

EPSIPRANTEL Veterinary—Oral-Local

A commonly used brand name for a veterinary-labeled product is *Cestex*.

Note: For a listing of dosage forms and brand names by country availability, see the *Dosage Forms* section(s).

Category: Anthelmintic.

Indications

Note: The text between ^{ELUS} and ^{EL} describes uses that are not included in U.S. product labeling. Text between ^{ELCAN} and ^{EL} describes uses that are not included in Canadian product labeling.

The ^{ELUS} or ^{ELCAN} designation may signify a lack of product availability in the country indicated. See the *Dosage Forms* section of this monograph to confirm availability.

Cats and dogs

Accepted

Cestode, gastrointestinal, infection (treatment)—Epsiprantel tablets are indicated in the treatment of tapeworms, *Dipylidium caninum* in cats and dogs, *Taenia taeniaeformis* in cats, and *Taenia pisiformis* in dogs.^{R-1}

Potentially effective

Cestode, gastrointestinal, infection (treatment)—*Cats and dogs:* ^{ELUS,CAN} There is evidence to suggest that epsiprantel is effective in the treatment of *Echinococcus granulosus* and *Echinococcus multilocularis*; however, there are insufficient data to recommend a dosage that can be relied upon to clear the infection in all animals treated (Evidence rating: A-1).^{{R-9-11}EL}

Chemistry

Chemical group: Pyrazino benzazepine.^{R-5}

Chemical name: (±)-2-(Cyclohexylcarbonyl)-2,3,6,7,8,12b-hexahydropyrazino[2, 1-a][2]benzazepin-4(1*H*)-one.^{R-4}

Molecular formula: C₂₀H₂₆N₂O₂.^{R-4}

Molecular weight: 326.43.^{R-1; 4}

Description: A stable, white solid.^{R-1}

Solubility: Sparingly soluble in water.^{R-1}

Pharmacology/Pharmacokinetics

Mechanism of action/Effect: The mechanism of action of epsiprantel appears to be similar to that of praziquantel, a drug that disrupts the regulation of calcium and other cations. Tetanic muscle contraction and paralysis occurs in the parasite, and the tegument becomes vacuolized.^{R-8; 10}

Absorption: Minimal absorption occurs in cats and dogs after oral administration.^{R-1; 5}

Biotransformation: There is no evidence that epsiprantel is metabolized.^{R-8}

Concentrations: Peak plasma concentration—

Cats: In 83% of cats in one study, the plasma concentration of epsiprantel was below the level of detection in all samples taken after an oral dose of 5.5 mg per kg of body weight (mg/kg).^{R-8} When plasma epsiprantel could be measured, the peak concentration was 0.21 mcg/mL at 30 minutes after administration of the dose.^{R-8}

Dogs: 0.13 mcg/mL (range, <0.5–0.36) at 1 hour after an oral dose of 5.5 mg/kg.^{R-8}

Elimination: *Cats and dogs*—Because only trace amounts are absorbed, epsiprantel is predominantly eliminated in the feces.^{R-8} Less than 0.1% of the dose is eliminated in the urine in dogs.^{R-8}

Precautions to Consider

Reproduction/Pregnancy

There is no information on the safety of administering epsiprantel to breeding or pregnant animals.^{R-1}

Evidence ratings

Evidence Quality

- A Good evidence to support a recommendation for use
- B Moderate evidence to support a recommendation for use
- C Insufficient evidence to support a recommendation for use
- D Moderate evidence to support a recommendation against use
- E Good evidence to support a recommendation against use

Evidence Type

- 1 Species-specific evidence from at least one large randomized and controlled trial (RCT) or multiple small RCTs
- 2 Species-specific evidence from a small RCT, disease models, large case studies, pharmacokinetic studies using surrogate endpoints, or evidence from well-designed trials in a different species that is considered appropriate for comparison
- 3 Dramatic results from either well-designed, species-specific trials without controls, controlled trials without randomization, or small case studies
- 4 Pharmacokinetic studies without surrogate endpoints or well designed pharmacodynamic studies in healthy animals
- 5 *In vitro* studies
- 6 Opinions of respected authorities on the basis of clinical experience or reports of expert committees

Pediatrics

Because studies have not been performed in very young animals, the manufacturer's product labeling does not recommend administering epsiprantel to kittens or puppies less than 7 weeks of age.^{R-1}

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Drug interactions have not been reported with the administration of epsiprantel to animals. It was administered concurrently with diethylcarbamazine citrate, anti-inflammatory agents, insecticides, and nematocides with no interactions reported during clinical field studies.^{R-1} The administration of pyrantel to dogs concurrently with epsiprantel did not affect the cestocidal efficacy of epsiprantel.^{R-6}

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; » = major clinical significance):

Fecal exam; or

Observation for motile proglottids

(reinfection may be noted by eggs or proglottids on fecal examination or by observation of motile proglottids on the feces or perineal region of the animal)

Side/Adverse Effects

Note: Side/adverse effects have not been reported with recommended dosing.

