MACROCYCLIC LACTONES (Veterinary—Systemic)

This monograph includes information on the following avermectins: Doramectin; Eprinomectin; Ivermectin; Selamectin. It also contains information on the following milbemycins: Milbemycin; Moxidectin.

Some commonly used *brand names* are:

For veterinary-labeled products—

Agri-Mectin Equine Paste Dewormer 1.87% [Ivermectin]
AmTech Phoenectin Injection for Cattle and Swine [Ivermectin]
AmTech Phoenectin Liquid for Horses [Ivermectin]
AmTech Phoenectin Paste 1.87% [Ivermectin]
AmTech Phoenectin Pour-On [Ivermectin]
Bimectin Pour-On [Ivermectin]
Comectrin Injection for Cattle and Swine [Ivermectin]
Comectrin Pour-On [Ivermectin]
Coopermec Cattle Pour-On [Ivermectin]
Cooper's Best Ivermectin Paste 1.87% [Ivermectin]
Cydectin Injectable Solution [Moxidectin]
Cydectin Injection [Moxidectin]
Cydectin Pour-On [Moxidectin]
Dealer Select Horse Care Ivermectin Paste 1.87% [Ivermectin]
Dectomax Injectable Solution [Doramectin]
Dectomax Pour-On [Doramectin]
Double Impact [Ivermectin]
DVMectin [Ivermectin]
Ecomectin Cattle Pour-On [Ivermectin]
Eprinex Pour-On [Eprinomectin]
Equell Paste 1.87% [Ivermectin]
Equimectrin Paste 1.87% [Ivermectin]
Eqvalan Liquid [Ivermectin]
Eqvalan Oral Paste [Ivermectin]
Eqvalan Paste 1.87% [Ivermectin]
Heartgard Chewables [Ivermectin]
Heartgard-30 Chewables [Ivermectin]
Heartgard-30 Chewables For Cats [Ivermectin]
Heartgard For Cats [Ivermectin]
Heartgard Tablets [Ivermectin]
Heartgard-30 Tablets [Ivermectin]
Horse Health Equine Ivermectin Paste 1.87% [Ivermectin]
Interceptor Flavor Tabs [Milbemycin]
Ivercare [Ivermectin]
Ivercide Equine Paste 1.87% [Ivermectin]
Ivercide Injection for Cattle and Swine [Ivermectin]
Ivercide Liquid for Horses [Ivermectin]
Ivercide Pour-On for Cattle [Ivermectin]
Ivermax Drench for Sheep [Ivermectin]
Ivermax Equine Oral Drench [Ivermectin]
Iver-On [Ivermectin]
Iversol Liquid for Horses [Ivermectin]
Ivomec Drench for Sheep [Ivermectin]
Ivomec Injection [Ivermectin]
Ivomec 1% Injection for Cattle and Swine [Ivermectin]
Ivomec Injection for Grower and Feeder Pigs [Ivermectin]
Ivomec 1% Injection for Swine [Ivermectin]
Ivomec Pour-On [Ivermectin]
Ivomec Premix for Swine [Ivermectin]
Ivomec Premix for Swine Type C Medicated Feed 0.02% [Ivermectin]
Ivomec Sheep Drench [Ivermectin]
Noramectin Pour-On [Ivermectin]
Panomec Oral Paste [Ivermectin]
ParaGARD [Ivermectin]
Parid EQ Liquid for Horses [Ivermectin]
Parid EQ Paste 1.87% [Ivermectin]
Privermectin Drench for Sheep [Ivermectin]
Privermectin Equine Oral Liquid [Ivermectin]
Privermectin Pour-On [Ivermectin]
Produmec Injection for Cattle and Swine [Ivermectin]
Produmec Pour-On [Ivermectin]
ProHeart 6 [Moxidectin]
ProMectin B Pour-On [Ivermectin]
ProMectin E Liquid [Ivermectin]
ProMectin E Paste [Ivermectin]
ProMectin Injection for Cattle and Swine [Ivermectin]
Prozap Pour-On [Ivermectin]
Quest Gel [Moxidectin]
Revolution [Selamectin]
Rotation 1 [Ivermectin]
SparMectin-E [Ivermectin]
Top Line [Ivermectin]
Ultramectrin Injection for Cattle and Swine [Ivermectin]
Ultramectrin Pour-On [Ivermectin]
Zimecterin [Ivermectin]

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

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

Category: Anthelmintic (systemic).

Indications

Note: Text between [EL-US] and [EL] describes uses not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses not included in Canadian product labeling.

The [EL-US] or [EL-CAN] designation may signify a lack of product availability in the country indicated. See the *Dosage Forms* section of this monograph to confirm availability.

General considerations

The macrocyclic lactones are effective against certain acarines, insects, and nematodes.{R-1} They have no measurable effect on cestodes or trematodes.{R-1}

Development of resistance to these anthlemintics by some nematodes in small ruminants and by roundworms in horses has been reported in the United States.{R-47; 49; 100-104} Resistant parasites have been transferred between goats and sheep farmed on the same pasture.{R-100} Animal management and carefully designed anthelmintic protocols are important strategies to limit resistance to macrocyclic lactones. There is cross resistance between the avermectins and milbemycins.{R-49; 101}

Accepted

Bot infection (treatment)—

Horses: Ivermectin oral paste and oral solution are indicated in the treatment and control of oral and gastric stages of *Gasterophilus* species, including *G. intestinalis* and third instars of *G. nasalis*.{R-8-11; 17-19} Moxidectin oral gel is indicated in the treatment of second and third instars of *G. intestinalis* and third instars of *G. nasalis*.{R-38}

Sheep: Ivermection oral solution and [EL-US]injection[EL] are indicated in the treatment and control of all larval stages of the nasal bot, *Oestrus ovis*.{R-12; 14; 15}

Eyeworm infection (treatment)—*Cattle:* Doramectin injection, doramectin topical solution, [EL-US]ivermectin injection[EL] and [EL-US]ivermectin topical solution[EL] are indicated in the treatment and control of adult *Thelazia* species.{R-13; 14; 23-26}

Flea infestation (prophylaxis and treatment)—*Cats* and *dogs:* Selamectin topical solution is indicated in the treatment and prevention of *Ctenocephalides canis* and *C. felis* infestation.{R-29; 30}

Grub (warble) infection (treatment)—

[EL-CAN]*Buffalo (Bison), American*[EL]: Ivermectin injection is indicated in the treatment and control of *Hypoderma bovis*.{R-1}

Cattle: Doramectin injection, doramectin topical solution, eprinomectin topical solution, ivermectin injection, ivermectin topical solution, moxidectin injection, and moxidectin topical solution are indicated in the treatment and control of parasitic stages of *Hypoderma bovis* and *H. lineatum*.{R-1; 2; 13; 14; 23-28; 31-33; 174}

[EL-CAN]*Reindeer*[EL]: Ivermectin injection is indicated in the control of *Oedemagena tarandi*.{R-2}

Habronemiasis, cutaneous (treatment); or

Onchocerciasis, cutaneous (treatment)—*Horses:* Ivermectin oral paste, ivermectin oral solution, and [EL-US]moxidection oral gel[EL] are indicated in the treatment and control of neck threadworm microfilariae, *Onchocerca* species, associated with dermatitis.{R-8-11; 17-19; 38} Ivermectin oral paste and oral solution are indicated in the treatment and control of dermatoses (summer sores) caused by cutaneous third-stage larvae (L_3) of *Draschia* and *Habronema* species.{R-8-11; 17; 18} Significant lesions may require medical therapy other than anthelmintic treatment.{R-8}

Heartworm disease (prophylaxis)—

Cats: Ivermectin tablets, milbemycin oxime tablets, and selamectin topical solution are indicated in the prevention of *Dirofilaria immitis* infection by the elimination of tissue stage larvae.{R-7; 29; 30; 34; 36}

Dogs: Ivermectin tablets, milbemycin oxime tablets, [EL-US]moxidectin for sustained-release injection[EL], and selamectin topical solution are indicated in the prevention of *Dirofilaria immitis* infection by the elimination of tissue stage larvae.{R-5; 6; 20; 29; 30; 35; 36; 39; 40}

Horn flies (treatment)—*Cattle:* Doramectin, eprinomectin, ivermectin, and [EL-CAN]moxidectin[EL] topical solutions are indicated in the treatment and control of *Haematobia irritans*.{R-1; 13; 23; 25; 27; 28; 31}

