IVERMECTIN

(eye-ver-*mek*-tin) Heartgard®, Ivomec®

ANTIPARASITIC

Prescriber Highlights

- Prototype avermectin drug used in variety of species as an antiparasiticide
- Contraindications: Label specific due to lack of safety data (foals, puppies, etc.) or public health safety (lactating dairy animals)
- Caution in breeds susceptible to MDR1-allele mutation (Collies, Australian Shepherds, Shelties, Long-haired Whippet, "white feet"); at higher risk for CNS toxicity
- Adverse Effects: HORSES: Swelling & pruritus at the ventral mid-line can be seen approximately 24 hours after ivermectin administration due to a hypersensitivity reaction to dead *Onchocerca* spp. microfilaria. DOGS: May exhibit a shock-like reaction when ivermectin is used as a microfilaricide, presumably due to a reaction associated with the dying microfilaria. CATTLE: Ivermectin can induce serious adverse effects by killing the larva when they are in vital areas; may also cause discomfort or transient swelling at the injection site. MICE & RATS: May cause neurologic toxicity at doses slightly more than usually prescribed. BIRDS: Death, lethargy, or anorexia may be seen. Orange-cheeked Waxbill Finches & budgerigars may be more sensitive to ivermectin than other species

Uses/Indications

Ivermectin is approved in horses for the control of: large strongyles (adult) (*Strongylus vulgaris, S. edentatus, S. equinus, Triodontophorus* spp.), small strongyles, pinworms (adults and 4th stage larva), ascarids (adults), hairworms (adults), large-mouth stomach worms (adults), neck threadworms (microfilaria), bots (oral and gastric stages), lungworms (adults and 4th stage larva), intestinal threadworms (adults), and summer sores (cutaneous 3rd stage larva) secondary to *Hebronema* or *Draschia* Spp.

In cattle, ivermectin is approved for use in the control of gastrointestinal roundworms (adults and 4th stage larva), lungworms (adults and 4th stage larva), cattle grubs (parasitic stages), sucking lice, and mites (scabies). For a listing of individual species covered, refer to the product information.

In swine, ivermectin is approved for use to treat GI roundworms, lungworms, lice, and mange mites. For a listing of individual species covered, refer to the product information.

In reindeer, ivermectin is approved for use in the control of warbles.

In American Bison, ivermectin is approved for use in the control of grubs.

In dogs and cats, ivermectin is approved only for use as a preventative for heartworm. It has also been used as a microfilaricide, slow-kill adulticide, ectoparasiticide, and endoparasiticide.

Pharmacology/Actions

Ivermectin enhances the release of gamma amino butyric acid (GABA) at presynaptic neurons. GABA acts as an inhibitory neurotransmitter and blocks the post-synaptic stimulation of the adjacent neuron in nematodes or the muscle fiber in arthropods. By stimulating the release of GABA, ivermectin causes paralysis of the parasite and eventual death. As liver flukes and tapeworms do not use GABA as a peripheral nerve transmitter, ivermectin is ineffective against these parasites.

Pharmacokinetics

In simple-stomached animals, ivermectin is up to 95% absorbed after oral administration. Ruminants only absorb ¼–⅓ of a dose due to inactivation of the drug in the rumen. While there is greater bioavailability after SC administration, absorption after oral dosing is more rapid than SC. It has been reported that ivermectin's bioavailability is lower in cats than in dogs, necessitating a higher dosage for prophylaxis of heartworm in this species.

Ivermectin is well distributed to most tissues, but does not readily penetrate into the CSF, thereby minimizing its toxicity. Collie-breed dogs with a specific gene defect allow more ivermectin into the CNS than other breeds/species.

Ivermectin has a long terminal half-life in most species (see below). It is metabolized in the liver via oxidative pathways and is primarily excreted in the feces. Less than 5% of the drug (as parent compound or metabolites) is excreted in the urine.