Overdose

For more information in cases of overdose or unintentional ingestion, **contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center** (888-426-4435 or 900-443-0000; a fee may be required for consultation) **and/or the drug manufacturer.**

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs in parentheses where appropriate)—not necessarily inclusive:

Kittens

With a single oral dose of 50 mg/kg (18 times the recommended dose).^{R-2}

Trembling, transient; vomiting

Note: Epsiprantel is highly tolerated in cats. With the above dose, one of five kittens exhibited signs. A single oral dose of 30 mg/kg produced no evidence of toxicity in 7-week old kittens or adult cats.^{R-3} A group of six cats tolerated the administration of 100 mg/kg a day for four days, with no adverse effects reported.^{R-1}

Dogs

With an oral dose of 100 to 500 mg/kg a day for fourteen days (18 to 91 times the recommended dose).^{R-1; 2}

Alkaline phosphatase, increased—with the 500-mg/kg dose only; **lymphocyte count, decreased**—females only; **proteinuria, slight; total white cell count, decreased**—with the 500-mg/kg dose only

Note: Epsiprantel is highly tolerated in dogs. With the above dosage administration, food intake by the dogs was unaffected. Other than isolated instances of vomiting by dogs in all dosing groups in this study (10-, 100-, and 500-mg/kg doses), no adverse physical signs were reported. No significant effects were described in post-treatment tissue samples for histopathology.^{R-2}

A single oral dose of 100 mg/kg administered to 7- to 10-week old puppies produced no overt signs of toxicity.^{R-3}

Treatment of overdose

There is no specific antidote for epsiprantel overdose. If toxicity occurs, recommended treatment consists of the following:

- Decrease absorption with early gastric lavage.
- Supportive treatment

Client Consultation

In providing consultation, consider emphasizing the following selected information:

Taking steps to control exposure to intermediate hosts should be considered in preventing reinfection. For *Taenia taeniaeformis*, intermediate hosts are mice, rats and other rodents. For *Taenia pisiformis*, intermediate hosts are rabbits and other rodents. For prevention of *Dipylidium caninum* infection, effective flea control is important.^{R-1}

Veterinary Dosing Information

Diet

Fasting before treatment is not necessary and, therefore, is not recommended.^{R-1}

Dosing and Dosage Forms

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The ^{ELUS} or ^{ELCAN} designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

DOSAGES

Cats and dogs—For *Epsiprantel Tablets*

Cestode, gastrointestinal, infection—

Cats: Oral, 2.75 mg per kg of body weight.^{R-1} With ongoing exposure, retreatment may be necessary.^{R-1; 3}

Dogs: Oral, 5.5 mg per kg of body weight.^{R-1} With ongoing exposure, retreatment may be necessary.^{R-1; 3}

Note: Cestode, gastrointestinal, infection—^{ELUS,CAN} For the treatment of *Echinococcus* species:

Cats: Although the efficacy has not been established, one study of 15 cats suggests that a dose of 2.75 to 5.5 mg per kg of body weight can be effective in the treatment of *Echinococcus* species.^{R-9}

Dogs: Although the efficacy has not been established, there is evidence to suggest that a single dose of 7.5 and 10 mg per kg of body weight may be necessary to treat adult and immature *Echinococcus* species worms, respectively.^{R-9-11} In some animals, a higher dose or repeated dosing may be necessary to completely clear immature worms.^{EL}

DOSAGE FORMS

Oral

EPSIPRANTEL TABLETS

Strength(s) usually available:

U.S.—^{R-1}

Veterinary-labeled product(s):

12.5 mg (Rx) [*Cestex*].

25 mg (Rx) [*Cestex*].

50 mg (Rx) [*Cestex*].

