

# TETRAHYDROPYRIMIDINES (Veterinary—Oral-Local)

This monograph includes information on the following: Morantel; Pyrantel.

Some commonly used *brand names* are:

For veterinary-labeled products—

<i>Anthelban V</i> [Pyrantel]	<i>Liquid Wormer</i> [Pyrantel]
<i>Banminth 48</i> [Pyrantel]	<i>Liquid Wormer-2X</i> [Pyrantel]
<i>Champion Protector</i> [Pyrantel]	<i>LiquiVict-2X</i> [Pyrantel]
<i>Continuex</i> [Pyrantel]	<i>Nemex-2</i> [Pyrantel]
<i>Cooper's Best Pyrantel Canine</i> [Pyrantel]	<i>Nemex Tabs</i> [Pyrantel]
<i>Cooper's Best Pyrantel Canine 2X</i> [Pyrantel]	<i>Pellet-Care P</i> [Pyrantel]
<i>Cooper's Best Pyrantel Equine Paste</i> [Pyrantel]	<i>Primex Canine</i> [Pyrantel]
<i>D-Worm 60</i> [Pyrantel]	<i>Primex Canine-2X</i> [Pyrantel]
<i>D-Worm 120</i> [Pyrantel]	<i>Primex Equine</i> [Pyrantel]
<i>D-Worm Chewable Tablets For Large Dogs</i> [Pyrantel]	<i>Pro-Banminth</i> [Pyrantel]
<i>D-Worm Chewable Tablets For Puppies/Small Dogs</i> [Pyrantel]	<i>Pyran 35</i> [Pyrantel]
<i>D-Worm Tablets For Large Dogs</i> [Pyrantel]	<i>Pyran 125</i> [Pyrantel]
<i>D-Worm Tablets For Puppies/Small Dogs</i> [Pyrantel]	<i>Pyr-A-Pam</i> [Pyrantel]
<i>Equi-Aid CW</i> [Pyrantel]	<i>Pyr-A-Pam II</i> [Pyrantel]
<i>Equi-Cide</i> [Pyrantel]	<i>Rotectin P</i> [Pyrantel]
<i>Equi-Phar Horse and Colt Wormer</i> [Pyrantel]	<i>Rumatel 88</i> [Morantel]
<i>Equi-Phar Pro-Tal Paste</i> [Pyrantel]	<i>Rumatel Goat and Cattle Wormer</i> [Morantel]
<i>Equi-Phar Pro-Tal Suspension</i> [Pyrantel]	<i>Strongid C</i> [Pyrantel]
<i>Exodus Equine Anthelmintic Paste</i> [Pyrantel]	<i>Strongid C 2X</i> [Pyrantel]
<i>Exodus Paste</i> [Pyrantel]	<i>Strongid P</i> [Pyrantel]
<i>Happy Jack ProDog Multi-Wormer</i> [Pyrantel]	<i>Strongid Paste</i> [Pyrantel]
<i>Happy Jack ProPup Multi-Wormer</i> [Pyrantel]	<i>Strongid T</i> [Pyrantel]
<i>Horse and Colt Wormer</i> [Pyrantel]	<i>Sure Shot Liquid Wormer for Dogs</i> [Pyrantel]
<i>K-9 Wormbgone 2X</i> [Pyrantel]	<i>Worm Protector 2X Double Strength</i> [Pyrantel]
<i>Liqui-Care P</i> [Pyrantel]	

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

**Category:** Anthelmintic (systemic).

## Indications

Note: The text between <sup>ELUS</sup> and <sup>EL</sup> describes uses that are not included in U.S. product labeling. Text between <sup>ELCAN</sup> and <sup>EL</sup> describes uses that are not included in Canadian product labeling.

The <sup>ELUS</sup> or <sup>ELCAN</sup> designation can signify a lack of product availability in the country indicated. See the *Dosage Forms* section of this monograph to confirm availability.

## General considerations

The tetrahydropyrimidines are effective in the treatment of gastrointestinal nematodes. In horses, pyrantel is considered somewhat effective in the treatment of adult cestodes, specifically *Anoplocephala* species.

Some resistance to pyrantel by parasites, including cyathostomes in horses, has been reported in the United States.<sup>{R-48-50}</sup> Animal management and carefully designed anthelmintic protocols are important strategies to limit development of resistance.

## Accepted

<sup>ELUS</sup>Cestode, gastrointestinal, infection (treatment)<sup>EL</sup>—*Horses and ponies*: Pyrantel pamoate oral paste and oral suspension are indicated in the treatment of adult common tapeworms, *Anoplocephala perfoliata*.<sup>{R-33-35; 45; 46}</sup>

Nematode, gastrointestinal, infection (prophylaxis)—

*Horses*: Pyrantel tartrate medicated feed, administered daily, is indicated in the prevention of *Strongylus vulgaris* larval infections.<sup>{R-27-29}</sup>

*Pigs*: Pyrantel tartrate for medicated feed is indicated in the prevention of large roundworm, *Ascaris suum*, migration and infection and <sup>ELCAN</sup> in the prevention of nodular worm, *Oesophagostomum* species, infection.<sup>{EL}{R-30; 38}</sup>

Nematode, gastrointestinal, infection (treatment)—

<sup>ELUS</sup>*Cats*<sup>EL</sup>: Pyrantel pamoate tablets are indicated in the treatment of gastrointestinal nematodes, including hookworms, *Ancylostoma* species, and roundworms, *Toxocara cati*.<sup>{R-36; 37; 40-42}</sup>