Kidneyworm infection (treatment)—*Pigs:* Doramectin injection and ivermectin medicated feed are indicated in the treatment and control of adult *Stephanurus dentatus*.{R-4; 16; 24; 26}

Lungworm infection (treatment)—

Cattle: Doramectin injection, doramectin topical solution, eprinomectin topical solution, ivermectin injection, ivermectin topical solution, moxidectin injection and moxidectin topical solution are indicated in the treatment and control of adult and fourth-stage larvae (L_4) of *Dictyocaulus viviparus*.{R-1; 2; 13; 14; 23-28; 31-33; 174}

[EL-US]*Deer*[EL]: Eprinomectin topical solution is indicated in Canadian product labeling for the treatment of adult and L_4 *Dictyocaulus viviparus*.{R-28}

Horses: Ivermectin oral paste and oral solution are indicated in the control of adult and L_4 *Dictyocaulus arnfieldi*.{R-8-11}

Pigs: Doramectin injection, ivermectin injection, and ivermectin medicated feed are indicated in the treatment and control of adult *Metastrongylus* species.{R-2-4; 14; 16; 24; 26}

Sheep: Ivermectin oral solution and [EL-US]injection[EL] are indicated in the treatment and control of adult and L_4 *Dictyocaulus filaria*.{R-12; 14; 15}

Mite dermatosis (treatment)—

Cattle: Doramectin injection, doramectin topical solution, eprinomectin topical solution, ivermectin injection, ivermectin topical solution and [EL-US]moxidectin topical solution[EL] are indicated in the treatment and control of *Sarcoptes scabiei* variant *bovis*.{R-1; 2; 13; 14; 23-28; 32} Doramectin injection, ivermectin injection, moxidectin injection, and moxidectin topical solution are also indicated in the treatment and control of *Psoroptes bovis*.{R-2; 13; 14; 24; 26; 31; 32; 174} Doramectin topical solution, eprinomectin topical solution, [EL-US]ivermectin topical solution[EL], and moxidectin topical solution are indicated in the treatment and control of *Chorioptes bovis*.{R-13; 25; 27; 28; 31}

Dogs:

Selamectin topical solution is indicated in the treatment and control of *Sarcoptes scabiei*.{R-29; 30} [EL-US,CAN]Ivermectin injection (Evidence rating: A-1,2), administered either orally or subcutaneously,{R-112-114} is used in the treatment and control of sarcoptic mange.[EL]

[EL-US,CAN]Ivermectin injection, administered either orally or subcutaneously, is used in the treatment and control of cheyletiellosis (Evidence rating: A-2).[EL]{R-66}

[EL-US,CAN]Orally administered ivermectin injection or oral solution (Evidence rating: A-3){R-122-125} has been used in the treatment of demodicosis, in conjunction with diagnosis and treatment of any underlying disease.[EL]

Pigs: Doramectin injection, ivermectin injection, and ivermectin medicated feed are indicated in the treatment and control of *Sarcoptes scabiei* variant *suis*.{R-2-4; 14; 16; 24; 26}

[EL-US,CAN]*Cats*[EL]: Ivermectin injection, administered either orally or subcutaneously, has been used in the treatment and control of cheyletiellosis (Evidence rating: A-3).{R-119}

Mite, ear, infestation (treatment)—

Cats and *dogs:* Selamectin topical solution is indicated in the treatment and control of *Otodectes cynotis*.{R-29; 30}

[EL-US,CAN]Ivermectin injection is used in the treament of *Otodectes cynotis* infestation (Evidence rating: A-1).[EL]{R-114; 159}

[EL-CAN]*Foxes,* ranch raised: Ivermectin injection is indicated in the treatment and control of *Otodectes cynotis*.[EL]{R-3}

Nematode, gastrointestinal, infection (treatment)—

Cats:

Ivermectin tablets are indicated in the removal of adult and immature hookworms, *Ancyclostoma tubaeforme* [EL,CAN]and *A. braziliense*.[EL]{R-7}

Milbemycin oxime tablets and selamectin topical solution are indicated in the removal of adult hookworms, *Ancyclostoma tubaeforme,* and roundworms, *Toxocara cati*.{R-29; 30; 34; 36}

Cattle:

Doramectin injection is indicated in the treatment and control of gastrointestinal roundworms, including adult *Bunostomum phlebotomum*, adult and L_4 *Cooperia oncophora,* adult *C. pectinata,* adult and L_4 *C. punctata,* adult and L_4 *C. surnabada* (syn. *mcmasteri*), adult and L_4 *Haemonchus placei,* [EL,US]adult *Nematodirus spathiger*[EL], adult and L_4 *Oesophagostomum radiatum,* adult *Ostertagia lyrata,* adult and L_4 *O. ostertagi* (including inhibited L_4), adult *Strongyloides papillosus,* adult and L_4 *Trichostrongylus axei,* adult and L_4 *T. colubriformis,* [EL,CAN]adult and L_4 *T. longispicularis*[EL], and adult *Trichuris* species.{R-24; 26}

Doramectin topical solution is indicated in the treatment and control of gastrointestinal roundworms, including adult *Bunostomum phlebotomum*, [EL,CAN]adult[EL] and L_4 *Cooperia oncophora,* adult *C. pectinata,* adult and L_4 *C. punctata,* adult *C. surnabada* (syn. *mcmasteri*), adult and L_4 *Haemonchus placei,* adult and L_4 *Oesophagostomum radiatum,* adult and [EL,US]L_4[EL] *Ostertagia lyrata,* adult and L_4 *O. ostertagi* (including inhibited L_4), adult and L_4 *Trichostrongylus axei,* adult and L_4 *T. colubriformis,* and adult *Trichuris* species.{R-23; 25}

Eprinomectin topical solution is indicated in the treatment and control of gastrointestinal roundworms, including adult and L_4 *Bunostomum phlebotomum,* adult and L_4 *Cooperia oncophora,* [EL,US]adult and L_4 *Cooperia pectinata*[EL], adult and L_4 *Cooperia punctata,* adult and L_4 *Cooperia surnabada,* adult and L_4 *Haemonchus placei,* adult and L_4 *Nematodirus helvetianus,* adult and L_4 *Oesophagostomum radiatum,* [EL,US]adult *Ostertagia lyrata*[EL], adult and L_4 *Ostertagia ostertagi* (including inhibited stage), adult *Strongyloides papillosus,* adult and L_4 *Trichostrongylus axei,* adult and L_4 *Trichostrongylus colubriformis,* adult *Trichostrongylus longispicularis,* and adult *Trichuris* species.{R-27; 28}

Ivermectin injection is indicated in the treatment and control of gastrointestinal roundworms, including [EL,CAN]adult and L_4 *Bunostomum phlebotomum*[EL], adult and L_4 *Cooperia oncophora,* adult and [EL,CAN]L_4[EL] *C. punctata,* [EL,CAN]adult and L_4 *C. pectinata*[EL], adult and L_4 *Haemonchus placei,* [EL,CAN]adult *Nematodirus helvetianus*, adult *N. spathiger*[EL], adult and L_4 *Oesophagostomum radiatum,* adult and L_4 *Ostertagia lyrata,* adult and L_4 *Ostertagia ostertagi* (including inhibited stage), [EL,US]*Strongyloides papillosus*[EL], adult and L_4 *Trichostrongylus axei* and adult and [EL,CAN]L_4[EL] *Trichostongylus colubriformis*.{R-2; 14}

Ivermectin topical solution is indicated in the treatment and control of gastrointestinal roundworms, including adult and L_4 *Cooperia* species, adult and L_4 *Haemonchus placei,* [EL,US]L_4 *Nematodirus* species[EL], adult and L_4 *Oesophagostomum radiatum,* [EL,US]adult *Oesophagostomum venulosum*[EL], adult and L_4 *Ostertagia ostertagi* (including inhibited stage), adult *Strongyloides papillosus,* adult and L_4 *Trichostrongylus axei,* adult and L_4 *T. colubriformis,* and adult *Trichuris* species.{R-1; 13}

Moxidectin injection is indicated in the treatment of gastrointestinal roundworms, including [EL,US]adult and L_4 *Bunostomum phlebotomum*[EL], [EL,CAN]adult and L_4 *Cooperia oncophora*[EL], [EL,US]adult *C. pectinata*[EL], adult and L_4 *C. punctata,* [EL,CAN]adult and L_4 *Cooperia surnabada*[EL] ,adult and [EL,US]L_4[EL] *Haemonchus placei,* [EL,US]adult and L_4 *Nematodirus helvetianus*[EL], adult and L_4 *Oesophagostomum radiatum,* adult and L_4 *Ostertagia ostertagi* [EL,US](including inhibited L_4)[EL], adult and [EL,US]L_4[EL] *Trichostrongylus axei,* adult and L_4 *T. colubriformis,* adult *Trichuris* species and adult *T. ovis*.{R-33; 174}