Pharmacokinetic parameters of ivermectin have been reported for various species:

Cattle: Volume of distribution = 0.45–2.4 L/kg; elimination half-life = 2–3 days; total body clearance = 0.79 L/kg/day.

Dogs: Bioavailability = 0.95; volume of distribution = 2.4 L/kg; elimination half-life = 2 days.

Swine: Volume of distribution = 4 L/kg; elimination half-life = 0.5 days.

Sheep: Bioavailability = 1 (intra-abomasal), 0.25 (intra-ruminal); volume of distribution = 4.6 L/kg; elimination half-life = 2–7 days.

Contraindications/Precautions/Warnings

The manufacturer recommends that ivermectin not be used in foals less than 4 months old, as safety of the drug in animals this young has not been firmly established. However, foals less than 30 days of age have tolerated doses as high as 1 mg/kg without signs of toxicity.

Ivermectin is not recommended for use in puppies less than 6 weeks old. After receiving heartworm prophylaxis doses, the manufacturer recommends observing Collie-type breeds for at least 8 hours after administration. Most clinicians feel that ivermectin should not be used in breeds susceptible (Collies, Shelties, Australian shepherds, etc.) to the mdr1 gene mutation at the doses specified for treating microfilaria or other parasites unless the patient has been tested and found not to have the gene defect. A specific test for identifying dogs that have the gene defect (deletion mutation of the mdr1 gene) is now available. Contact the veterinary clinical pharmacology lab at www.vetmed.wsu.edu.

Ivermectin is reportedly contraindicated in chelonian species.

Because milk withdrawal times have not been established, the drug is not approved for use in lactating dairy animals or females of breeding age.

The injectable products for use in cattle and swine should be given subcutaneously only; do not give IM or IV.

If using a product in a species not labeled for that product (extra-label), be certain of the dosage and/or dilutions. There are many reports of overdoses in small animals when large animal products have been used.

Adverse Effects

In horses, swelling and pruritus at the ventral mid-line can be seen approximately 24 hours after ivermectin administration due to a hypersensitivity reaction to dead *Onchocerca* spp. microfilaria. The reaction is preventable by administering a glucocorticoid just prior

to, and for 1–2 days after ivermectin. If untreated, swelling usually subsides within 7–10 days and pruritus will resolve within 3 weeks.

Dogs may exhibit a shock-like reaction when ivermectin is used as a microfilaricide, presumably due to a reaction associated with the dying microfilaria. Other adverse effects when used as a microfilaricide include depression, hypothermia, and vomiting. Pretreatment with diphenhydramine (2 mg/kg IM) and dexamethasone (0.25 mg/kg IV) can help prevent adverse reactions (Atkins 2005).

When used to treat *Hypoderma bovis* larva (Cattle grubs) in cattle, ivermectin can induce serious adverse effects by killing the larva when they are in vital areas. Larva killed in the vertebral canal can cause paralysis and staggering. Larva killed around the gullet can induce salivation and bloat. These effects can be avoided by treating for grubs immediately after the Heal fly (Warble fly) season or after the stages of grub development where these areas would be affected. Cattle may experience discomfort or transient swelling at the injection site. Using a maximum of 10 mL at any one-injection site can help minimize these effects.

Neurotoxicity is possible in dogs, particularly in those with the gene defect (deletion mutation of the mdr1 gene) that has been seen in certain genetic lines of Collie-type breeds.

In mice and rats, ivermectin may cause neurologic toxicity at doses slightly more than usually prescribed (less than 0.5 mg/kg).

In birds, death, lethargy or anorexia may be seen. Orange-cheeked Waxbill Finches and budgerigars may be more sensitive to ivermectin than other species.

For additional information refer to the Overdosage/Acute Toxicity section below.

