxidation.[5] In ruminants, FBZ undergoes enterohepatic cycling.

INDICATIONS

In general, FBZ is effective against the major GI and lung parasites of many different animal species. Notable exceptions are discussed.

In **dogs** and **cats**, FBZ has good efficacy against hookworms, ascarids, whipworms, and *Taenia* at the labeled dose. In puppies, more than 99% of hookworms and 90% of ascarids are removed when bitches are treated daily starting at the 40th day of gestation to the 14th day of whelping.[1] FBZ causes over 94% reduction in third- and fourth-stage *Toxocara canis* and *Toxocara leonina*. FBZ has been found to be effective in treating *Paragonimus*, *Crenosoma*, and *Giardia* infections in dogs.[6–8] FBZ was found to be safe in cats at up to five times the labeled dose for dogs and three times the duration of dosing.[9] I have used FBZ (50 mg/kg for 5 days PO) to treat acute idiopathic small bowel diarrhea in dogs and cats. This represents an extralabel usage.

In **horses**, FBZ causes over 90% reduction in adult and large and small strongyles; encysted early third-, late third-, and fourth-stage cyathostomes; ascarids; mature *Oxyuris equi;* arteritis caused by fourth-stage *Strongylus vulgaris*; and *Trichostrongylus axei*. A notable exception is its lack of activity against stomach bots.[1] FBZ is approved for use with trichlorfon to remove stomach bots. Repeated dosing after 2 weeks is recommended to maintain reduced egg production and minimize pasture contamination.[10]

In **cattle**, FBZ is 75% effective in eliminating adult and migrating rumen flukes (*Paramphistomum*); reduces by over 90% the number of all major GI parasites (stomach worms, intestinal worms) as fourth- and fifth-stage larvae and over 99% reduction as adults and lungworms; re-

Table 1. Dosing and Administration of Fenbendazole

Species	*Parasite*	*Dosage*[a]
Dog	*Toxocara,*[b] *Toxascaris,*[b] *Trichuris,*[b] *Ancyclostoma,*[b] *Uncinaria*[b]	50 mg/kg for 3 days
	Capillaria plica, Filaroides hirthi	50 mg/kg for 3 days (repeat in 3 weeks or dose for 3–10 days)[18]
	Capillaria aerophila	50 mg/kg for 10–14 days[18] or 22–55 mg/kg for 5–21 days[21]
	Taenia[b]	50 mg/kg for 3 days[1]
	Paragonimus kellicotti	50–100 mg/kg for 10–14 days,[6] 50 mg/kg for 10–14 days[18]
	Crenosoma vulpis,[8] *Giardia*[9]	50 mg/kg for 3 days
	Eucoleus boehmi,[18] *Nanophytes salmincola*[22]	50 mg/kg for 10–14 days
	Heterobilharzia americanum	40 mg/kg for 10 days[1]
Cats	*Toxocara, Ancyclostoma, Strongyloides, Taenia*[18,23]	50 mg/kg for 3 days
	Aelurostrongylus abstrusus	20 mg/kg for 5 days (repeat in 5 days), 25–50 mg/kg q12h for 10–14 days, 50 mg/kg for 10 days, 20–50 mg/kg for 5 days (repeat in 5 days),[18] or 22–55 mg/kg for 5–21 days[22]
	C. aerophila, P. kellicotti[18]	50 mg/kg for 10–14 days
	Capillaria feliscati[18]	50 mg/kg for 3–10 days
	Eurytrema procyonis[1]	30 mg/kg for 6 days
	Ollulanus[1]	20–50 mg/kg for 3 days
Cattle	*Haemonchus,*[b] *Ostertagia,*[b] *Trichostrongylus,*[b] *Bunostomum,*[b] *Nematodirus,*[b] *Cooperia,*[b] *Oesphagostomum,*[b] *Dictyocaulus*[b]	5 mg/kg once[b]
	Monezia,[b] fourth-stage *Ostertagia*[b]	10 mg/kg once
	Paramphistomum[1]	7.5 mg/kg for 6 days
	Fasciola gigantica[1]	5 mg/kg once
	Taenia saginata, cysticerci[1]	50 mg/kg once
	Giardia[11] (calves)	5 mg/kg for 3 days
Sheep and goats	*Muellerius*[1]	15 mg/kg once
	Dicrocoelum[1]	100 mg/kg once
	Monezia[1]	15 mg/kg once
	Thysamosoma actinoides[1]	10 mg/kg once
Horses	*Strongylus,*[b] *Cyathostomum,*[b] *Cylicocylus,*[b] *Cylicostephanus,*[b] *Triodontophorus,*[b] *Oxyuris*[b]	5 mg/kg once
	Third- and fourth-stage strongyles	10 mg/kg for 5 days (paste)
	Parascaris[b]	10 mg/kg once
Birds	Ascarids, *Capillaria,* tapeworms	8 mg/kg for 6 days[1]
Turkeys	Ascarids,[b] *Heterakis,*[b] *Capillaria obsignata*[b]	45 ppm for 6 days
Swine	*Trichuris suis*[b]	15 mg/kg once (65% reduction) or 3 mg/kg for 3 days (99%)
	Stephanurs dentatus,[b] *Metastrongylus,*[b] *Ascaris*[b] (stages adult, L_3, L_4), *Oesophagostumum dentatum*[b] (nodular), *Trichuris*[b] (stages adult, L_2, L_3, L_4)	3 mg/kg for 3 days
	Hyostrongylus[b]	3 mg/kg for 3 days or 6 mg/kg once