Moxidectin topical solution is indicated in the treatment and control of gastrointestinal roundworms, including adult *Bunostomum phlebotomum,* adult and L_4 *Cooperia oncophora,* adult *C. pectinata,* adult and L_4 *C. punctata,* [EL,CAN]adult *C. spatulata*[EL], adult and L_4 *C. surnabada,* adult and L_4 *Haemonchus placei,* adult and L_4 *Nematodirus helvetianus*, adult and L_4 *Oesophagostomum radiatum,* adult and L_4 *Ostertagia ostertagi* (including inhibited L_4), adult and L_4 *Trichostrongylus axei,* adult and L_4 *T. colubriformis* and [EL,US]*Trichuris discolor*[EL].{R-31; 32}

[EL,US]*Deer*[EL]: Eprinomectin topical solution is indicated in Canadian product labeling in the treatment of gastrointestinal roundworms, including adult *Ostertagia*-like species (including *O. mossi/dikmansi, O. lyrata, O. leptospicularis, Spiculopteratia spiculoptera,* and *S. asymmetrica*), adult *Mazamastrongylus* species, adult *Oesophagostomum* species, and adult and L_4 *Trichostrongylus* species.{R-28}

Dogs:

Milbemycin oxime tablets are indicated in the control of adult hookworms, *Ancyclostoma caninum;* the removal and control of adult roundworms, *Toxocara canis* and *Toxascaris leonina;* and in the removal and control of adult whipworms, *Trichuris vulpis*.{R-35; 36}

[EL,US]Moxidectin for sustained-release injection[EL] is indicated in the treatment of larval and adult hookworms, *Ancyclostoma caninum* and *Uncinaria stenocephala,* present at the time of treatment.{R-39; 40}

[EL,US]Selamectin topical solution[EL] is indicated as an aid in the treatment and control of *T. canis*.{R-30}

[EL,US,CAN]Ivermectin injection, administered either orally or subcutaneously, can be effective in the treatment of hookworms, *Ancyclostoma braziliense* and adult and larval *A. caninum*, and whipworms, *T. vulpis* (Evidence rating: A-1); however, it is relatively ineffective in the treatment of ascarids.[EL]{R-134}

Horses:

Ivermectin oral paste and oral solution are indicated in the treatment and control of hairworms, adult *Trichostrongylus axei;* intestinal threadworms, adult *Stongyloides westeri;* large mouth stomach worms, adult *Habronema muscae;* pinworms, adult and L_4 *Oxyuris equi;* roundworms, adults, L_3, and L_4 *Parascaris equorum;* large strongyles, including adult and [EL,CAN]tissue stages[EL] of *Strongylus edentatus*, adult *Stronylus equinus,* adult *Strongylus vulgaris* (and early forms in blood vessels) and adult *Triodontophorus* species; and small strongyles, including [EL,CAN]*Coronocyclus* species[EL], *Cyathostomum* species, *Cylicocyclus* species, *Cylicodontophorus* species, *Cyclicostephanus* species, [EL,US]*Gyalocephalus* species[EL], and *Petrovinema poculatum*.{R-8;-11; 17-19; 44}

Moxidectin oral gel is indicated in the treatment and control of hairworms, adult *Trichostrongylus axei;* large mouth stomach worms, adult and [EL,US]gastric L_4[EL] *Habronema muscae;* pinworms, adult and L_4 *Oxyuris equi;* roundworms, adult and L_4 *Parascaris equorum;* large strongyles, including adult and tissue stages of *Strongylus edentatus*, adult and arterial larval stages of *S. vulgaris*, adult *Triodontophorus brevicauda,* and adult *T. serratus;* and small strongyles, including adult *Coronocyclus* species, adult *Cyathostomum* species, adult *Cylicocyclus* species, [EL,US]adult *Cylicodontophorus* species[EL], adult *Cylicostephanus* species, adult *Gyalocephalus capitatus,*

undifferentiated lumenal larvae; and encysted late L_3 and L_4 mucosal cyathostome larvae.{R-37; 38}

Regular treatment is expected to decrease the risk of verminous arteritis and colic caused by early forms of *S. vulgaris* in the blood vessels (verminous arteritis).{R-8-11}

Pigs:

Doramectin injection is indicated in the treatment and control of gastrointestinal roundworms, including adult and L_4 *Ascaris suum,* adult *Hyostrongylus rubidus*, adult and L_4 *Oesophagostomum dentatum,* adult *Oesophagostomum quadrispinulatum,* and adult *Strongyloides ransomi*.{R-24; 26}

Ivermectin injection and medicated feed are indicated in the treatment and control of gastrointestinal roundworms, including adult and L_4 *Ascaris suum*, *Hyostrongylus rubidus*, and *Oesophagostomum* species; and adults and somatic larvae of *Strongyloides ransomi*.{R-2-4; 14; 16} [EL,US]In Canada, ivermectin medicated feed is also indicated in the treatment and control of adult *Ascarops strongylina*.[EL]{R-16}

Sheep:

Ivermectin oral solution is indicated in the treatment and control of gastrointestinal roundworms, including adult *Chabertia ovina,* adult and L_4 *Cooperia curticei,* [EL,CAN]adult *Cooperia onchophora*[EL], adult and L_4 *Haemonchus contortus,* [EL,CAN]adult *Haemonchus placei*[EL], adult and [EL,CAN]L_4[EL] *Nematodirus battus,* [EL,CAN]adult[EL] and L_4 *N. spathiger,* adult and L_4 *Oesophagostomum columbianum,* [EL,US]adult[EL] and [EL,CAN]L_4[EL] *Oesophagostomum venulosum,* adult and L_4 *Ostertagia circumcincta,* adult *Strongyloides papillosus,* adult and L_4 *Trichostrongylus axei,* adult and L_4 *T. colubriformis,* and adult *Trichuris ovis*.{R-12; 15}

[EL,US]Ivermection injection[EL] is indicated in the treatment and control of gastrointestinal roundworms, including adult and immature *Chabertia ovina,* adult and immature *Cooperia curticei,* adult and immature *Haemonchus contorus,* adult and immature *Oesophagostomum columbianum,* adult *Oesophagostomum venulosum,* adult and immature *Ostertagia circumcincta,* adult *Trichostrongylus axei,* adult and immature *T. colubriformis,* and adult *Trichuris ovis*.{R-14}

Pediculosis (treatment)—

Cattle: Doramectin injection, doramectin topical solution, eprinomectin topical solution, ivermectin injection, ivermectin topical solution, moxidectin injection, and moxidectin topical solution are indicated in the control of *Haematopinus eurysternus, Linognathus vituli,* and *Solenopotes capillatus*.{R-1; 14; 24-28; 31-33; 174} Doramectin, eprinomectin, ivermectin, and moxidectin topical solutions are also indicated in the control of *Damalinia bovis*.{R-2; 13; 23; 25; 27; 28; 31; 32}

Pigs: Doramecin injection, ivermectin injection, and ivermectin medicated feed are indicated in the control of *Haematopinus suis*.{R-2-4; 14; 16; 24; 26}

Tick infestation (treatment)—*Dogs:* Selamectin topical solution is indicated in the control of *Dermacentor variabilis*{R-29} and [EL,US]the treatment and control of *Rhipicephalus sanguineus.*[EL]{R-30}

Potentially effective

Mite dermatosis (treatment)—

Dogs:

[EL,US,CAN]For cheyletiellosis—There is some evidence to suggest that milbemycin (Evidence rating: B-3) and selamectin (Evidence rating: B-3) can be effective in the treatment of cheyletiellosis.[EL]{R-121; 133}

[EL,US,CAN]For demodicosis—There is some evidence to suggest that doramectin (Evidence rating: B-3) or milbemycin (Evidence rating: B-2) can be effective in the treatment of demodicosis.[EL]{R-126-130}

[EL,US,CAN]For sarcoptic mange—There is some evidence to suggest that ivermectin topical solution (Evidence rating: B-2) or milbemycin tablets (Evidence rating: B-2) can be effective in the treatment of sarcoptic mange. [EL]{R-112; 115-117; 160}

[EL,US,CAN]*Cats:*

For cheyletiellosis—There is some evidence to suggest that selamectin (Evidence rating: B-3) can be effective in the treatment of cheyletiellosis.{R-120}