Reproductive/Nursing Safety

Ivermectin is considered safe to use during pregnancy. Reproductive studies performed in dogs, horses, cattle and swine have not demonstrated adverse effects to fetuses. Reproductive performance in male animals is apparently unaltered. 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.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as in class: ***A*** (*Probably safe. Although specific studies may not have proved the safety of all drugs in dogs and cats, there are no reports of adverse effects in laboratory animals or women.*)

Ivermectin is excreted in milk in low concentrations; it is unlikely to pose significant risk to nursing offspring.

Overdosage/Acute Toxicity

There were 660 exposures to ivermectin reported to the ASPCA Animal Poison Control Center (APCC) during 2005–2006. In these cases 575 were dogs with 104 showing clinical signs, 47 cats with 8 showing clinical signs, 9 wild felines with 3 showing clinical signs, 5 reported bird cases with 2 showing clinical signs, and 2 reported turtle cases with 1 showing clinical signs. The remaining 22 cases consisted of 12 rodents, 3 lagomorphs, 2 caprine, 2 equine, 1 ovine, and 2 unknown species none of which showed clinical signs. Common findings in dogs recorded in decreasing frequency included ataxia, blindness, mydriasis, tremors and vomiting. Common findings in cats recorded in decreasing frequency included ataxia, mydriasis, tremors, hyperesthesia and hypothermia. Common findings in wild felines recorded in decreasing frequency included ataxia, blindness and disorientation. Common findings in birds recorded in decreasing frequency included abasia, ataxia, head held low, lethargy and paresis. Common findings in turtles in decreasing frequency included flaccid paralysis and unresponsiveness.

In dogs (non-sensitive breeds), signs of acute toxicity rarely occur at single dosages of 1 mg/kg (1000 microgram/kg) or less. At 2.5 mg/kg, mydriasis occurs, and at 5 mg/kg, tremors occur. At doses of 10 mg/kg, severe tremors and ataxia are seen. Deaths occurred when dosages exceeded 40 mg/kg, but the LD_{50} is 80 mg/kg. Dogs (Beagles) receiving 0.5 mg/kg PO for 14 weeks developed no signs of toxicity, but at 1–2 mg/kg for the same time period, developed mydriasis and had some weight decreases. Half of the dogs receiving 2 mg/kg/day for 14 weeks developed signs of depression, tremors, ataxia, anorexia, and dehydration.

Ivermectin is actively transported by the p-glycoprotein pump and certain breeds susceptible to MDR1-allele mutation (Collies, Australian Shepherds, Shelties, Long-haired Whippets, etc.) are at higher risk for CNS toxicity. At the dosage recommended for heartworm prophylaxis, it is generally believed that the drug is safe to use in these animals.

Dogs who receive an overdosage of ivermectin or develop signs of acute toxicity (CNS effects, GI, cardiovascular) should receive supportive and symptomatic therapy. Emptying the gut should be considered for recent massive oral ingestions in dogs or cats. For both oral and injected ivermectin overdoses, the use of repeated activated charcoal doses is advised to interrupt enterohepatic recirculation.

Ivermectin has a large safety margin in cats. Kittens receiving doses of at least 110 mcg/kg and adult cats receiving at least 750 mcg/kg showed no untoward effects. Acute toxic signs associated with massive overdoses in cats will appear within 10 hours of ingestion. Signs may include agitation, vocalization, anorexia, mydriasis, rear limb paresis, tremors, and disorientation. Blindness, head pressing, wall climbing, absence of oculomotor menace reflex, and a slow and incomplete response to pupillary light may also be seen. Neurologic signs usually diminish over several days and most animals completely recover within 2–4 weeks. Symptomatic and supportive care is recommended.

In horses, doses of 1.8 mg/kg (9x recommended dose) PO did not produce signs of toxicity, but doses of 2 mg/kg caused signs of visual impairment, depression and ataxia.

In cattle, toxic effects generally do not appear until dosages of 30x those recommended are injected. At 8 mg/kg, cattle showed signs of ataxia, listlessness, and occasionally, death.

Sheep showed signs of ataxia and depression at ivermectin doses of 4 mg/kg.