100 mg (Rx) [*Cestex*].

Canada—^{R-3}

Veterinary-labeled product(s):

12.5 mg (Rx) [*Cestex*].

25 mg (Rx) [*Cestex*].

Packaging and storage: Store between 15 and 30 °C (59 and 86 °F),^{R-1; 3} unless otherwise specified by the manufacturer. Store in a tight container.

Additional information: Keep out of the reach of children.^{R-1}

Developed: 12/01/08

References

1. Cestex Veterinary Tablets product labeling (Pfizer—US), Rev 11/00. Available at www.pfizerah.com. Accessed on September 26, 2008.
2. Freedom of information summary. Cestex (epsiprantel) tablets. NADA 140-893. Sponsor: Beecham Laboratories. Approval date: December 1, 1989. Available at www.fda.gov/cvm. Accessed on September 26, 2008.
3. Cestex product information (Pfizer—Canada). Available at www.pfizer.ca. Accessed on September 26, 2008.
4. USP dictionary of USAN and international drug names, 2008 ed. Rockville, MD: The United States Pharmacopeial Convention Inc; 2008.
5. Manger BR, Brewer MD. Epsiprantel, a new tapeworm remedy. Preliminary efficacy studies in dogs and cats. *Br Vet J* 1989; 145: 384-8.
6. Jacobs DE, Fisher MA, Pilkington JG, et al. Evaluation of the efficacy of an epsiprantel/pyrantel combination against gastrointestinal helminths of dogs. *J Small Anim Pract* 1990; 31: 59-63.
7. Corwin RM, Green SP, Keefe TJ. Dose titration and confirmation tests for determination of cesticidal efficacy of epsiprantel in dogs. *Am J Vet Res* 1989 Jul; 50(7): 1076-7.
8. Reinemeyer CR, Courtney CH. Anticestodal drugs. In: Adams HR, editor. *Veterinary pharmacology and therapeutics*, 8th ed. Ames, Iowa: Blackwell Publishing, 2001. p. 983-4.
9. Eckert J, Thompson RC, Bucklar H, et al. Efficacy evaluation of epsiprantel (Cestex) against *Echinococcus multilocularis* in dogs and cats. *Berl Munch Tierarztl Wochenschr* 2001 Mar-Apr; 114(3-4): 121-6.
10. Thompson RC, Reynoldson JA, Manger BR. *In vitro* and *in vivo* efficacy of epsiprantel against *Echinococcus granulosus*. *Res Vet Sci* 1991; 51: 332-4.
11. Arru E, Garippa G, Manger BR. Efficacy of epsiprantel against *Echinococcus granulosus* infections in dogs. *Res Vet Sci* 1990; 49: 378-9.

Epsiprantel in the treatment of *Echinococcus* species in cats and dogs

Revision date: October 1, 2008

The following tables are not intended to be in-depth reviews of each article. Instead, they are brief overviews/reviews of the studies, assuming reviewers are already familiar with the cited references. If you would like additional information about these studies, please contact veterinary@usp.org.

Back to the indication.

Study 1 of 3: Eckert J, Thompson RC, Bucklar H, et al. Efficacy evaluation of epsiprantel (Cestex) against *Echinococcus multilocularis* in dogs and cats. Berl Munch Tierarztl Wochenschr 2001 Mar-Apr; 114(3-4): 121-6 (from abstract; article in German).