<sup>ELCAN</sup>*Cattle*<sup>EL</sup>: Morantel tartrate for medicated feed and morantel tartrate medicated feed are indicated in the treatment and control of adult gastrointestinal nematodes, including *Cooperia* species, *Haemonchus* species, *Nematodirus* species, *Oesophagostomum radiatum*, *Ostertagia* species, and *Trichostrongylus* species.<sup>{R-1-3}</sup>

*Dogs*: Pyrantel pamoate <sup>ELCAN</sup>oral suspension<sup>EL</sup> and tablets are indicated in the treatment and control of hookworms, *Ancylostoma caninum* and *Uncinaria stenocephala*, and large roundworms, *Toxocara canis* and *Toxascaris leonina*.<sup>{R-5; 21; 36; 37}</sup> <sup>ELCAN</sup>Pyrantel pamoate oral suspension is also indicated in the control of *T. canis* in puppies by treatment of lactating dogs after whelping.<sup>{EL}{R-5; 9; 21}</sup>

<sup>ELCAN</sup>*Goats*<sup>EL</sup>: Morantel tartrate for medicated feed and morantel tartrate medicated feed are indicated in the treatment and control of adult gastrointestinal nematodes, including *Haemonchus contortus*, *Ostertagia (Teladorsagia) circumcincta*, and *Trichostrongylus axei*.<sup>{R-1; 3}</sup>

*Horses and ponies*: Pyrantel pamoate oral paste and oral suspension, and pyrantel tartrate medicated feed are indicated in the treatment and control of adult gastrointestinal nematodes, including

## 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 or small case studies
- 4 Pharmacokinetic studies without surrogate endpoints
- 5 *In vitro* studies
- 6 Opinions of respected authorities on the basis of clinical experience or reports of expert committees

pinworms, *Oxyuris equi*; large roundworms, *Parascaris equorum*; large strongyles, *Strongylus edentatus*, *S. equinus*, and *S. vulgaris*; and small strongyles.<sup>(R-6; 7; 10; 17; 24-26; 33-35)</sup>

Canadian product labeling also lists the small strongyles, *Cyathostomum* species and *Cylicostephanus* species, as susceptible.<sup>(R-33-35)</sup>

Pyrantel tartrate medicated feed, administered daily, is indicated in the control of gastrointestinal nematodes, including adult and fourth stage larvae (L<sub>4</sub>) of pinworms, *Oxyuris equi*; adult and L<sub>4</sub> of large roundworms, *Parascaris equorum*; adult large strongyles, *Strongylus edentatus*, *S. vulgaris*, and *Tridontophorus* species; and adult and L<sub>4</sub> of small strongyles, *Cyathostomum* species, *Cylicocycclus* species, *Cylicostephanus* species, *Cylicodontophorus* species, and *Poteriostomum* species.<sup>(R-27-29)</sup>

<sup>EL,CAN</sup> **Pigs**<sup>EL</sup>: Pyrantel tartrate for medicated feed is indicated in the treatment and control of gastrointestinal nematodes, including large roundworms, *Ascaris suum*, and nodular worms, *Oesophagostomum* species.<sup>(R-30; 44)</sup>

### Potentially effective

<sup>EL,US</sup> **Cestode, gastrointestinal, infection (treatment)—Horses**: There is some evidence to suggest that the <sup>EL,CAN</sup> daily administration of pyrantel tartrate medicated feed, at the recommended dose, may be effective in the control of adult tapeworms (Evidence rating: B-2).<sup>(R-45; 47)</sup>

**Nematode, gastrointestinal, infection (treatment)—**<sup>EL,US,CAN</sup> For *Physaloptera* species: **Dogs**—Pyrantel pamoate is used in the treatment of *Physaloptera* species infection in dogs, based on limited case information (Evidence rating: B-6).<sup>(R-52; 53)</sup>

## Regulatory Considerations

U.S.—

Withdrawal times have been established for morantel tartrate for medicated feed, morantel tartrate medicated feed, and pyrantel tartrate for medicated feed.

Canada—

Withdrawal times have been established for pyrantel tartrate for medicated feed.

## Chemistry

**Chemical group**: Tetrahydropyrimidines.<sup>(R-5; 6)</sup>

### Chemical name:

Morantel tartrate—Pyrimidine, 1,4,5,6-tetrahydro-1-methyl-2-[2-(3-methyl-2-thienyl)ethenyl]-, (E)-, [R-(R\*,R\*)]-2,3-dihydroxybutanedioate (1:1).<sup>(R-39)</sup>

Pyrantel pamoate—Pyrimidine, 1,4,5,6-tetrahydro-1-methyl-2-[2-(2-thienyl)ethenyl]-, (E)-, compd. with 4,4'-methylenebis[3-hydroxy-2-naphthalenecarboxylic acid](1:1).<sup>(R-39)</sup>

Pyrantel tartrate—Pyrimidine, 1,4,5,6-tetrahydro-1-methyl-2-[2-(2-thienyl)ethenyl]-, (E)-, [R-(R\*,R\*)]-2,3-dihydroxybutanedioate (1:1).<sup>(R-39)</sup>

### Molecular formula:

Morantel tartrate—C<sub>12</sub>H<sub>16</sub>N<sub>2</sub>S·C<sub>4</sub>H<sub>6</sub>O<sub>6</sub>.<sup>(R-39)</sup>

Pyrantel pamoate—C<sub>11</sub>H<sub>14</sub>N<sub>2</sub>S·C<sub>23</sub>H<sub>16</sub>O<sub>6</sub>.<sup>(R-39)</sup>

Pyrantel tartrate—C<sub>11</sub>H<sub>14</sub>N<sub>2</sub>S·C<sub>4</sub>H<sub>6</sub>O<sub>6</sub>.<sup>(R-39)</sup>