Swine showed signs of toxicosis (lethargy, ataxia, tremors, lateral recumbency, and mydriasis) at doses of 30 mg/kg. Neonatal pigs may be more susceptible to ivermectin overdosages, presumably due to a more permeable blood-brain barrier. Accurate dosing practices are recommended.

Drug Interactions

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

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

Caution is advised if using other drugs that can inhibit **p-glycoprotein**. Those dogs at risk for MDR1-allele mutation (Collies, Australian Shepherds, Shelties, Long-haired Whippet, etc., "white feet") should probably not receive ivermectin with the following drugs, unless tested "normal"; drugs and drug classes involved include:

- **AMIODARONE**
- **CARVEDILOL**

- **CLARITHROMYCIN**
- **CYCLOSPORINE**
- **DILTIAZEM**
- **ERYTHROMYCIN**
- **ITRACONAZOLE**
- **KETOCONAZOLE**
- **QUINIDINE**
- **SPIRONOLACTONE**
- **TAMOXIFEN**
- **VERAPAMIL**

Laboratory Considerations

- When used at microfilaricide dosages, ivermectin may yield false-negative results in animals with occult heartworm infection.

Doses

- **DOGS:**

Note: When used for prophylaxis or treatment of dirofilariasis it is suggested to review the guidelines published by the American Heartworm Society at www.heartwormsociety.org for more information.

As a preventative for heartworm:

a) 6–12 mcg/kg PO once monthly (Knight 2000)

b) Minimum dosage of 6 micrograms/kg (0.006 mg/kg) PO per month. (Package insert; *Heartgard 30*®—MSD)

As a microfilaricide:

a) When used to kill third, fourth, and young fifth stage larvae for prophylaxis or to kill these larval stages prior to adulticide therapy along with microfilariae, ivermectin is dosed at 6–12 mcg/kg PO once a month. When only used to kill circulating microfilariae, ivermectin can be administered at 6 mcg/kg (the approved prophylactic dose) or at a dose of 50 mcg/kg (approximately 10 times the prophylactic dose). Microfilariae numbers decrease gradually to, or close to, zero within several months at the lower dose. The chance of adverse reactions with this approach is minimal. The higher dose results in a rapid kill that is associated with more adverse effects. (Kittleson 2006b)

As an ectoparasiticide (miticide):

a) For generalized demodicosis: **Note:** Do not consider use in MDR1 mutation susceptible breeds unless tested "normal/normal" for mutation www.vetmed.wsu.edu. If normal/normal, drug reaction is very unlikely. Start at low dosage and increase:

Day 1: 100 mcg/kg PO q24h,

Day 4: 200 mcg/kg PO q24h,

Day 7: 300 mcg/kg; continue to increase by 100 mcg/kg every 3rd day until reach target dose of 600 mcg/kg PO daily and continue treatment 1–2 months after 2 negative skin scrapes. Treatment usually requires 10–33 weeks. (Hillier 2006g)

b) For demodicosis: 400–600 mcg/kg PO daily. Consider using the test dose method: Start at 100 mcg/kg PO and increase by 100 mcg/day until target dose is reached. Treatment typically required for 2–4 months. If toxicity is noted, discontinue. Do not use in collies, Shelties, Old English Sheepdogs and other herding dogs. (DeManuelle 2000)

c) As scabicide: 300–400 mcg/kg PO or SC once weekly for weeks. If using the 1% injection, 1 mL = 10,000 mcg. Beware in sensitive breeds (*e.g.,* Collies, etc.; "white feet, don't treat"). Check heartworm status prior to treatment. Adverse effects are rare outside of sensitive breeds. (Foil 2003c)

As an endoparasiticide:

a) For treatment of parasitic lung disease (*Capillaria* spp.): 0.2 mg/kg PO once (Bauer 1988)

b) For *Oslerus osleri*: 0.4 mg/kg SC once (Reinemeyer 1995)

c) For *Eucoleus boehmi*: 0.2 mg/kg PO once (Reinemeyer 1995)

d) For *Pneumonyssoides caninum*: 0.2 mg/kg SC once (Reinemeyer 1995)