For demodicosis—There is some evidence to suggest that doramectin (Evidence rating: B-3) can be effective in the treatment of demodicosis.{R-126}

For notoedric mange—There is some evidence to suggest that doramectin (Evidence rating: B-3) and selamectin (Evidence rating: B-3) can be effective in the treatment of notoedric mange.[EL]{R-131; 132}

[EL,US,CAN]Mite, nasal, infestation (treatment)—*Dogs:* There is some evidence to suggest that ivermectin injection (Evidence rating: B-3), milbemycin oxime tablets (Evidence rating: B-2), or selamectin topical solution (Evidence rating: B-2) can be effective in the treatment of *Pneumonyssoides caninum* infestation in dogs.[EL]{R-169-173}

Nematodes, gastrointestinal (treatment): [EL,US,CAN]*Goats*[EL]—There is some evidence to suggest ivermectin oral solution (Evidence rating: A-1,3){R-135-137} or oral moxidectin (Evidence rating: B-2){R-104; 138} can be effective in the treatment of gastrointestinal nematodes; however, experts warn against routine administration of macrocyclic lactone anthelmintics to goats because of concern that efficacy could be short-lived for the herd treated as well as for the general goat population because of the potential for parasite resistance.{R-104} In some locations, resistance may already compromise efficacy.{R-104} Use is reserved for situations where other parasite control measures have failed, where a survey in the population of goats to be treated documents parasite susceptibility, and where a parasite control strategy is in place to maximize efficacy and minimize resistance.

Regulatory Considerations

U.S.—

Withdrawal times have been established for doramectin injection, doramectin topical solution, eprinomectin topical solution, ivermectin injection, ivermectin medicated feed, ivermectin oral solution, ivermection topical solution, and moxidectin topical solution. See the *Dosage Forms* section of this monograph for more information.

Canada—

Withdrawal times have been established for doramectin injection, doramectin topical solution, eprinomectin topical solution, ivermectin injection, ivermectin medicated feed, ivermectin oral solution, ivermection topical solution, moxidectin injection, and moxidectin topical solution. See the *Dosage Forms* section of this monograph for more information.

Chemistry

Source:

Avermectins—Derivatives of fermentation products of the soil organism, *Streptomyces avermitilis*.{R-2; 25}

Milbemycin oxime—Fermentation product of *Streptomyces hygroscopicus* subspecies *aureolacrimosus*.{R-45}

Moxidectin—A semi-synthetic methoxine derivative of nemadectin, a fermentation product of *Streptomyces cyaneogriseus* subspecies *noncyanogenus*.{R-39}

Chemical group: Macrocyclic lactones. The avermectins and milbemycins are closely related chemically, each having a 16-membered lactone ring.{R-47}

Chemical name:

Doramectin—Avermectin A_{1a}, 25-cyclohexyl-5-*O*-demethyl-25-de(1-methylpropyl)-.{R-43}

Eprinomectin—A mixture of two components:

At least 90% eprinomectin component B_{1a}—Avermectin A_{1a}, 4”-(acetylamino)-5-*O*-demethyl-4”-deoxy-, (4”R)-.{R-43}

Up to 10% eprinomectin component B_{1b}—Avermectin A_{1a}, 4”-(acetylamino)-5-*O*-demethyl-25-de(1-methylpropyl)-4”-deoxy-25-(1-methylethyl)-, (4”R)-.{R-43}

Ivermectin—A mixture of two components:{R-43; 53}

At least 80% ivermectin component B_{1a}—Avermectin A_{1a}, 5-*O*-demethyl-22,23-dihydro-.

Up to 20% ivermectin component B_{1b}—Avermectin A_{1a}, 5-*O*-demethyl-25-de(1-methylpropyl)-22,23-dihydro-25-(1-methylethyl)-.

Milbemycin oxime—A mixture of two components:{R-43; 53}

About 80% milbemycin A_4 5-oxime.

About 20% milbemycin A_3 5-oxime.

Moxidectin—Milbemycin B, 5-*O*-demethyl-28-deoxy-25-(1,3-demethyl-1-butenyl)-6,28-epoxy-23-(methoxyimino)-, [6*R*,23*E*,25*S*(*E*)]-.{R-43}

Selamectin—(5*Z*,25S)-25-cyclohexyl-4'-*O*-de(2,6-dideoxy-3-*O*-methyl-*alpha*-L-arabino-hexopyranosul)-5-demethoxy-25-de(1-methylpropyl)-22,23-dihydro-5-hydroxyiminoavermectin A_{1a}.{R-29}

Molecular formula:

Doramectin—$C_{50}H_{74}O_{14}$.{R-43}

Eprinomectin—{R-43}

Eprinomectin component B_{1a}: $C_{50}H_{75}NO_{14}$.

Eprinomectin component B_{1b}: $C_{49}H_{73}NO_{14}$.

Ivermectin—{R-43}

Ivermectin component B_{1a}: $C_{48}H_{74}O_{14}$.

Ivermectin component B_{1b}: $C_{47}H_{72}O_{14}$.

Milbemycin oxime—{R-35; 53}

Milbemycin A_4 5-oxime: $C_{32}H_{45}NO_7$.

Milbemycin A_3 5-oxime: $C_{31}H_{43}NO_7$.

Moxidectin—$C_{37}H_{53}NO_8$.{R-43}

Selamectin—$C_{43}H_{63}NO_{11}$.{R-53}

Molecular weight:

Doramectin—899.11.{R-43}

Eprinomectin—{R-43}

Eprinomectin component B_{1a}: 914.13.

Eprinomectin component B_{1b}: 900.10.{R-43}

Ivermectin—{R-58}

Ivermectin component B_{1a}: 875.10.

Ivermectin component B_{1b}: 861.17.

Milbemycin oxime—{R-35; 53}

Milbemycin A_4 5-oxime: 555.71.

Milbemycin A_3 5-oxime: 541.68.

Moxidectin—639.82.{R-43}

Selamectin—769.96.{R-53}

Description:

Eprinomectin—Crystalline solid with a melting point of 163.3 to 165.7 °C.{R-53}

Ivermectin—Off-white powder.{R-53}

Milbemycin oxime—Practically odorless white to pale yellow powder with a melting point of 169.6 to 177.4 °C. The pH of an aqueous solution is 6.3.{R-53}

Moxidectin—White to yellow powder with a melting point of 145 to 154 °C.{R-60}

Solubility:

Doramectin—Essentially insoluble in water (25 parts per billion at 25 °C) but freely soluble in methylene chloride or methanol and soluble in isopropanol.{R-61}

Eprinomectin—Freely soluble in polar organic solvents.{R-59}

Ivermectin—Solubility in water is about 0.006 to 0.009 mg per liter.{R-67} It is virtually insoluble in saturated hydrocarbons, such as cyclohexane and highly soluble in methyl ethyl ketone, propylene glycol, and polyethylene glycol.{R-53}

Milbemycins—Soluble in n-hexane, benzene, acetone, ethanol, methanol, chloroform; very slightly soluble in water.{R-53}

Moxidectin—Solubility in water is 4.3 mg per liter.{R-67}

Pharmacology/Pharmacokinetics

Note: See also *Table 1* and *Table 2* at the end of this monograph for additional pharmacokinetic data.

Mechanism of action/Effect: The macrocyclic lactones bind to glutamate-gated chloride ion channels in invertebrate nerve and muscle cells.{R-2; 27} The cell membranes then develop an increased permeability to chloride ions causing hyperpolarization of affected cells and subsequent paralysis and death of the parasite.{R-2; 27} Medications in this class also interact with other ligand-gated chloride channels, including ones gated by gamma-aminobutyric acid (GABA).{R-2; 27}

Because mammals do not have glutamate-gated chloride channels and macrocyclic lactones have a low affinity for other mammalian ligand-gated chloride channels, mammals have low susceptibility to the effects of macrocyclic lactones. Also, these medications are slow to penetrate the blood-brain barrier, protecting the GABA-gated channels in mammalian central nervous systems.{R-2; 27} See also the *Breed sensitivity* information under *Precautions to Consider* in this monograph for information pertaining to animals believed to have a defect in active transport across the blood-brain barrier.

Absorption:

Oral administration: Slowing the movement of food through the gastrointestinal tract increases the bioavailability of orally administered macrocyclic lactones due to their tendency to associate with digesting food.{R-46} For more information on the effect of diet and body weight on the pharmacokinetics of macrocyclic lactones, see also the *Veterinary Dosing Information* section in this monograph.