<p>Design</p> <ul style="list-style-type: none"> Controlled study of induced infection <p>N = 16 dogs (4 per group) and 15 cats (5 per group)</p>	<p>Goal: To evaluate the effectiveness of the label dose of epsiprantel against <i>E. multilocularis</i> infection in cats and dogs.</p> <p>Methods:</p> <ul style="list-style-type: none"> Helminth-free cats and dogs were infected with protozoocoles of <i>E. multilocularis</i>. They entered the treatment period 20 days later. Animals were necropsied 4 days after treatment. <p>Dose and duration:</p> <ul style="list-style-type: none"> Canine study 1— <ul style="list-style-type: none"> Treatment group: Oral, 5.1 mg/kg (range, 4.9-5.3 mg/kg) Untreated controls Canine study 2— <ul style="list-style-type: none"> Treatment group: Oral, 5.4 mg/kg (range, 5.2-5.8 mg/kg) Untreated controls Feline study— <ul style="list-style-type: none"> Treatment group 1: Oral, 2.7 mg/kg (range, 2.7-2.8 mg/kg) Treatment group 2: Oral, 5.5 mg/kg Untreated controls Duration of study—4 days after treatment <p>Results:</p> <ul style="list-style-type: none"> No adverse effects were reported. Canine studies— <ul style="list-style-type: none"> In each control group, all animals were infected and had large numbers of intestinal worms, with average individual worm burdens of 59,500 to 149,800 and 20,500 to 43,200 <i>E. multilocularis</i> in dogs in studies 1 and 2, respectively. Four treated dogs were free of worms but the other four had residual worm burdens (10 to 70 worms in three dogs and 1480 in one dog). The treated dogs had reduction of their worm burdens by 99.6% in study 1 and by 99.9% in study 2. Feline study— <ul style="list-style-type: none"> In the untreated cats, the average worm burden was 2864 per animal. Both doses were 100% effective in eliminating <i>E. multilocularis</i> in the 10 treated cats. <p>Conclusions:</p> <ul style="list-style-type: none"> Epsiprantel eliminated at least 99% of <i>E. multilocularis</i> in cats and dogs. Residual worm burdens continued in some animals. 	
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Study 2 of 3: Thompson RC, Reynoldson JA, Manger BR. *In vitro* and *in vivo* efficacy of epsiprantel against *Echinococcus granulosus*. Research in Veterinary Science 1991; 51: 332-4.

<p>Design</p> <ul style="list-style-type: none"> • Preliminary <i>in vitro</i> efficacy and an <i>in vivo</i>, controlled, randomized study of dogs with induced infection <p>N = <i>In vivo</i> studies: Trial 1—18 dogs Trial 2—30 dogs</p>	<p>Goal: To evaluate the effectiveness of epsiprantel against <i>in vitro</i> worms and against canine infection with <i>E. granulosus</i> at different stages of the life cycle.</p> <p>Methods:</p> <ul style="list-style-type: none"> • Protoscoleces were collected from sheep hydatid cysts. Juvenile worms were derived from protoscoleces incubated in evaginating solutions for 7 days. Adult worms for the <i>in vitro</i> study were taken from experimentally infected dogs. • <i>In vitro</i> study— <ul style="list-style-type: none"> - Protoscoleces, juvenile worms, and adults were exposed to epsiprantel at a concentration of 10 mcg/mL, either as a single dose, or as multiple doses applied as culture medium was changed every 36 hours. • <i>In vivo</i> study— <ul style="list-style-type: none"> - Helminth-free, mixed breed dogs, 2 to 12 months of age, were administered protoscoleces of <i>E. granulosus</i>. - Dogs were treated either at 7 days or 28 days postinfection. All dogs were autopsied 35 days after infection. <p>Dose and duration:</p> <ul style="list-style-type: none"> • <i>In vivo</i> study (single-dose)— <table border="0" style="width: 100%;"> <tr> <td style="width: 50%; vertical-align: top;"> <p><u>Trial 1 (Treated 7 days postinfection)</u></p> <ul style="list-style-type: none"> -Group 1—Oral epsiprantel, 5 mg/kg -Group 2—Oral epsiprantel, 7.5 mg/kg -Group 3—Oral epsiprantel, 10 mg/kg -Group 4—Oral praziquantel, 5 mg/kg -Group 5—Untreated controls </td> <td style="width: 50%; vertical-align: top;"> <p><u>Trial 2 (Treated 28 days postinfection)</u></p> <ul style="list-style-type: none"> -Group 1—Oral epsiprantel, 2.5 mg/kg -Group 2—Oral epsiprantel, 5 mg/kg -Group 3—Oral epsiprantel, 7.5 mg/kg -Group 4—Oral praziquantel, 5 mg/kg -Group 5—Untreated controls </td> </tr> </table> • Duration—35 days after treatment <p>Results:</p> <ul style="list-style-type: none"> • No adverse effects were reported. • <i>In vitro</i> study—Single-dose treatment killed 70% of protoscoleces by day 15. The majority of protoscoleces in control dogs were alive with no visible change. Repeated doses killed 95% by day 15. All juvenile and adult worms were dead by 15 days. • <i>In vivo</i> study— <p>Worm count reduction - infections cleared:</p> <table border="0" style="width: 100%;"> <tr> <td style="width: 50%; vertical-align: top;"> <p><u>7-day-old infections</u></p> <ul style="list-style-type: none"> Group 1: >94% - 0 dogs/3 treated Group 2: >90% - 1/3 Group 3: 99.9% - 2/3 Group 4: 100% - 3/3 </td> <td style="width: 50%; vertical-align: top;"> <p><u>28-day-old infections</u></p> <ul style="list-style-type: none"> Group 1: 96% - 1 dog/5 treated Group 2: 99.9% - 2/5 Group 3: 99.99% - 4/5 Group 4: 100% - 5/5 </td> </tr> </table> <p>Conclusions:</p> <ul style="list-style-type: none"> • Adult worms responded more quickly to <i>in vitro</i> epsiprantel treatment than more immature stages. Protoscoleces were least affected. • Epsiprantel is anticestodal and has activity <i>in vivo</i> at doses of 2.5 to 10 mg/kg. 	<p><u>Trial 1 (Treated 7 days postinfection)</u></p> <ul style="list-style-type: none"> -Group 1—Oral epsiprantel, 5 mg/kg -Group 2—Oral epsiprantel, 7.5 mg/kg -Group 3—Oral epsiprantel, 10 mg/kg -Group 4—Oral praziquantel, 5 mg/kg -Group 5—Untreated controls 	<p><u>Trial 2 (Treated 28 days postinfection)</u></p> <ul style="list-style-type: none"> -Group 1—Oral epsiprantel, 2.5 mg/kg -Group 2—Oral epsiprantel, 5 mg/kg -Group 3—Oral epsiprantel, 7.5 mg/kg -Group 4—Oral praziquantel, 5 mg/kg -Group 5—Untreated controls 	<p><u>7-day-old infections</u></p> <ul style="list-style-type: none"> Group 1: >94% - 0 dogs/3 treated Group 2: >90% - 1/3 Group 3: 99.9% - 2/3 Group 4: 100% - 3/3 	<p><u>28-day-old infections</u></p> <ul style="list-style-type: none"> Group 1: 96% - 1 dog/5 treated Group 2: 99.9% - 2/5 Group 3: 99.99% - 4/5 Group 4: 100% - 5/5 	
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Study 3 of 3: Arru E, Garippa G, Manger BR. Efficacy of epsiprantel against *Echinococcus granulosus* infections in dogs. Research in Veterinary Science 1990; 49: 378-9.