(continues on next page)

Table 1. *Continued*

Species	*Parasite*	*Dosage*[a]
Primates	*Acanthocephalan, Prosthenorchis, Physaloptera*[1]	30 mg/kg/day once
Reptiles and amphibians	Gastrointestinal parasites	30–50 mg/kg once[1]
	Spirurides, Oxyurids, Capillaria	50–100 mg/kg once or 30–50 mg/kg for 2 days[1]
Rodents	*Syphacia muris*	150 ppm (8–12 mg/kg/day) for 7 days (repeat in 1 week for 7 days)[1]

[a]Fenbendazole is administered orally.
[b]FDA-approved species and dose; all other listed uses and doses are considered extralabel.

duces by over 75% the number of *Fasciola gigantica*; and kills 100% of *Taenia saginata* tissue cysts. FBZ eliminates *Giardia* infection in calves[11] and can be used in lactating dairy cattle with no milk withdrawal.[12] Sheep and goats have a similar spectrum of use.

Fenbendazole in **swine** is over 99% effective in killing lungworms, kidney worms, and whipworms; is 100% effective for ascarids and nodular worms; and causes a 75% reduction of fourth-stage and 99% reduction of fifth-stage stomach worms. FBZ was found to be 100% effective against fourth-stage ascarids.[13]

Fenbendazole is labeled to treat many **zoo** and **wildlife species**. In zoo ruminants and feral swine, FBZ is indicated for the treatment of lungworms *(Protostrongylus)*, kidney worms *(Stephanurus)*, roundworms *(Ascaris)*, nodular worms *(Oesophagostomum)*, small stomach worms *(Trichostrongylus)*, thread-necked intestinal worms *(Nematodirus)*, barber's pole worms *(Haemonchus)*, and whipworms *(Trichuris)*. In Felidae and Ursidae, FBZ is indicated for the treatment of ascarids, hookworms, whipworms, and tapeworms.[12] FBZ has been used to treat raccoons for ascarid infection[14] and rodents, reptiles, primates, and birds for GI parasites and pinworms.[1]

Fenbendazole is ovicidal against eggs of ruminant trichostrongylids, stomach worms in pigs, ascarids in chickens, and hookworms and whipworms in dogs. Egg production is inhibited in these species within 1 hour of dosing.[1]

Client Counseling Information

- Fenbendazole is safe in many species, including cats.
- It is best to treat on a full stomach or administer with a meal.
- For large animals (e.g., horses, cattle), make sure the mouth is empty of food before administering paste or suspension.
- Store the unused portion at 59°F to 86°F.
- Contact your veterinarian if any adverse signs (e.g., vomiting, diarrhea) occur.
- Repeated doses may need to be given depending on the parasite present. Cattle require a withdrawal time of 8 days before slaughter when given paste products, 11 days when given medicated blocks, 16 days when given natural protein deworming blocks, and 13 days when given medicated top dress pellets.
- There is no withdrawal for milk.
- There is no withdrawal for swine or turkeys.