Subcutaneous administration: Minor differences in vehicle may alter the bioavailability of subcutaneously administered ivermectin. One study showed significant variations in absorption, peak plasma concentration, and mean residence time among generic ivermectin injection productions.{R-142}

Topical administration: *Sheep*—Topical administration is not an effective method of drug delivery in sheep because of wool and wool grease.{R-46}

Selamectin—Bioavailability:

Cats—

Oral administration: F was calculated to be 109%, with a dose of 24 mg per kg of body weight (mg/kg).{R-90}

Topical administration: 74%, with a dose of 24 mg/kg.{R-90}

Dogs—

Oral administration: F was calculated to be 62%, with a dose of 24 mg/kg.{R-90}

Topical administration: 4.4%, with a dose of 24 mg/kg.{R-90}

Distribution: Macrocyclic lactones are widely distributed in the body and, as lipophilic substances, concentrate in adipose tissue, thereby leading to extended residence in plasma because of slow release over time.{R-67; 96; 143; 144} Moxidectin is said to be 100 times more lipophilic than ivermectin.{R-72} After topical administration of moxidectin to calves, it is found in the highest concentration in fat and in the skin on the topline where it is applied.{R-144} Distribution to skin varies according to location: backline > rib cage area > thigh > face.{R-144}

Protein binding: The protein binding of macrocyclic lactones has not been reported in animals.{R-47}

Ivermectin—*Human data:* 93.2 ± 4.4%.{R-48}

Duration of action: Days of persistant activity after administration, as stated in product labeling—{R-1; 2; 13; 14; 23-28; 31-33; 174}

Note: Small variations in vehicle among products could impact the duration of activity.{R-67}

Cattle:

U.S.—

	Doramectin Injection	Doramectin Topical	Eprinomectin Topical	Ivermectin Injection	Ivermectin Topical	Moxidectin Injection	Moxidectin Topical
Gastrointestinal roundworms							
Cooperia oncophora	14	28		14	14		
C. punctata	28	35		21	21		
C. surnabada					14		
Haemonchus placei	14	35		14	14	35	14
Nematodirus helvetianus							
Oesophagostomum radiatum	28	28		28	28	42	28
Ostertagia ostertagi	21	28		21	14	14	28
Trichostrongylus axei				21	21	14	
Horn flies							
Haematobia irritans		7	7		28		7
Lice							
Bovicola (Damalinia) bovis		77			56		
Lingonathus vituli		42					
Solenopotes capillatus							
Lungworms							
Dictyocaulus viviparus	28	28	21	28	28	42	42

Canada—

	Doramectin Injection	Doramectin Topical	Eprinomectin Topical	Ivermectin Injection	Ivermectin Topical	Moxidectin Injection	Moxidectin Topical
Gastrointestinal roundworms							
Cooperia oncophora		21	21	14			
C. punctata	21		21	14			
C. surnabada			21				
Haemonchus placei			14	14			14
Nematodirus helvetianus			28				
Oesophagostomum radiatum		28	14	21			28
Ostertagia ostertagi	21	28	28	21	14	21	28
Trichostrongylus axei		28	14	14			
Trichostrongylus colubriformis			14				
Horn flies							
Haematobia irritans		7			35		
Lice							
Bovicola (Damalinia) bovis		42					
Lingonathus vituli		42					
Solenopotes capillatus		35					
Lungworms							
Dictyocaulus viviparus	28	42	28	21	28	28	42

Dogs: Moxidectin sustained-release injection has persistent activity against *Dirofilaria immitis* larvae for 6 months after treatment; however, there is no residual efficacy against hookworm infection.{R-39; 40}

Horses: Moxidectin oral gel has persistent activity suppressing strongyle egg production for 84 days.[R-37]

Elimination: The predominant route of elimination for the macrocyclic lactones is by excretion through bile into the feces (50 to 96% of the dose), primarily as unmetabolized drug. Small amounts are eliminated in the urine.[R-46; 47; 96]

Precautions to Consider

Breed sensitivity

MDR1 gene mutation: It has been known for some time that certain Collie dogs are more sensitive to high doses of ivermectin than other dogs. This sensitivity has been associated with a deletion mutation of the *MDR1* gene that encodes a transmembrane protein pump called P-glycoprotein.[R-149; 150] P-glycoprotein actively transports foreign chemicals out of cells; it has been identified in brain capillary endothelial cells, intestinal epithelial cells, biliary canalicular cells, renal proximal tubular epithelial cells, as well as placental and testicular cells.[R-150] Dogs homozygous for a mutant allele of *MDR1* have a nonfunctional P-glycoprotein.[R-149; 150] Gene studies have shown that the mutation of the of the *MDR1* gene can also be found in members of breeds other than Collie dogs.[R-154]

P-glycoprotein is believed to transport ivermectin, and possibly milbemycin, moxidectin, and selamectin, out of brain tissue and into circulation.[R-150] Lack of a functional protein leads to accumulation of medications in tissues. Because P-glycoprotein transports many substances other than macrocyclic lactones, affected dogs could be susceptible to other toxicities. For example, many Collies are sensitive to recommended doses of loperamide and may be more prone to toxic effects of chemotherapeutic drugs, among others.[R-150]

Further research is necessary to investigate the possible benefits of disabling P-glycoprotein in dogs without the mutation by blocking its action with other medications. One goal is the development of strategies to improve absorption and delivery of medications to target tissues with fewer side effects.[R-150]

Collie dogs: Collie dogs with the *MDR1* gene mutation can develop signs of ivermectin toxicity with single doses as low as 0.1 mg/kg.[R-150; 151] A sample population study of 40 Collie dogs in the northwestern United States found 35% to be homozygous for the mutation and 42% to be heterozygous carriers of the mutant allele.[R-152]

Australian Shepherds, Miniature Australian Shepherds, English Shepherds, German Shepherds (white),[R-175] *Longhaired Whippets, McNabs, Old English Sheepdogs, Shetland Sheepdogs, Silken Windhounds:* Gene studies have shown that the mutation of the *MDR1* gene can be found in members of these breeds, generally at a much lower frequency than has been reported in Collie dogs.[R-110; 154] The Longhaired Whippet is an exception; 15.7% of the dogs in one subpopulation were found to be homozygous for the mutation. The frequencies of the mutation in reported studies are only relevant for the subpopulations of the breeds that were tested.[R-154]

Australian Cattle Dogs, Bearded Collies, Border Collies: The *MDR1* mutation has not been found in the members of these breeds that have been tested.[R-154] However, sensitivity to ivermectin has been reported in some individuals.[R-154]

Testing for mutation of the *MDR1* gene: A test is currently available to screen for the presence of the mutation in individual dogs by submitting buccal mucosal cells to Dr. Katrina Mealey at the Veterinary Clinical Pharmacology Laboratory in the College of Veterinary Medicine at Washington State University (www.vetmed.wsu.edu/depts-vcpl).[R-154; 155] This test will also identify whether the mutation is homozygous or heterozygous.[R-155]

Reproduction/Pregnancy

Doramectin: *Cattle*—No adverse effects were observed when doramectin topical solution was administered at a dose of 1.5 mg/kg (three times the recommended dose) to breeding bulls and cows.[R-23; 25]

Eprinomectin: *Cattle*—Application of 1.5 mg/kg (three times the recommended topical dose) caused no adverse effects on breeding performance of bulls and cows.[R-27; 28]

Ivermectin:

Cats, cattle, dogs, pigs, or sheep—Ivermectin is expected to have a wide margin of safety when administered to pregnant or breeding animals.[R-6-8; 13; 14; 17; 18]

Horses: Mares administered ivermectin oral paste at a dose of 0.6 mg/kg every two weeks for a total of six doses during the first three months of gestation showed no decrease in fertility and no evidence of teratogenic anatomic defects compared to controls that received no medication.[R-111]

Milbemycin:

Cats—Although studies are not available for milbemycin administered alone,[R-34; 36] administration of the labeled dose of milbemycin oxime and praziquantel once a week during anestrus, proestrus, pregnancy, and lactation showed no significant measurable difference between treatment and control groups in length of pregnancy, number of kittens alive and dead, or congenital abnormalities.[R-164]

Dogs—No adverse effects were observed in breeding males, pregnant females, or their litters when 1.5 mg/kg (three times the labeled oral dose) was given daily from breeding to one week before weaning the pups.[R-35]