- **CATS:**

Note: When used for prophylaxis or treatment of dirofilariasis it is suggested to review the guidelines published by the American Heartworm Society at www.heartwormsociety.org for more information

As a preventative for heartworm:

a) Minimum effective dosage: 0.024 mg/kg (24 micrograms/kg) PO every 30–45 days (**Note:** also controls hookworms at this dosage) (Knight 1995)

For *Aelurostrongylus abstrusus*:

a) 0.4 mg/kg SC once (Reinemeyer 1995); (Hawkins 2000)

- **FERRETS:**

For prevention of heartworm disease:

a) 0.02 mg/kg PO monthly (Hoeffer 2000)

- **RABBITS/RODENTS/SMALL MAMMALS:**

a) Rabbits: For *Sarcoptes scabiei, Notoedres cati*: 0.3–0.4 mg/kg SC, repeat in 14 days.

For ear mites (Psoroptes) 0.2–0.44 mg/kg PO, SC repeat in 8–18 days (Ivey and Morrisey 2000)

b) Rabbits: For treatment of ear mites: 200 mcg/kg SC and repeated in two weeks. All rabbits in colony should be treated and cages cleaned and disinfected. (Burke 1999)

c) Rodents and lagomorphs: For treatment of sarcoptoid and some fur mites: 200–250 mcg/kg SC. Cages should be thoroughly cleaned and disinfected. (Burke 1999)

d) Mice, Rats, Gerbils, Guinea pigs, Chinchillas: 200 mcg/kg SC or PO every 7 days for 3 weeks Hamsters: 200–500 mcg/kg SC or PO every 14 days for 3 weeks (Adamcak and Otten 2000)

e) Guinea pigs for *Trixacarus caviae* mites: 500 mcg/kg SC, repeated at 14 and 28 days. (Johnson 2006d)

- **CATTLE:**

For susceptible parasites:

a) 200 micrograms/kg SC. Doses greater than 10 mL should be given at two separate sites. (Paul 1986)

b) For psoroptic mange: 200 mg/kg IM (**Note:** Reference was written before approval of the SC labeled bovine product); isolate from other cattle for at least 5 days after treatment. (Mullowney 1986)

c) 200 micrograms/kg (0.2 mg/kg) SC under the loose skin in front of or behind the shoulder (Product Information; *Ivomec® Inj. for Cattle 1%*—MSD)

- **HORSES:**

For susceptible parasites:

a) 200 micrograms/kg (0.2 mg/kg) PO using oral paste or oral liquid (Product Information; *Eqvalan®*—MSD)

b) 0.2 mg/kg PO; 0.2 mg/kg PO at 4 day intervals for lice and mange (Robinson 1987)

c) As a larvicidal for arterial stages of *S. vulgaris*: 0.2 mg/kg once (Herd 1987)

- **SWINE:**

For susceptible parasites:

a) 300 micrograms/kg (0.3 mg/kg) SC in the neck immediately behind the ear (Product Information; *Ivomec® Inj. for Swine 1%*—MSD)

b) For general control of endo- and ectoparasites in potbellied pigs: 300 micrograms/kg SC or IM once for internal parasites and repeated in 10–14 days for external parasites (only partially effective against whipworms—see fenbendazole) (Braun 1995)

■ **SHEEP:**

For susceptible parasites:

a) 200 micrograms/kg for nasal bot infection (Bennett 1986)

b) 200 micrograms/kg SC for one dose (goats also) (Upson 1988)

■ **LLAMAS:**

For susceptible parasites:

a) 0.2 mg/kg PO or SC for one dose (Cheney and Allen 1989), (Fowler 1989)

■ **BIRDS:**

For susceptible parasites:

a) For ascarids, Capillaria and other intestinal worms, *Knemidocoptes pilae* (scaly face and leg mites): Dilute to a 2 mg/mL concentration. After diluting product, use immediately.