CAUTIONS

Adverse Reactions

In 1997, the adverse reactions most frequently reported to the FDA regarding animals that had been dosed with FBZ included trembling in cats; diarrhea and death in cattle; death in chickens; anorexia in dogs; and vomiting, abdominal pain, and death in horses.[15] In 1998, the most frequently reported adverse reactions were diarrhea and vomiting in dogs; abdominal pain in horses; and anorexia, depression, and death in sheep.[16] Vomiting and diarrhea may occur in dogs and cats during treatment for *Giardia*.[17] FBZ should not be administered in ruminants given bromsalan (a flukicide) because it causes abortions in cattle and death in sheep.[18]

Contraindications

In food animals, there is a withholding time for FBZ (except for milk from dairy cattle) because of

minute residues detectable in tissues.[1] Drug residues are near the lowest level of detection by 2 days after dosing, but residual quantities are still detectable in the liver 14 days later.[1] FBZ should not be administered to animals with a known hypersensitivity to the drug or to horses intended for food.[12]

Use in Pregnancy

Fenbendazole is safe to use in pregnant bitches and mares at all stages of gestation.[12] There are no known teratogenic or embryotoxic effects in rats, sheep, or cattle.[19] In rabbits, FBZ is fetotoxic but not teratogenic.[19]

ACUTE TOXICITY

The minimum lethal dose of FBZ in cattle is 750 mg/kg, which is 100 times the therapeutic dose.[1] Consecutive daily dosing in dogs was administered at 250 mg/kg for 30 days,[1] 125 mg/kg for 90 days,[1] and 4 mg/kg for 180 days[17] with no adverse effects. Sheep have been dosed at 45 mg/kg for 30 days with no adverse effects.[1] The LD_{50} for rats and mice is more than 10 g/kg.[17] Lifetime exposure in rodents demonstrated no carcinogenesis.[17]

DRUG INTERACTIONS

There is one reported case,[20] published in 1987, of an adverse drug interaction with FBZ. One dog developed aplastic anemia during simultaneous dosing of FBZ and trimethoprim–sulfadiazine. Anemia was resolved after both drugs were discontinued. Which drug might have caused the bone marrow aplasia was not determined. A similar drug combination was given to a healthy animal, but no anemia developed.[20]

DOSAGE AND ADMINISTRATION

Dosing and administration guidelines for FBZ are presented in Table 1. No special monitoring is needed during FBZ administration. Animals with heavy parasite burdens may experience a hypersensitivity reaction when the death of the parasite causes an immune reaction in the host.[18] FBZ has minimal long-term effects on parasites; thus repeated dosing is usually necessary.[18] In horses, treatment should be repeated at 2 weeks and in cattle at 4 to 6 weeks.[10,12]

PREPARATIONS

Commercial preparations are numerous, including granules at 22.2% concentration; a suspension at 10% concentration; a paste at 10% concentration; and a variety of medicated feeds, salt blocks, pellets, and premix products.