Moxidectin: *Cattle, dogs,* and *horses*—Moxidectin administered at three times the labeled dose had no observed effect on reproductive performance of female or male cattle or horses.[R-31-33; 56] Moxidectin administered in a sustained-release formulation at a dose of 0.51 mg/kg had no observed effect on the reproductive performance of dogs.[R-39]

Selamectin: *Cats* and *dogs*—No adverse effects were observed in breeding males or females or their offspring when selamectin was administered at a dose of 18 mg/kg (three times the labeled minimum dose) every 14 days to breeding males and every 28 days to females during gestation.[R-29; 30]

Lactation

Because macrocyclic lactones are highly lipophilic, they are generally well distributed into milk.[R-46] An exception is eprinomectin, which has a relatively low milk distribution.[R-75; 76]

Doramectin:

Goats—After a subcutaneous dose of 0.2 mg/kg, doramectin reached a peak milk concentration of 22.83 ± 1.55 nanograms/mL at 1.65 ± 1.03 days after treatment. It could be measured in the milk for 21.0 ± 2.9 days after treatment; 2.9 ± 0.88% of the dose administered was recovered in the milk.[R-88]

Sheep—After a subcutaneous dose of 0.2 mg/kg, doramectin reached a peak milk concentration of 79.8 ± 14.9 nanograms/mL at 3.00 ± 0.32 days after treatment. Concentrations of doramectin in milk were higher than concentrations in plasma in each sample taken from 12 hours to 35 days after treatment. The milk-to-plasma ratio was 2.88 ± 0.30; 2.44 ± 0.44% of the dose was distributed into the milk.[R-94]

Eprinomectin:

Cattle—After a topical dose of 0.5 mg/kg, a milk-to-plasma ratio of 0.1 was measured in lactating cattle; only 0.1% of the dose administered is distributed into milk.[R-75]

Goats—After a topical dose of 0.5 mg/kg, eprinomectin reached a peak milk concentration of 0.32 ± 0.08 nanograms/mL at 0.54 ± 0.29 days.[R-92] After a topical dose of 1 mg/kg, eprinomectin reached a peak milk concentration of 0.82 ± 0.25 nanograms/mL at 1.07 ± 0.64 days.[R-92] The milk-to-plasma ratio was 0.122 ± 0.070 with the 0.5 mg/kg dose and

0.254 ± 0.179 with the 1 mg/kg dose.[R-92] Of the dose administered, 0.3 to 0.5% is distributed into the milk.[R-92]

Ivermectin:

Cattle—After a subcutaneous dose of 0.2 mg/kg, ivermectin reached a peak milk concentration of 40.51 ± 9.67 nanograms/mL at 1.76 ± 1.04 days after treatment. Ivermectin could be measured in the milk for 17.8 ± 6.34 days after treatment. The milk-to-plasma ratio was 0.77 ± 0.26; 5.46 ± 1.19% of the dose was recovered in the milk.[R-51]

Goats—After a subcutaneous dose of 0.2 mg/kg, ivermectin reached a peak milk concentration of 7.26 ± 1.49 nanograms/mL at 2.82 ± 0.36 days after administration. The milk-to-plasma ratio was 1.08 ± 0.23.[R-95]

Sheep—After a subcutaneous dose of 0.2 mg/kg, ivermectin reached a peak milk concentration of 22.67 ± 18.27 nanograms/mL at 1.28 ± 1.07 days after treatment. Ivermectin could be measured in the milk for 23 days. The milk-to-plasma ratio was 1.67 ± 0.50 for the first 7 days; 0.7% of the dose was recovered in the milk.[R-83]

Milbemycin: *Dogs*—When administered to lactating dogs at a dose of 1.5 mg/kg (three times the recommended dose), on a daily rather than monthly basis, milbemycin oxime was distributed into milk. Nursing puppies received enough drug to show clinical effects. However, another study using the same daily dose in pregnant dogs through parturition and lactation until one week before weaning showed no apparent effect on dogs or their puppies. In another study, pregnant dogs were given a single 1.5-mg/kg dose just before or shortly after whelping; no effects were observed in the puppies.[R-35]

Moxidectin: *Goats*—After an oral or subcutaneous dose of 0.2 mg/kg, moxidectin was measured in milk up to 40 days after treatment. After oral administration, 5.7 ± 1.04% of the dose was recovered in the milk and after subcutaneous administration, 22.53 ± 1.09% was recovered.[R-88]

Pediatrics

Doramectin: *Calves*—No evidence of toxicity was seen when neonatal calves were administered up to 1.5 mg/kg (three times the labeled topical dose).[R-23]

Eprinomectin—No signs of toxicity were observed in neonatal calves given topical eprinomectin at a dose of 1.5 mg/kg (three times the recommended dose) or in 8-week-old calves given 2.5 mg/kg (five times the recommended dose).[R-27]

Ivermectin:

Calves, horses, and *kittens*—Very young animals may be more sensitive to ivermectin overdosage, developing more severe adverse effects than adults.[R-107; 109]

Mice and *rats:* Newborn mice and rats are susceptible to neurotoxicity when mothers are administered ivermectin during pregnancy and nursing; the threshold dose is unknown but fetal mortality and newborn neurotoxicity occur with high doses (1 to 4 mg/kg). Neurotoxicity has been reported in newborns but not adults treated with the same therapeutic dose.[R-106; 107]

Milbemycin:

Kittens—Young cats and kittens given milbemycin oxime at a dose of 2 mg/kg, 6 mg/kg, or 10 mg/kg (one to five times the recommended dose) showed no drug-related effects.[R-34; 36] Tolerability studies of kittens and young cats demonstrated no drug-related adverse effects when an exaggerated dose of 20 mg/kg (ten times the recommended dose) was administered.[R-34] However, milbemycin oxime is not recommended for use in kittens less than six weeks of age or under 1.5 pounds of body weight.[R-34]

Puppies—No evidence of toxicity was seen in 2-, 4-, or 6-week-old puppies administered oral milbemycin oxime at a dose of 0.5 mg/kg. Nursing puppies that were 2, 4, and 6 weeks of age developed transient tremors, vocalization, and ataxia when administered 9.6 mg/kg (19 times the recommended dose of 0.5 mg/kg); signs had resolved within 24 to 48 hours.[R-35] However, milbemycin oxime is not recommended for use in puppies less than four weeks of age or 2 pounds of body weight.[R-35]

Moxidectin:

Calves—No signs of toxicity were observed in neonatal calves given moxidectin topical solution at a dose of 1.5 mg/kg (three times the recommended dose) within twelve hours of birth or in calves nursing from cows treated with 0.5 mg/kg (the recommended dose).[R-31]

Foals—Moxidectin gel is not recommended for foals less than six months of age. Caution is advised in dosing small animals, foals or miniature horses, to avoid overdosage. Transient depression, ataxia, and recumbency have been reported with moxidectin administration to very young or debilitated animals.[R-37]

Puppies—No signs of systemic toxicity were noted in 7- to 8-month-old puppies given a single dose of up to 0.85 mg/kg (five times the dose recommended in product labeling on moxidectin for sustained-release injection).[R-39]

Selamectin—*Kittens* and *puppies:* No signs of toxicity were observed in six-week-old kittens or puppies administered a dose of 18 to 60 mg/kg (three to ten times the labeled topical dose) every 28 days for seven treatments.[R-57]

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.

Verapamil

(concurrent administration of ivermectin with verapamil, a p-glycoprotein transport substrate, significantly increases the plasma availability of ivermectin in sheep; in the same study, verapamil had no effect on the pharmacokinetics of moxidectin)[R-80]

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).