Most birds: Inject 220 mcg/kg IM;

Parakeets: 0.02 mg/30 g (2000 mcg/30 gram) IM;

Amazons: 0.1 mg IM;

Macaws: 0.2 mg IM;

Finches: 0.02 mg (Stunkard 1984)

b) For ascarids, coccidia and other intestinal nematodes, Oxysipura, gapeworms, *Knemidocoptes pilae* (scaly face and leg mites): Dilute bovine preparation (10 mg/mL) 1:4 with propylene glycol.

For most species: 200 mcg/kg IM or orally; repeat in 10–14 days.

Budgerigars: 0.01 mL of diluted product (see above) IM or PO (Clubb 1986)

c) 200 mcg/kg (0.2 mg/kg) SC; dilute using propylene glycol. (Sikarskie 1986)

d) Ratites: 200 mcg/kg PO, IM or SC. Has efficacy against *Chandlerella quiscali* in emus. (Jenson 1998)

■ **REPTILES:**

For most nematodes, ectoparasites:

a) For lizards, snakes, and alligators: 0.2 mg/kg (200 mcg/kg) IM, SC, or PO once; repeat in 2 weeks **Note:** Ivermectin is toxic to chelonians (Gauvin 1993)

Monitoring

- Clinical efficacy
- Adverse effects/toxicity (see Adverse Effects and Overdosage Sections)

Client Information

- When using large animal products the manufacturer recommends not eating or smoking and to wash hands after use. Avoid contact with eyes.
- Dispose of unused products and containers by incineration or in approved-landfills. Ivermectin may adversely affect fish or other water-borne organisms if disposed in water.
- Contact veterinarian if any treated animal exhibits signs of toxicity (see Adverse effects and Overdosage sections above).

Chemistry/Synonyms

An avermectin anthelmintic, ivermectin occurs as an off-white to yellowish powder. It is very poorly soluble in water (4 micrograms/mL), but is soluble in propylene glycol, polyethylene glycol, and vegetable oils.

Ivermectin may also be known as MK 933, Ivermectine, Ivermectinum or Ivermectina; many trade names are available.

Storage/Stability/Compatibility

Ivermectin is photolabile in solution; protect from light. Unless otherwise specified by the manufacturer, store ivermectin products at room temperature (15–30°C).

Ivermectin 1% oral solution (equine tube wormer product) is stable at 1:20 and 1:40 dilutions with water for 72 hours when stored in a tight container, at room temperature, and protected from light.

Dosage Forms/Regulatory Status

VETERINARY APPROVED PRODUCTS:

Note: As ivermectin is no longer patent protected in the USA, there are a variety of "generic" products available with many trade names. The following may not be a complete listing.

Ivermectin for Injection: 10 mg/mL (1%) in 50 mL, 200 mL and 500 mL packs; *Ivomec®* (Merial); (OTC); Approved for use in swine. Slaughter withdrawal (at labeled doses) = 18 days.

Ivermectin for Injection: 10 mg/mL (1%) and Clorsulon 100 mg/mL; *Ivomec® Plus Injection for Cattle* (Merial); (OTC). Approved for use in cattle (not female dairy cattle of breeding age). Slaughter withdrawal (at labeled doses) = 40 days. No milk withdrawal has been established.

Ivermectin for Injection: 10 mg/mL (1%) in 50 mL, 200 mL, 500 mL bottles; *Ivomec® 1% Injection for Cattle* and *Swine* (Merial), *Double Impact®* (AgriLabs); *Ultramectrin® Injection* (RXV); (OTC). Approved for use in cattle (not female dairy cattle of breeding age) and swine. Slaughter (when used as labeled): cattle = 35 days, swine = 18 days, reindeer = 56 days, bison = 56 days. No milk withdrawal time has been established.