### Molecular weight:

Morantel tartrate—370.42.<sup>(R-39)</sup>

Pyrantel pamoate—594.68.<sup>(R-39)</sup>

Pyrantel tartrate—356.39.<sup>(R-39)</sup>

### Description:

Pyrantel Pamoate USP—Yellow to tan solid.<sup>(R-4)</sup>

Pyrantel tartrate—White crystals.<sup>(R-32)</sup>

Note: Exposure of aqueous solutions of pyrantel salts to light can cause photoisomerization and decreased potency.<sup>(R-56)</sup>

**Solubility**: Pyrantel pamoate—Practically insoluble in water and in methanol; soluble in dimethyl sulfoxide; slightly soluble in dimethylformamide.<sup>(R-4)</sup>

## Pharmacology/Pharmacokinetics

**Mechanism of action/Effect**: The mechanism of action of morantel and pyrantel is believed to be interference with acetylcholine receptors at autonomic ganglion, the adrenal medulla, chemoreceptors of the carotid and aortic bodies, and neuromuscular junctions. One result is contracture of parasite musculature, producing paralysis, similar to that induced by nicotine, that is 100 times more potent than acetylcholine and is not easily reversible.<sup>(R-54-56)</sup> Helminths are unable to maintain their position in the intestinal lumen and are expelled by peristalsis.<sup>(R-68)</sup>

**Absorption**: Tetrahydropyrimidines are believed to be most effective when retained in the gastrointestinal tract, making minimal absorption a positive factor in efficacy.<sup>(R-59)</sup> Pyrantel pamoate is poorly water soluble and, therefore, poorly absorbed by the intestinal mucosa.<sup>(R-37)</sup> Orally administered pyrantel tartrate is well absorbed from the intestinal tract of monogastric animals,<sup>(R-60)</sup> but the tartrate salts of morantel and pyrantel are poorly absorbed in ruminants.<sup>(R-62)</sup>

Oral bioavailability—**Pigs**:

Pyrantel citrate—F = 41.34 ± 3.33%.<sup>(R-59)</sup>

Pyrantel pamoate—F = 15.88 ± 3.48%.<sup>(R-59)</sup>

**Distribution**: Volume of distribution—**Pigs**: Steady state—2.74 ± 0.37 L/kg.<sup>(R-59)</sup>

**Biotransformation**: When morantel is absorbed from the gastrointestinal tract in pigs, studies have suggested it is quickly metabolized to inactive compounds.<sup>(R-59)</sup>

Biotransformation is believed to occur rapidly to a complex array of metabolites.<sup>(R-64)</sup> Three pathways have been described: 1) oxidation of the thiophene ring 2) glutathione conjugation 3) oxidation of the tetrahydropyrimidine ring.<sup>(R-63)</sup>

**Half-life**: Elimination—

Intravenous administration of pyrantel citrate: **Pigs**—1.75 ± 0.19 hours.<sup>(R-59)</sup>

Oral administration:

**Horses**: 13.43 ± 1.38 hours, with an oral pyrantel pamoate dose of 13 mg/kg.<sup>(R-59)</sup>

**Pigs**: 6.26 ± 0.66 hours, with an oral pyrantel pamoate dose of 33 mg/kg.<sup>(R-59)</sup>

### Concentrations:

Morantel tartrate—

**Cattle**: No morantel could be detected (minimum detection limit of 0.05 mcg/mL) in the plasma of calves 30 minutes to 8 hours after oral administration of morantel tartrate.<sup>(R-62)</sup> However, using tritium-labeled morantel, peak plasma concentration of morantel and metabolites in lactating dairy cattle was 170 parts per billion (ppb; range, 92 to 223 ppb) 8 hours after administration of a 10-mg/kg dose.<sup>(R-63; 65)</sup>

**Goats**—No morantel could be detected (limit of 0.05 mcg/mL) in the plasma 30 minutes to 72 hours after oral administration of morantel tartrate at a dose of 10 mg/kg.<sup>(R-62)</sup>

Pyrantel pamoate—

**Horses**: A peak plasma concentration of 0.09 ± 0.02 mcg/mL was reached at 7.5 ± 1.41 hours after oral administration of 13 mg/kg.<sup>(R-60)</sup>

**Pigs**: A peak plasma concentration of 0.23 ± 0.06 mcg/mL was reached at 3.26 ± 0.64 hours after oral administration of 33 mg/kg.<sup>(R-59)</sup>

**Elimination**: Tetrahydropyrimidine salts that are poorly absorbed in the gastrointestinal tract, such as pyrantel pamoate, are more

predominately eliminated in the feces, while more soluble salts, such as pyrantel tartrate, are eliminated to a larger degree in the urine.<sup>(R-59)</sup>

**Morantel tartrate—Cattle:** Eliminated predominately in the feces (68% of the dose) but also in urine (14 to 20%) in the first 96 hours.<sup>(R-63; 65)</sup>

**Pyrantel—**

**Dogs:** Pyrantel pamoate is primarily eliminated in the feces, with <15% eliminated in the urine.<sup>(R-37)</sup>

**Pigs:** The fecal:urine elimination ratio is 34:42 for pyrantel tartrate and 72:9 for pyrantel pamoate.<sup>(R-59)</sup>

**Clearance—Pigs:**  $18.2 \pm 2.17$  mL/min/kg.<sup>(R-59)</sup>

## Precautions to Consider

### Reproduction/Pregnancy

**Cats:** No adverse effects were reported in 32 kittens born to 7 cats given pyrantel pamoate every two weeks at a dose of 20 mg per kg of body weight (mg/kg), beginning with several doses before breeding and continuing through gestation to birth of the kittens.<sup>(R-42)</sup>