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

Existing *Dirofilaria immitis* infection

(dogs with circulating microfilariae can have a hypersensitivity-type reaction to preventative treatment with macrocyclic lactones [ivermectin, milbemycin, moxidectin]; in laboratory studies, intravenous injection of extracts made from microfilaria or adult heartworms causes shock-like reactions in dogs that have not been infected with heartworms or other parasites with common antigenicity;[R-166] the specific pathophysiologic mechanisms that cause microfilaremia-induced distributive shock following drug treatment are not well defined;[R-167] pretreatment with corticosteroids may aid in prevention of clinical signs associated with a shock-like reaction that can occur[R-165])

(with ivermectin administration, the most typical sign in microfilaremic dogs appears to be a mild transient diarrhea, although there have been reports of melena, salivation, vomiting, and on occasion, death, with more severe reactions; also, the dose administered for prevention is not effective for clearance of microfilariae)[R-5; 6; 47]

(with the first administration of oral milbemycin, some microfilaremic dogs have had hypersensitivity reactions that included coughing, labored respiration, lethargy, salivation, and vomiting; signs resolved within 48 hours)[R-35; 63]

(moxidectin in a sustained-release formulation was administered to dogs with heartworm infection at a dose of 0.51 mg/kg [three times the labeled dose] with no adverse effects; however, the manufacturer cautions that heartworm-positive dogs treated with moxidectin sustained-release injection may develop cardiopulmonary signs, including coughing or dyspnea)[R-39]
(no treatment-related adverse effects were seen in cats and dogs with heartworm infection when administered selamectin at a dose of 18 mg/kg [three times the minimum labeled dose])[R-29]

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):

Note: No specific tests have been recommended for animals during treatment with macrocyclic lactones. Due to relevant factors of local parasite incidence levels, seasonal environmental variations, owner compliance, and potential parasite resistance, periodic review of parasite load is an essential part of any control program.[R-167]

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:

Those indicating need for medical attention

Buffalo, cattle, reindeer

Incidence unknown

Inflammatory reaction to death of migrating first instar grub larvae—if anthelmintics are administered when larvae are migrating; signs are dependent on location of larvae[R-1; 2; 13; 14; 23-28; 31-33; 47]

Note: In cattle, *death of migrating larvae* in the esophagus can cause dysphagia, drooling, esophagitis, and bloat. If in the spinal canal, ataxia, muscular weakness, stiffness, and paralysis of the hind limbs can occur.

Cattle, sheep

Incidence unknown

Local tissue reaction—with ivermectin injection[R-2; 14]

Note: Pain at the site of subcutaneous injection has been reported in animals. Occasionally, visible soft tissue swelling that resolves without treatment occurs in cattle. Because of the risk of a *local tissue reaction* developing into a clostridial infection that would require aggressive antibacterial therapy, animals should be monitored for site reactions.[R-2]

Cats

With oral *ivermectin* administration[R-7]

Incidence rare

Diarrhea (≤0.2% of animals treated in clinical trials); ***vomiting*** (≤0.3%)

With topical *selamectin* administration[R-29]

Incidence less frequent (1% of animal treated in field studies)

Local cutaneous reactions (alopecia, inflammation)

Incidence rare (≤0.5%)

Anorexia; diarrhea; lethargy; muscle tremors; salivation; vomiting

Incidence unknown

Ataxia; erythema; fever; pruritis; seizure; urticaria

Dogs

With *ivermectin* administered orally, *milbemycin, moxidectin,* and *selamectin*[R-5; 6; 29; 35; 39]

Incidence unknown, except where reported in field studies

Anaphylaxis/anaphylatoid reactions—with moxidectin sustained-release injection; ***anorexia—***unknown incidence, except ≤0.5% with selamectin in field study; ***ataxia***—not yet reported with moxidectin; ***convulsions***—unknown incidence, except 1% with moxidectin sustained-release injection in field study; ***depression/lethargy/ listlessness***—unknown incidence, except 1% with moxidectin sustained-release formulation and ≤0.5% with selamectin, in field studies; ***diarrhea***—unknown incidence, except 1% with moxidectin sustained-release formulation and ≤0.5% with selamectin, in field studies; ***edema, facial and head***—with moxidectin sustained-release injection; ***erythema***—with moxidectin sustained-release injection and selamectin; ***increased body temperature***—reported with moxidectin sustained-release injection (1% in field study) and selamectin; ***hypersalivation***—unknown incidence, except ≤0.5% with selamectin in field study; ***hypersensitivity reaction to death of Dirofilaria immitis microfilaria***—reported with ivermectin, milbemycin, and moxidectin administration;[R-5; 35; 39; 47] ***muscle tremors***—with selamectin, ≤0.5% in field study; ***mydriasis***—with ivermectin; ***pruritis***—with selamectin; ***local swelling or pruritis at the injection site***—with moxidectin sustained-release injection;[R-57] ***tachypnea***—with selamectin, ≤0.5% in field study; ***urticaria***—with moxidectin sustained-release injection and selamectin; ***vomiting***—unknown incidence, except 1% with moxidectin sustained-release injection and ≤0.5% with selamectin, in field studies; ***weight loss***—reported with moxidectin sustained-release injection,1% in field study

Note: *Moxidectin for sustained-release injection* has been recalled from the market in the United States, based on concerns about adverse reactions associated with its administration. The manufacturer and the Food and Drug Administration are continuing to investigate this issue.[R-158]

Hypersensitivity reactions have been reported in dogs with circulating microfilaria when treated for heartworm prevention with ivermectin, milbemycin, or moxidectin. See also the *Medical considerations/Contraindications* section in this monograph for more information.

Some dogs develop transient local inflammatory *injection site reactions* to moxidectin sustained-release injection that are visible for up to three weeks and are sometimes pruritic; three of eight dogs in one clinical trial had local inflammatory reactions.[R-39; 66] Local granulomas were reported on histologic exam five months later in some dogs.[R-39] Recommendations to alternate injection sites every six months are intended to decrease injection site reactions.

Horses

Incidence unknown

Cutaneous swelling and itching—believed to be a reaction to death of heavy loads of *Onchocerca* microfilariae [R-17]

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

Sheep

Incidence unknown

Coughing—for several minutes after oral drenching[R-12]

Environmental impact

Macrocyclic lactones are excreted as active drug in the feces. Studies have been published pertaining to the effect of abamectin, doramectin, eprinomectin, ivermectin, milbemycin, and moxidectin on dung-feeding insects as well as the process of dung degradation and nutrient recycling.[R-55] Avermectins are considered toxic to the dung-dependent insects studied, including *Diptera* and *Coleoptera,* and to aquatic vertebrates.[R-54] The milbemycins appear to be relatively less toxic to invertebrates.[R-54; 55] In general, the macrocyclic lactones are considered relatively nontoxic to birds, plants, and earthworms, with the exception that eliminating coprophagous insects in dung appears to discourage the use of the dung by earthworms, thereby delaying processing of nutrients.[R-54] It is not clear what the overall impact of the macrocyclic lactones on pastural ecosystems worldwide will be because so many variables, including climate, native species

populations, frequency of dosing, long-acting formulations, number of animals treated, and additional parasite control methods, can impact the effect. Research is needed to more clearly define this issue.

At this time, because avermectins have a low solubility in water, a high octanol/water partition coefficient, and a high degree of binding to soil, and because of their spatial and temporal distribution, they have not been expected to have a significant impact on dung-dependent insects;[{R-54}] however, guidelines for the use of each product to minimize environmental impact is included on product labeling (see *Additional information* subsections for each product in the *Dosage Forms* section of this monograph.)

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: The macrocyclic lactones have high therapeutic indices because of their high potency and the low dosages required for efficacy. When acute toxicity occurs, signs are often associated with neurotoxicity.[{R-47}] Examples of tolerance include:

Doramectin—No signs of toxicity were observed in cattle given doramectin topical solution at a dose of 12.5 mg per kg of body weight (mg/kg) or twenty-five times the recommended dose.[{R-25}]

Ivermectin—No treatment-related adverse effects on feed intake or body temperature were noted in cattle administered 1 to 5 mg/kg (two to ten times the labeled topical dose).[{R-62}] No treatment-related adverse effects on clinical exam, feed intake, weight gain, clinical pathology, or necropsy were observed in pigs administered up to 10 parts per million in the feed (five times the labeled dose) for twenty-one days.[{R-64}]

The manufacturer reported no signs of toxicity in sensitive Collies when ivermectin was administered orally at ten times the dose for heartworm prevention (0.06 mg/kg).[{R-5; 6}]

Milbemycin—No signs of toxicity were noted in adult beagle dogs given up to 16 mg/kg (32 times the labeled dose) once a week for four weeks or 2.5 mg/kg (five times the labeled dose) daily for thirty-six days.[{R-63}]

When roughcoated collies were administered up to twenty times the recommended dose of milbemycin oxime (10 mg/kg), no evidence of toxicity was seen. When given twenty-five times the recommended dose (12.5 mg/kg) one of fourteen collies developed ataxia, periodic recumbency, and pyrexia.[{R-35}] In a study of dogs known to be sensitive to ivermectin, an oral milbemycin oxime dose of 10 mg/kg (20 times the recommended dose) produced transient, mild ataxia and depression, and, in some cases, mydriasis or excessive salivation; signs had resolved within twenty-four to forty-eight hours.[{R-168}]

Moxidectin—No signs of toxicity were observed in cattle given moxidectin topical solution at a dose of 12.5 mg/kg (twenty-five times the recommended dose).[{R-31}]

See also the *Pediatrics* information pertaining to toxicity under *Precautions* in this monograph.