Ivermectin for Injection: 2.7 mg/mL (0.27%) in 200 mL bottles; *Ivomec® 0.27% Injection for Feeder* and *Grower Pigs* (Merial); (OTC). Approved for use in swine. Slaughter (when used as labeled) = 18 days

Ivermectin Oral Paste: 1.87% (18.7 mg/gram) in 6.08 g syringes; *Equimectrin® Paste 1.87%* (Farnam), *Eqvalan® Paste 1.87%* (Merial), *Rotectin® 1 Paste 1.87%* (Farnam), *Zimectrin® Paste* (Farnam); (OTC). Approved for use in horses (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; *Zimecterin Gold®*(Merial); (OTC). Approved for use in horse or ponies not intended for food purposes.

Ivermectin Liquid: 1% (10 mg/mL) in 50 mL and 100 mL btls (for tube administration; **NOT** for injection); *Amtech Phoenectin® Liquid for Horses* (Phoenix Scientific), *Eqvalan® Liquid* (Merial), *Ivercide® Liquid for Horses* (Phoenix Pharmaceutical); (Rx). Approved for use in horses (not intended for food purposes).

Ivermectin Oral Tablets: 68 mcg, 136 mcg, 272 mcg (Plain or Chewable) in 6 chewables in carton in 10 carton trays, *Heartgard® Tablets* (Merial), *Heartgard® Chewables* (Merial); (Rx). Approved for use in dogs.

Ivermectin Oral Chewable Tablets: 55 mcg or 165 mcg in cartons of 6 in 10 cartons per tray. *Heartgard® for Cats* (Merial); (Rx) Approved for use in cats.

Ivermectin/Pyrantel Oral Tablets: 68 mcg/57 mg, 136 mcg/114mg, 272 mcg/228 mg); *Heartgard® Plus Chewables* (Merial); *Tri-Heart® Plus Chewable Tablets* (Schering); (Rx). Approved for use in dogs.

Ivermectin Oral Solution: 0.08% in 960 mL and 4,800 mL containers; *Ivomec® Sheep Drench* (Merial); (OTC); Approved for use in sheep. Slaughter withdrawal time = 11 days.

Ivermectin Bolus: 1.72 g; *Ivomec® SR Bolus* (Merial); (OTC). Approved for use in cattle (not female dairy cattle of breeding age). Slaughter withdrawal time = 180 days. No milk withdrawal time has been established.

Ivermectin Medicated feeds: *Ivomec® Premix for Swine Type A Medicated Article* (Merial) 0.6% in 50 lb. *Ivomec® Premix for Swine Type C Medicated Feed 0.02%* (Merial) in 20 lb one-ton bag and 40 lb two-ton bag, *Ivomec® Premix for Swine Type C medicated feed 0.1%* (Merial) in 20 lb one-ton bag. Approved for use in swine. Slaughter withdrawal = 5 days

Ivermectin Topical Parasiticide Pour-on for Cattle: 5 mg/mL 250 mL, 500 mL, 1 liter and 1 gallon bottles. Approved for use in cattle (not female dairy cattle of breeding age). Slaughter withdrawal time = 48 days, milk withdrawal has not been established. *Amtech Phoenectin® Pour-on for Cattle* (Phoenix Scientific), *Bimectin® Pour-On* (Bimeda), *Ivercide® Pour-On for Cattle* (Phoenix Pharmaceutical), *Ivermectin® Pour-On* (Aspen, Durvet), *Ivomec® Eprinex® Pour-on for Beef and Dairy Cattle* and *Ivomec® Pour-on for Cattle* (Merial), *Prozap® Ivermectin Pour-on* (Loveland), *Top Line®* (AgriLabs), *Ultramectrin® Pour-On* (RXV); (OTC)

An otic product *Acarexx®* is also available.