**Cattle:** No adverse effects were reported when morantel tartrate was administered to cows at a dose of 200 mg/kg (twenty times the recommended dose) during pregnancy and lactation.<sup>(R-2)</sup>

**Dogs:** No adverse effects were reported from clinical studies of the administration of pyrantel pamoate to pregnant dogs or male dogs at stud.<sup>(R-5)</sup>

**Horses:** No adverse effects were reported when pyrantel pamoate was administered to pregnant mares or breeding stallions.<sup>(R-6)</sup> Pyrantel pamoate products are labeled for administration to mares one month before foaling.<sup>(R-6; 17)</sup> No adverse effects were reported when pyrantel tartrate was administered daily at the recommended dose to mares during all stages of pregnancy or when it was administered to breeding stallions.<sup>(R-27-29)</sup>

### Lactation

**Cattle:** Peak concentration of tritium-labeled morantel and metabolites in milk was measured to be 84 ppb (range, 71 to 93 ppb) at the second milking (24 hours) after administration of a 10-mg/kg dose of morantel tartrate.<sup>(R-63-65)</sup>

**Goats:**

Twelve hours (first sample time) after oral administration of morantel tartrate, 10 mg/kg, the marker residue for morantel was measured to be 15.17 parts per billion (ppb) in milk and diminished in subsequent samples. The acceptable upper limit set by the Food and Drug Administration for residues in milk was 90 ppb.<sup>(R-61)</sup>

Morantel was not detected (minimum detection limit of 0.05 mcg/mL) in milk from 1 to 72 hours after oral administration of morantel tartrate, 10 mg/kg, to six goats, with the exception of one goat that had a milk concentration of 0.092 mcg/mL at 8 hours.<sup>(R-62)</sup>

### Pediatrics

**Dogs:** No adverse effects were reported from clinical studies of the administration of pyrantel pamoate to nursing puppies.<sup>(R-5)</sup>

Pyrantel pamoate products are labeled for use in lactating dogs two to three weeks after whelping and in puppies beginning at 2 weeks of age.<sup>(R-5; 21)</sup>

**Horses:** Pyrantel pamoate products are labeled for administration to lactating mares ten days to two weeks after the foal's birth, while treatment of foals can begin at 2 months of age and be repeated every 4 weeks.<sup>(R-6; 17)</sup>

No adverse effects were reported when pyrantel tartrate was administered daily at the recommended dosage to mares during lactation.<sup>(R-27-29)</sup> No adverse effects were reported when pyrantel tartrate was administered to one- to three-month-old foals at a dose of 26.4 mg/kg a day (ten times the recommended daily dose) for up to 98 days.<sup>(R-31)</sup>

## 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:** Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Levamisole and<sup>(R-54; 55)</sup>

Nicotine-like cholinergic agents, other

(when pyrantel is administered concurrently with levamisole, toxicity of levamisole can be increased; the lethal dose [LD<sub>50</sub>] of levamisole was lowered from 39.8 mg/kg to 27.5 mg/kg in pigs when pyrantel tartrate was administered at a dose of 25 mg/kg; this effect may also occur with other nicotinic acetylcholine receptor blocking agents, including morantel, but concurrent administration of organophosphates with tetrahydropyrimidines does not lead to the same potentiation of effect)

Piperazine<sup>(R-68)</sup>

(there have been suggestions that the paralysis and muscle relaxation caused by the anticholinergic action of piperazine could counteract the muscle contractile effect of pyrantel if they were administered concurrently; the clinical significance of this potential interaction has not been demonstrated and has been questioned)

## Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance).

**Note:** No specific medical considerations or contraindications have been reported in animals, although product labeling contains warnings against use of tetrahydropyrimidines in severely debilitated animals.

## Human medical considerations/contraindications<sup>(R-68)</sup>

The following medical considerations/contraindications have been reported in human beings, and are included in the human monograph *Pyrantel (Oral-Local)* in *USP DI Volume I*; the following are intended for informational purposes only and may or may not be applicable to the use of morantel or pyrantel in the treatment of animals:

**Risk-benefit should be considered when the following medical problems exist:**

Hypersensitivity to morantel or pyrantel

Liver disease

**Note:** Worsening of pre-existing myasthenia gravis has been reported in one patient.

## 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 examinations

(periodic monitoring of fecal shedding and parasite load is important in structuring and adjusting gastrointestinal parasite control programs)

## Side/Adverse Effects

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

**Note:** With recommended dosages, reports of side/adverse effects in association with administration of the tetrahydropyrimidines are rare.

## Human side/adverse effects<sup>(R-68)</sup>

The following side/adverse effects have been reported in human beings, and are included in the human monograph *Pyrantel (Oral-Local)* in *USP DI Volume I*; the following are intended for informational purposes only and may or may not be applicable to the use of morantel or pyrantel in the treatment of animals:

### Those indicating need for medical attention

Incidence rare

**Hypersensitivity** (skin rash)

### Those indicating need for medical attention only if they continue or are bothersome

Incidence less frequent

**Central nervous system effects** (dizziness, drowsiness, headache, irritability, trouble in sleeping); **gastrointestinal disturbances** (abdominal or stomach cramps or pain, diarrhea, loss of appetite, nausea or vomiting)

### Environmental impact

Morantel is extremely persistent in fecal material that is not washed into the soil or directly exposed to sunlight, including core samples of cattle feces.<sup>(R-62)</sup> However, some researchers have reported that morantel does not affect the development of dung flies even at high fecal concentrations.<sup>(R-62)</sup>

### 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.**

Note: Because it is poorly absorbed with oral administration, pyrantel pamoate carries a lower risk of toxicity than other tetrahydropyrimidine salts in monogastric species.