<p>Design</p> <ul style="list-style-type: none"> • Randomized study of induced infection with positive and negative controls <p>N = 20 dogs</p>	<p>Goal: To evaluate the effectiveness of epsiprantel against <i>E. granulosus</i> infection in dogs.</p> <p>Methods:</p> <ul style="list-style-type: none"> • Four-month-old Beagles orally infected with 20,000 to 50,000 protoscoleces of <i>E. granulosus</i> harvested from hepatic hydatid cysts of sheep. Dogs were housed individually and fed prepackaged food. • Dogs were treated 41 days after infection. Fecal testing and observation was performed daily after treatment. Dogs were euthanized 4 days after treatment and necropsies were performed. <p>Dose and duration:</p> <ul style="list-style-type: none"> • Treatment group 1—Oral, 2.5 mg/kg, as a single dose • Treatment group 2— Oral, 5 mg/kg, as a single dose • Treatment group 3— Oral, 7.5 mg/kg, as a single dose • Control group—Oral placebo (lactose-filled capsule) <ul style="list-style-type: none"> • Duration—4 days after treatment <p>Results:</p> <ul style="list-style-type: none"> • No adverse effects were reported. • In untreated control animals, numbers of individual worms were so high that only one-tenth of the intestinal worm content could be counted in each dog. Estimated total worm counts ranged from 4700 to 6900. • No entire worms were found in any treated dog, although a few scoleces and fragments were noted. Counts of partial worms ranged from 0 to 18 in each treated dog, with the exception of two dogs in the 7.5-mg/kg treatment group that were completely cleared of worms and worm parts. • As expected, epsiprantel appeared to have no effect on naturally acquired gastrointestinal nematodes in these dogs. <p>Conclusions:</p> <ul style="list-style-type: none"> • Epsiprantel was highly effective against young adult <i>E. granulosus</i> infection in dogs. • Remaining worm numbers were extremely low in treated dogs. • With the labeled dose for dogs (5.5 mg/kg), an efficacy of 99.9% could be expected, based on the results of this study. 	
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