STORAGE AND HANDLING

Fenbendazole should be stored at 59°F to 86°F.[12]

REFERENCES

1. Reinemeyer CR, Courtney CH: Chemotherapy of parasitic disease, in Adams HR (ed): *Veterinary Pharmacology and Therapeutics*, ed 7. Ames, Iowa State University Press, 1995, pp 889–953.
2. McKellar QA, Harrison P, Galbraith EA, et al: Pharmacokinetics of fenbendazole in dogs. *J Vet Pharmacol Ther* 13(4):386–392, 1990.
3. McKellar QA, Galbraith EA, Baxter P: Oral absorption and bioavailability of fenbendazole in the dog and the effect of concurrent ingestion of food. *J Vet Pharmacol Ther* 16(2):189–198, 1993.
4. Aiello S, Mays A (eds): Pharmacology, in *Merck Veterinary Manual*. Rahway, NJ, Merck & Co, 1998, pp 1807–1809.
5. Petersen MB, Friis C: Pharmacokinetics of fenbendazole following intravenous and oral administration to pigs. *Am J Vet Res* 61(5):573–576, 2000.
6. Dubey JP, Miller TB, Sharma SP: Fenbendazole for the treatment of *Paragonimus kellicotti* infection in dogs. *JAVMA* 174(8):835–837, 1979.
7. Peterson EN, Barr SC, Gould WJ, et al: Use of fenbendazole for treatment of *Crenosoma vulpis* infection in a dog. *JAVMA* 202(9):1483–1484, 1993.
8. Barr SC, Bowman DD, Heller RL: Efficacy of fenbendazole against giardiasis in dogs. *Am J Vet Res* 55(7):988–990, 1994.
9. Schwartz RD, Donoghue AR, Baggs RB, et al: Evaluation of the safety of fenbendazole in cats. *Am J Vet Res* 61(3):330–332, 2000.
10. Lumdsen GG, Quan-Taylor R, Smith SM, et al: Field efficacy of ivermectin, fenbendazole and pyrantel embonate paste anthelmintics in horses. *Vet Rec* 125(20):497–499, 1989.
11. O'Handley RM, Cockwill C, Jelinski M, et al: Effects of repeat fenbendazole treatment in dairy calves with giardiosis on cyst excretion, clinical signs and production. *Vet Parasitol* 89(3):209–218, 2000.
12. Product information. Panacur®. Millsboro, DE, Intervet, 1996.
13. Stewart TB, Rowell TJ: Susceptibility of fourth-stage *Ascaris suum* larvae to fenbendazole and to host response in the pig. *Am J Vet Res* 47(8):1671–1673, 1986.
14. Bauer C, Gey A: Efficacy of six anthelmintics against luminal stages of *Baylisascaris procyonis* in naturally infected raccoons *(Procyon lotor)*. *Vet Parasitol* 60(1-2):155–159, 1995.
15. FDA: Adverse Drug Experiences, 1997 CVM Annual Summary. Available at: www.fda.gov/cvm/index/ade/ann97.pdf; accessed February 26, 2002.
16. FDA: Adverse Drug Experiences, 1998 CVM Annual Summary. Available at: www.fda.gov/cvm/index/ade/ann98.pdf; accessed February 26, 2002.
17. Lynn RC: Drugs for the treatment of Protozoal infections, in Boothe D (ed): *Small Animal Clinical Pharmacology and Therapeutics*. Philadelphia, WB Saunders Co, 2001, p 265.
18. Plumb DC: *Veterinary Drug Handbook*, ed 3. Ames, Iowa State University Press, 1999, pp 311–314.
19. Lynn RC: Drugs for the treatment of Helminth infections, in Boothe DM (ed): *Small Animal Clinical Pharmacology and Therapeutics*. Philadelphia, WB Saunders Co, 2001, p 267–271.
20. Weiss DJ, Adams LG: Aplastic anemia associated with trimethoprim–sulfadiazine and fenbendazole administration in a dog. *JAVMA* 191(9):1119–1120, 1987.
21. Boothe DM (ed): A systems approach, in *Small Animal Clinical Pharmacology and Therapeutics*. Philadelphia, WB Saunders Co, 2001, p 506.
22. Boothe DM (ed): Drugs affecting the respiratory system, in *Small Animal Clinical Pharmacology and Therapeutics*. Philadelphia, WB Saunders Co, 2001, p 619.
23. Roberson EL, Burke TM: Evaluation of granulated fenbendazole (22.2%) against induced and naturally occurring helminth infection in cats. *Am J Vet Res* 41(9):1499–1502, 1980.