No adverse effects were observed when pyrantel pamoate was administered to four- to six-month-old kittens at a daily dose of 100 mg (base) per kg of body weight (mg/kg) for three days.<sup>(R-40)</sup>

No significant adverse effects were observed when pyrantel pamoate was administered to dogs at a dose of 207 mg (base) per kg a day (forty times the recommended dose) for up to 90 days.<sup>(R-5)</sup>

No adverse effects were observed when pyrantel pamoate was administered by stomach tube to horses at a dose of 132 mg (base) per kg (ten times the recommended dose) or when administered by intratracheal injection at a dose of 6.6 mg (base) per kg (one-half the recommended dose).<sup>(R-6)</sup>

No adverse effects were observed when pyrantel tartrate was administered to horses at a dose of 26.4 mg/kg a day (ten times the daily dose) for 196 days.<sup>(R-31)</sup> The same dose administered daily to one- to three-month-old foals for up to 98 days caused no observed adverse effects.<sup>(R-31)</sup>

### 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:

#### Cattle

With a dose of 200 mg of pyrantel tartrate per kg of body weight.<sup>(R-56)</sup>

#### Ataxia

#### Horses

With a dose of 100 mg of pyrantel tartrate per kg of body weight a day.<sup>(R-56)</sup>

**Incoordination; respiration rate, increased; sweating, profuse**

Note: One out of three horses treated with this dose died.

### Human clinical effects of overdose<sup>(R-68)</sup>

The following clinical effects have been reported in human beings, and are included in the human monograph *Pyrantel (Oral-Local)* in *USP DI Volume 1*; the following are intended for informational purposes only and may or may not be applicable to the use of morantel or pyrantel in the treatment of animals:

**Asphyxia; autonomic dysfunction** (blurred vision; confusion; dizziness, faintness, or lightheadedness when getting up from a

lying or sitting position; irregular heartbeat; sweating; unusual tiredness or weakness); **muscle spasm, twitches, and weakness; prostration**

### Lethal dose

Acute oral LD<sub>50</sub>:

Morantel—*Mice*: 5000 mg/kg.<sup>(R-56)</sup>

Pyrantel pamoate—*Dogs*: Greater than 691 mg/kg.<sup>(R-5)</sup>

Pyrantel tartrate—

*Mice*: 175 mg/kg.<sup>(R-66)</sup>

*Rats*: 170 mg/kg.<sup>(R-66)</sup>

### Treatment of overdose

There is no specific antidote for morantel or pyrantel 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:

Importance of regular treatment when recommended and of follow-up fecal examinations

Zoonotic potential when appropriate

### Veterinary Dosing Information

#### Parasite management

*Cats and dogs*: The Centers for Disease Control and Prevention Division of Parasitic Diseases (CDC DPD) in association with the American Association of Veterinary Parasitologists (AAVP) recommends that pregnant dogs be treated with an appropriate anthelmintic to prevent transplacental and transmammary hookworm and roundworm infection. If the mother is not treated during pregnancy, it is recommended that puppies receive anthelmintic at 2, 4, 6, and 8 weeks of age, then monthly until 6 months of age, to protect against parasite infection and to reduce zoonotic potential.<sup>(R-67)</sup>

It is recommended that kittens receive anthelmintic at 3, 5, 7, and 9 weeks of age<sup>(R-67)</sup> and then monthly until 6 months of age.

Although many kittens and puppies are not examined by a veterinarian until 6 to 8 weeks of age, infected animals will already be shedding eggs by that age.

Adult cats and dogs should be regularly tested for gastrointestinal parasites and, if necessary, treated as part of routine health maintenance.

*Horses*: Management practices that have been recommended to control parasitism and minimize parasite resistance include.<sup>(R-48)</sup>

Assess anthelmintic efficacy by a fecal egg count reduction test (FECR) before developing a parasite control program.

Structure treatment to keep pasture larval burden low.<sup>(R-51)</sup> Do regular fecal egg counts (FEC) to monitor effectiveness of parasite control and for timing of intermittent anthelmintic dosing. Control of parasitism by reduction of FEC, rather than complete elimination of parasites, is recommended under certain conditions.

Administering anthelmintic too frequently can increase the development of resistance.

Avoid rapid rotation of anthelmintics in which a different anthelmintic is used for each treatment. Changing medication on an annual basis or pairing medications for simultaneous administration may be more effective in slowing anthelmintic resistance.

Quarantine new or visiting horses until larval stages are effectively treated.

#### Diet

Due to low water solubility, the bioavailability of pyrantel pamoate is not affected by fiber content of diet.<sup>(R-58)</sup>

Fasting is not required for administration of tetrahydropyrimidines. In pigs, the more soluble salts, such as the tartrate salt, may benefit from a diet

rapidly moving through the gastrointestinal tract to retain more pyrantel in the gut lumen and thereby increase efficacy.<sup>(R-58; 59)</sup>

## MORANTEL

### Oral Dosage Forms

Note: The following dosages are expressed in terms of the *morantel tartrate salt* (not morantel base).

The text between <sup>EL,US</sup> and <sup>EL</sup> describes uses not included in U.S. product labeling. Text between <sup>EL,CAN</sup> and <sup>EL</sup> describes uses that are not included in Canadian product labeling.