HUMAN-LABELED PRODUCTS:

Ivermectin Tablets: 3 mg and 6 mg; *Stromectol®* (Merck); (Rx)

KAOLIN/PECTIN

(***kay***-oh-lin/***pek***-tin) Kaopectolin

GI ADSORBENT/PROTECTANT

Prescriber Highlights

- Adsorbent for treatment of diarrhea & GI toxins; questionable efficacy
- Contraindications: Should not be relied on to control severe diarrheas or to replace adequate fluid/electrolyte monitoring or as replacement therapy in severe or chronic diarrheas
- Adverse Effects: Transient constipation
- Drug Interactions

Uses/Indications

Although its efficacy is in question, kaolin/pectin is used primarily in veterinary medicine as an oral anti-diarrheal agent. It has also been used as an adsorbent agent following the ingestion of certain toxins. Administration may be difficult due to the large volumes that may be necessary to give orally.

Pharmacology/Actions

Kaolin/pectin is thought to possess adsorbent and protective qualities. Presumably, bacteria and toxins are adsorbed in the gut and the coating action of the suspension may protect inflamed GI mucosa. The pectin component, by forming galacturonic acid, has been demonstrated to decrease pH in the intestinal lumen.

In one study in children with acute nonspecific diarrhea, stool fluidity was decreased, but stool frequency, water content, and weight remained unchanged. No studies documenting the clinical efficacy of this combination in either human or veterinary species were located.

Pharmacokinetics

Neither kaolin nor pectin are absorbed after oral administration. Up to 90% of the pectin administered may be decomposed in the gut.

Contraindications/Precautions/Warnings

There are no absolute contraindications to kaolin/pectin therapy, but it should not be relied on to control severe diarrheas. Kaolin/pectin should not replace adequate fluid/electrolyte monitoring or replacement therapy in severe or chronic diarrheas.

Adverse Effects

At usual doses, kaolin/pectin generally has no adverse effects. Constipation may occur, but is usually transient and associated with high dosages. High doses in debilitated, or in very old or young patients may rarely cause fecal impaction. In rats, kaolin/pectin has been demonstrated to increase fecal sodium loss in diarrhea.

In humans, kaolin/pectin is recommended for use only under the direct supervision of a physician, in patients less than 3 years of age or for longer than 48 hours.

Reproductive/Nursing Safety

Adsorbent (only) anti-diarrheal products should be safe to use during pregnancy and lactation. The addition of other active ingredients (*e.g.*, as opiates) may alter this recommendation.

Overdosage/Acute Toxicity

Overdosage is unlikely to cause any serious effects, but constipation requiring treatment may occur.

Drug Interactions

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

- **DIGOXIN**: Some evidence exists that kaolin/pectin may impair the oral absorption of digoxin. Separate doses by at least two hours.
- **LINCOMYCIN**: Kaolin/pectin may inhibit the oral absorption of lincomycin. If both drugs are to be used, administer kaolin/pectin at least 2 hours before or 3–4 hours after the lincomycin dose.

Doses

- **DOGS:**

  For diarrhea:
  a) 1–2 mL/kg PO q4–6h (Davis 1985a)
  b) 1–2 mL/kg PO four times daily (Johnson 1984)
  c) 1–2 mL/kg PO q2–6h (Kirk 1986)

  For enterotoxins secondary to garbage ingestion:
  a) 2–5 mL/kg PO q1–6 hours (Coppock and Mostrom 1986)
  b) 10–15 grams of kaolin/kg PO four times daily (Grauer and Hjelle 1988a)

- **CATS:**

  For diarrhea:
  a) 1–2 mL/kg PO q4–6h (Davis 1985a)
  b) 1–2 mL/kg PO four times daily (Johnson 1984)
  c) 1–2 mL/kg PO q2–6h (Kirk 1986)

- **FERRETS:**

  a) 1–2 mL/kg PO 3–4 times daily (Williams 2000)

- **RABBITS/RODENTS/SMALL MAMMALS:**

  a) Guinea pigs: 0.2 mL PO 3–4 times a day (Adamcak and Otten 2000)