The <sup>EL,US</sup> or <sup>EL,CAN</sup> designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

### MORANTEL TARTRATE FOR MEDICATED FEED

**Usual dose:** <sup>EL,CAN</sup>Nematode, gastrointestinal, infection<sup>EL</sup>—*Cattle* and *goats*: Oral, 10 mg morantel tartrate per kg of body weight,<sup>(R-1; 2)</sup> fed as a single dose to be consumed within six hours.<sup>(R-1; 2)</sup> Treatment may need to be repeated with ongoing parasite exposure.<sup>(R-2)</sup>

**Withdrawal times**—*Cattle*: US—Meat: 14 days, Milk: None.<sup>(R-2)</sup>  
*Goats*: US—Meat: 30 days, Milk: None.<sup>(R-1)</sup>

Note: For more accurate dosing, cattle may be grouped by size. Fresh water is made available during treatment.<sup>(R-2)</sup>

#### Strength(s) usually available:

U.S.—<sup>(R-1; 2)</sup>

Veterinary-labeled product(s):

193.6 grams per kg of premix (OTC) [*Rumatel 88*].

Canada—

Veterinary-labeled product(s):

Not commercially available.

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer.

**Preparation of dosage form:** This product is used in the manufacture of medicated feeds.<sup>(R-1)</sup> It should not be mixed with feeds containing bentonite.<sup>(R-2)</sup>

**Caution:** Workers handling this medication should minimize exposure, wear protective clothing and a mask or respirator to control dust, have sufficient ventilation of the area, and be alert for signs of an allergic reaction. If a reaction occurs, medical attention should be sought.<sup>(R-2)</sup>

Keep out of the reach of children.

**USP requirements:** Not in USP.<sup>(R-4)</sup>

### MORANTEL TARTRATE MEDICATED FEED

**Usual dose:** <sup>EL,CAN</sup>Nematode, gastrointestinal, infection<sup>EL</sup>—*Cattle* and *goats*: Oral, 10 mg morantel tartrate per kg of body weight,<sup>(R-3)</sup> administered as a single dose that may be given as the sole ration, mixed with complete feed, or administered as a top dress.<sup>(R-3)</sup> Treatment may need to be repeated with ongoing parasite exposure.

**Withdrawal times**—*Cattle*: US—Meat: 14 days, Milk: None.

*Goats*: US—Meat: 30 days, Milk: None.

Note: For more accurate dosing, cattle may be grouped by size. Fresh water is made available during treatment.<sup>(R-3)</sup>

#### Strength(s) usually available:

U.S.—<sup>(R-1; 2)</sup>

Veterinary-labeled product(s):

9.8 grams per kg of feed (OTC) [*Rumatel Goat and Cattle Wormer*].

Canada—

Veterinary-labeled product(s):

Not commercially available.

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer.

**Preparation of dosage form:** This product should not be mixed with feeds containing bentonite.

**USP requirements:** Not in USP.<sup>(R-4)</sup>

## PYRANTEL

### Oral Dosage Forms

Note: The dosing and strengths of the pyrantel pamoate dosage forms available are expressed in terms of *pyrantel base* (not the pyrantel pamoate salt). Pyrantel pamoate is a salt of tetrahydropyrimidine base and pamoic acid; it contains 34.7% pyrantel base.<sup>(R-5)</sup>

However, the dosing and strengths of the pyrantel tartrate dosage forms available are expressed in terms of *pyrantel tartrate salt*. Pyrantel tartrate contains 57.9% pyrantel base.

The text between <sup>EL,US</sup> and <sup>EL</sup> describes uses not included in U.S. product labeling. Text between <sup>EL,CAN</sup> and <sup>EL</sup> describes uses that are not included in Canadian product labeling.

The <sup>EL,US</sup> or <sup>EL,CAN</sup> designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

### PYRANTEL PAMOATE ORAL PASTE

#### Usual dose:

<sup>EL,US</sup>Cestode, gastrointestinal, infection<sup>EL</sup>—*Horses and ponies*: Oral, 13.2 mg (base) per kg of body weight as a single dose.<sup>(R-33; 34; 46)</sup> It may be necessary to repeat the dose as part of a parasite management program.<sup>(R-33; 45)</sup>

Nematode, gastrointestinal, infection—*Horses and ponies*: Oral, 6.6 mg (base) per kg of body weight as a single treatment.<sup>(R-17; 33; 34)</sup>

**Withdrawal times:** This product is not labeled for use in horses or ponies intended to be slaughtered for food production.<sup>(R-17; 33; 34)</sup>

Note: It is recommended that pyrantel pamoate oral paste be administered on the dorsum of the tongue.<sup>(R-17; 33; 34)</sup>

#### Strength(s) usually available:

U.S.—<sup>(R-16-20)</sup>

Veterinary-labeled product(s):

171 mg (base) per mL (OTC) [*Exodus Equine Anthelmintic Paste*].

180 mg (base) per mL (OTC) [*Strongid Paste*].

226 mg (base) per mL (OTC) [*Cooper's Best Pyrantel Equine Paste; Equi-Cide; Equi-Phar Pro-Tal Paste; Rotectin P; GENERIC*].

Canada—<sup>(R-33; 34)</sup>

Veterinary-labeled product(s):

180 mg (base) per mL (OTC) [*Exodus Paste* (apple flavoring); *Strongid P* (caramel flavoring)].

**Packaging and storage:** Store between 15 and 30 °C (59 and 86 °F), in a closed container,<sup>(R-17; 33; 34)</sup> unless otherwise specified by the manufacturer. Protect from light and from freezing.<sup>(R-33; 34)</sup>

**Caution:** Keep out of the reach of children.<sup>(R-17)</sup>

**USP requirements:** Not in USP.<sup>(R-4)</sup>

## PYRANTEL PAMOATE ORAL SUSPENSION USP

### Usual dose:

<sup>EL,US</sup>Cestode, gastrointestinal, infection<sup>EL</sup>—*Horses and ponies:*  
Oral, 13.2 mg (base) per kg of body weight as a single dose.<sup>(R-35; 46)</sup> It may be necessary to repeat the dose in eight weeks.<sup>(R-45)</sup>

**Withdrawal times:** This product is not labeled for use in horses or ponies intended for human consumption.<sup>(R-35)</sup>

Nematode, gastrointestinal, infection—

<sup>EL,CAN</sup>*Dogs*<sup>EL</sup>: Oral, 5 mg (base) per kg of body weight as a single treatment.<sup>(R-5)</sup>

Note: Pyrantel pamoate suspension may be mixed with a small amount of food, if necessary to increase palatability.<sup>(R-5; 35)</sup>

*Horses and ponies:* Oral, 6.6 mg (base) per kg of body weight as a single treatment.<sup>(R-5; 35)</sup>

**Withdrawal times:** This product is not labeled for use in horses or ponies intended for human consumption.<sup>(R-6; 35)</sup>

Note: Pyrantel pamoate suspension may be administered to horses by stomach tube, dose syringe, or mixed in the feed.<sup>(R-6)</sup>

### Strength(s) usually available:

U.S.—<sup>(R-5-16)</sup>

Veterinary-labeled product(s):

2.27 mg (base) per mL (OTC) [*Cooper's Best Pyrantel Canine; D-Worm 60* (vanilla flavoring); *Liquid Wormer* (butterscotch flavoring); *Primex Canine; Sure Shot Liquid Wormer for Dogs*].

4.54 mg (base) per mL (OTC) [*Champion Protector; Cooper's Best Pyrantel Canine 2X* (butterscotch flavoring); *D-Worm 120* (vanilla flavoring); *K-9 Wormbgone 2X* (butterscotch flavoring); *LiquiVict-2X* (butterscotch flavoring); *Nemex-2* (caramel flavoring); *Primex Canine-2X* (butterscotch flavoring); *Worm Protector 2X Double Strength* (caramel flavoring)].

50 mg (base) per mL (Rx) [*Anthelban V* (vanilla flavoring); *Equi-Phar Pro-Tal Suspension; Liqui-Care P* (vanilla flavoring); *Primex Equine* (mint flavoring); *Strongid T* (caramel flavoring)].

Note: Products listed above with a strength of 2.27 or 4.54 mg per mL (mg/mL) are labeled for use in dogs while those with a strength of 50 mg/mL are labeled for use in horses.

Canada—<sup>(R-35)</sup>

Veterinary-labeled product(s):

50 mg (base) per mL (OTC) [*Strongid T* (caramel flavoring)].

Note: The above product is labeled for use in horses only.

**Packaging and storage:** Store between 15 and 30 °C (59 and 86 °F), in a tight container, unless otherwise specified by the manufacturer.<sup>(R-4; 5; 35)</sup> Protect from light and from freezing.<sup>(R-6; 35)</sup>

**Preparation of dosage form:** Exposure of pyrantel pamoate oral suspension to direct sunlight should be avoided during handling.<sup>(R-6)</sup> For administration to horses by stomach tube, the suspension may be mixed with water just before dosing; the remaining diluted suspension should not be stored.<sup>(R-6)</sup>

**Caution:** Keep out of the reach of children.<sup>(R-5; 6)</sup>

**Additional information:** The bottle should be shaken thoroughly before each use to insure uniform suspension of medication.<sup>(R-6; 35)</sup>

**USP requirements:** Preserve in tight, light-resistant containers. A suspension of Pyrantel Pamoate in a suitable aqueous vehicle. Contains an amount of pyrantel pamoate equivalent to the labeled amount of pyrantel, within ±10%. Meets the requirements for Identification, Uniformity of dosage units (for oral suspension packaged in single unit containers), Deliverable volume (for oral suspension packaged in multiple-unit containers), and pH (4.5–6.0).<sup>(R-4)</sup>

## PYRANTEL PAMOATE TABLETS

**Usual dose:** Nematode, gastrointestinal, infection—

<sup>EL,US</sup>*Cats*<sup>EL</sup>: Oral, 20 mg (base) per kg of body weight as a single dose.<sup>(R-36; 37; 40-42)</sup>

*Dogs*: Oral, 5 mg (base) per kg of body weight as a single dose.<sup>(R-21; 36; 37)</sup>

Note: <sup>EL,US,CAN</sup>*Physaloptera* species infection<sup>EL</sup>—*Dogs:* There is some evidence to suggest that an oral dose of 5 to 15 mg (base) per kg of body weight may be effective in the treatment of *Physaloptera* species infection.<sup>(R-52; 53)</sup>

### Strength(s) usually available:

U.S.—<sup>(R-21-23)</sup>

Veterinary-labeled product(s):

22.7 mg (base) (OTC) [*D-Worm Chewable Tablets For Puppies/Small Dogs; D-Worm Tablets For Puppies/Small Dogs; Happy Jack ProPup Multi-Wormer* (chewable); *Nemex Tabs*].

113.5 mg (base) (OTC) [*D-Worm Chewable Tablets For Large Dogs; D-Worm Tablets For Large Dogs; Happy Jack ProDog Multi-Wormer* (chewable); *Nemex Tabs*].

Canada—<sup>(R-36; 37)</sup>

Veterinary-labeled product(s):

35 mg (base) (OTC) [*Pyran 35; Pyr-A-Pam*].

125 mg (base) (OTC) [*Pyran 125; Pyr-A-Pam III*].

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a tight container, unless otherwise specified by the manufacturer.<sup>(R-21; 36)</sup> Protect from light.<sup>(R-21; 36)</sup>

**Caution:** Keep out of the reach of children.<sup>(R-21; 36)</sup>

**USP requirements:** Not in USP.<sup>(R-4)</sup>

## PYRANTEL TARTRATE FOR MEDICATED FEED

**Usual dose:** Nematode, gastrointestinal, infection—*Pigs:*

<sup>EL,CAN</sup>For treatment and control of large roundworms and nodular worms<sup>EL</sup>—Oral, 22 mg of pyrantel tartrate per kg of body weight for pigs up to 91 kg (200 pounds), administered as the sole ration in an amount that will be consumed within a few hours to provide a single dose.<sup>(R-30)</sup> For pigs weighing more than 91 kg, the dose is 2000 mg per animal.<sup>(R-30)</sup> The complete feed for this therapeutic use contains 800 grams of pyrantel tartrate per ton (880 mg per kg) of feed.<sup>(R-30; 44)</sup>

Note: For single dose treatment, pigs may be fasted overnight to insure good consumption of medicated feed. For most accurate dosing, pigs can be separated by weight into different lots or pens for treatment. Water should be available during the fasting and treatment period.<sup>(R-30)</sup>

<sup>EL,CAN</sup>For treatment and control of large roundworm infection<sup>EL</sup>—Oral, 96 grams of pyrantel tartrate per ton of feed (106 mg per kg of feed), fed as the only ration for three days.<sup>(R-30)</sup>

For prevention of large roundworm migration or infection<sup>EL,CAN</sup> and prevention of nodular worm infection<sup>EL</sup>—Oral, 96 grams of pyrantel tartrate per ton of feed (106 mg per kg of feed), fed continuously as the only ration.<sup>(R-30; 38)</sup>

**Withdrawal time:** U.S.—Meat: 1 day (24 hours).<sup>(R-30)</sup> Canada—Meat: 7 days.<sup>(R-38)</sup>

**Strength(s) usually available:**U.S.—<sup>(R-30)</sup>Veterinary-labeled product(s):  
106 grams per kg (OTC) [*Banminth 48*].Canada—<sup>(R-38)</sup>Veterinary-labeled product(s):  
106 grams per kg (OTC) [*Pro-Banminth*].**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a tight container, unless otherwise specified by the manufacturer. Store in a cool, dry place.<sup>(R-30; 38)</sup>**Preparation of dosage form:** This product is used in the manufacture of medicated feeds.<sup>(R-30)</sup> It should not be mixed with feeds containing bentonite.<sup>(R-30)</sup>**Caution:** Workers handling this medication should minimize exposure, wear protective clothing and a mask or respirator to control dust, have sufficient ventilation of the area, and be alert for signs of an allergic reaction. If a reaction occurs, medical attention should be promptly sought.<sup>(R-30)</sup>

Keep out of the reach of children.

**USP requirements:** Not in USP.<sup>(R-4)</sup>**PYRANTEL TARTRATE MEDICATED FEED****Usual dose:** <sup>EL,CAN</sup>Nematode, gastrointestinal, infection<sup>EL</sup>—*Horses*:Treatment and control of susceptible parasites—Oral, 12.5 mg of pyrantel tartrate per kg of body weight as a single dose, administered in a quantity of feed normally consumed in one feeding.<sup>(R-24-26)</sup> With constant exposure to parasites, treatment may need to be repeated every two months.Prevention of *Strongylus vulgaris* larval infection and control of other susceptible parasites—Oral, 2.64 mg of pyrantel tartrate per kg of body weight a day, administered as a top-dress or mixed in the horse's daily grain ration.<sup>(R-27-29)</sup>Note: Animals that may already have a *S. vulgaris* infection from previous exposure should be treated with a larvicidal product before beginning daily administration of this medication.<sup>(R-27)</sup>Daily treatment of foals may begin once a consistent daily feed intake is apparent, usually between two to three months of age.<sup>(R-27)</sup>**Withdrawal times:** These products are not labeled for use in horses or ponies intended for food.<sup>(R-24-29)</sup>Note: Daily pyrantel tartrate administration may lose efficacy in the prevention of parasite infection when a horse is stressed.<sup>(R-51)</sup> Periods of decreased food consumption or decreases in drug absorption could affect protection from infection.<sup>(R-51)</sup><sup>EL,US,CAN</sup>Cestode, gastrointestinal, infection (treatment)<sup>EL</sup>—*Horses:* There is some evidence to suggest that an oral dose of 2.64 mg of pyrantel tartrate per kg of body weight a day may be effective in the control of adult tapeworms.<sup>(R-45; 47)</sup>**Strength(s) usually available:**U.S.—<sup>(R-16; 24-29)</sup>Veterinary-labeled product(s):  
*Labeled for single dose administration—*  
12.5 grams per kg of pellets (OTC) [*Equi-Phar Horse and Colt Wormer* (molasses flavoring); *Horse and Colt Wormer* (molasses flavoring); *Pellet-Care P* (molasses flavoring)].  
*Labeled for daily administration—*  
10.6 grams per kg of pellets (OTC) [*Strongid C* (molasses flavoring)].21.1 grams per kg of pellets (OTC) [*Continuex* (molasses flavoring); *Equi Aid CW*; *Strongid C 2X* (molasses flavoring)].

Canada—

Veterinary-labeled product(s):  
Not commercially available.**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer.<sup>(R-21)</sup>**Preparation of dosage form:** These products should not be mixed with feeds containing bentonite.<sup>(R-27)</sup>**Caution:** Keep out of the reach of children.<sup>(R-24-26)</sup>**USP requirements:** Not in USP.<sup>(R-4)</sup>Developed: 6/24/05**References**

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