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:

Cats

Adults

Reported with ivermectin administered at a dose of 0.5 mg/kg (21 times the labeled dose) or more:[{R-146}]
Anorexia; ataxia; bradycardia, central nervous system dysfunction (circling, disorientation, head pressing, sudden blindness, slow papillary light reflex, loss of menace reflex and other reflexes, mydriasis, signs progressing to coma and death); ***hypothermia; respiratory rate, decreased***

Kittens

With ivermectin administered orally to 6-week-old kittens at a dose of 0.12 mg/kg (five times the labeled dose) every 28 days for 8 months:[{R-65}]
Diarrhea—in one of seven kittens treated

With a subcutaneous ivermectin dose of 0.3 mg/kg (12.5 times the labeled dose), administered to a 3-month-old kitten[{R-108}]
Ataxia; depression; hyperesthesia; incoordination; miosis or mydriasis; tremors; recumbency and/or coma

Cattle

With eprinomectin administered at a dose of 5 mg/kg (ten times the labeled dose):[{R-27}]
Mydriasis—observed in one of six animals treated

With moxidectin administered at a dose of 2.5 mg/kg (five times the recommended dose):[{R-33}]
Ataxia; depression; drowsiness; salivation, transient—reported in 50% of animals overdosed, appearing 8 to 24 hours after treatment and generally resolving without treatment within 24 to 72 hours.

Dogs

Adults

Reported in breeds susceptible to toxicity with a single ivermectin dose as low as 0.1 mg/kg; in other dogs, with doses in the range of 2.5 to 4 mg/kg:[{R-147; 148}]
Ataxia; bradycardia; central nervous system dysfunction (with high doses, progressing to recumbency, coma, and death); ***depression; drooling; mydriasis; tremors***

Puppies, 8 to 12 weeks of age

With an oral milbemycin dose of 2.5 to 12.5 mg/kg (five to twenty-five times the recommended dose):[{R-63}]
Ataxia; prostration; ptyalism; tremors; vocalization—all signs resolved within 24 to 48 hours; older puppies were less affected than younger puppies

Horses

Adults

With ivermectin administered at a dose of 3 mg/kg (15 times the therapeutic dose):[{R-111}]
Mydriasis

With ivermectin administered at a dose of 2 to 6 mg/kg (10 to 30 times the recommended dose)[{R-109}]
Ataxia; depression; mydriasis; respiratory rate, decreased; drooping lower lip

Foals

With ivermectin administered at 2.1 mg/kg (10.6 times the recommended adult dosage) to a neonatal foal:[{R-109}]
Ataxia; depression; head-pressing; visual impairment

With moxidectin administered at a dose of 1.2 to 2 mg/kg (three to five times the labeled oral dose) to foals 7 days to 4 months of age or older (reported in order of progression):[{R-56}]
Ataxia; depression; difficulty rising; drooping ears and lip; protruding tongue; tremors; vacant stare; recumbency—resolved within two days

Note: Some foals were unaffected by a single dose of 1.2 mg/kg; continuing daily doses increased the number of foals affected.

Treatment of macrocyclic lactone toxicity

Recommended treatment consists of the following:

- Discontinue macrocyclic lactone administration. In safety studies, mild toxicity resolved without treatment within twenty-four to forty-eight hours.
- With more severe signs, recovery can require weeks to months; there is a report of full recovery by a dog comatose for seven weeks.[{R-167}]
- Treatment is symptomatic and supportive and may include intravenous fluid and electrolyte administration; special bedding and maintenance for long-term recumbency, parenteral nutrition, or

mechanical ventilation.{R-153}

- Medications that cause central nervous system depression, such as diazepam or barbiturates, should be avoided.

Client Consultation

In providing consultation, consider emphasizing the following selected information:

Never exceeding the prescribed amount without veterinary consultation; contacting a veterinarian if more than the recommended dose is administered

Contacting a veterinarian if any doses are missed or if a potential underdose occurs

Familiarizing clients with signs that may indicate an adverse reaction is occuring and instructing when to contact a veterinarian

For topical solutions—Instructing for effective administration, preventing human exposure, and procedures to follow if skin or eye contact occurs

Veterinary Dosing Information

Control programs

Best results from anthelmintic therapy are usually attained through use of a parasite control program structured to avoid adverse effects and effectively control parasites while minimizing the development of resistance.{R-1} In order for therapies to effectively treat and control parasites, medications and other control measures are strategically timed. Knowledge of local parasite life cycles, drug efficacy and pharmacology, and patterns of drug resistance are combined to develop a treatment schedule.

Resistance—For susceptible animal species or for farms with gastrointestinal parasites known to carry resistance to macrocyclic lactones, strategies have been recommended to minimize resistance. In foals, regular monitoring of the efficacy of treatment regimens has been suggested; also, alternating the administration of macrocyclic lactones with the administration of anthelmintics from other classes may slow development of resistance.{R-103} In small ruminants, suggested strategies have included good pasture management practices, treating and quarantining all new animals for 2 weeks to achieve a negative fecal exam before adding to the herd, treating only those animals that require it rather than using whole herd treatments, utilizing sequentially administered combinations of anthelmintics, regular monitoring of treatment efficacy, and restricting feed intake 24 hours before treatment and/or administering a second dose within 12 hours.{R-104; 157}

Grubs—Timing of systemic anthelmintic treatment for grubs is important to prevent killing larvae and creating an inflammatory response as they migrate through vital tissues. Death of *Hypoderma lineatum* in esophageal tissues can lead to bloat. Death of larvae in the vertebral canal can cause neurologic disease, including staggering and paralysis. To be most effective in cattle, treatment for *H. lineatum* just after the heel fly (warble fly) season is recommended. Subsequent treatment should be performed after larval migration.{R-27}

Pigs—Manufacturer-generated product labeling includes the following recommendations for parasite control: At the start of a parasite control program, all breeding animals in the herd are treated; retreatments are performed, depending on exposure.{R-2; 4; 14; 24} All weaner and feeder pigs are treated when moved to clean quarters. {R-2; 4; 14; 24} To prevent gastrointestinal roundworms in piglets, sows are treated with doramectin or ivermectin injection seven to fourteen days before farrowing while gilts are treated seven to fourteen days before breeding and again before farrowing.{R-2; 14; 24} With ivermectin medicated feed, sows and gilts are treated fourteen to twenty-one days before farrowing and gilts fourteen to twenty-one days before breeding.{R-4} Boars are treated regularly, depending on exposure.

Effect of licking topical applications

Cattle allowed to freely lick themselves and others treated with topical ivermectin have been shown to have a significant difference in plasma and fecal disposition of the medication when compared to cattle prevented from licking.{R-141} Oral ingestion by other cattle of medication applied topically has the potential to cause some treated animals to have subtherapeutic ivermectin concentrations and may impact the selection of anthelmintic resistant parasite populations.{R-141; 157} Higher than expected concentrations in untreated animals licking medications from others could lead to unexpected tissue residues.{R-141} Oral ingestion also significantly increases the elimination of parent drug in the feces.{R-141}

Effect of fasting or diet restriction

Horses and sheep—Slowing the movement of food through the gastrointestinal tract increases the bioavailability of orally administered macrocyclic lactones due to their tendency to strongly associate with digesting food material.{R-46} Fasting horses before oral administration of moxidectin significantly increases bioavailability, as does the fasting of sheep before administration of ivermectin.{R-46; 50}

Pigs—A reduction in the rate of deposition of body fats due to a restriction in diet during and after treatment had no effect on the pharmacokinetics of ivermectin in 4-month-old pigs compared to pigs with similar body condition given a diet for growth.{R-78} However, the persistence of moxidectin, a more highly lipophilic medication, in the plasma was reduced (>2 nanograms/mL for 49 days) in pigs on the restricted diet compared to the pigs with a higher rate of fat deposition (>2 nanograms/mL to the end of the study, 63 days).{R-78}

Effect of type of feed

Sheep—Peak plasma concentrations and overall availability of oral ivermectin and fenbendazole were reduced in lambs grazing on pasture when compared to lambs fed hay and a small amount of concentrated ration.{R-105}

Effect of body condition

Pigs—With poor body condition or lean body weight, pigs have an earlier peak plasma concentration of subcutaneously administered ivermectin or moxidectin as well as a reduction in the persistence of drug in plasma and adipose tissue.{R-77} The pharmacokinetics of intravenously administered ivermectin in pigs is not affected by body composition.{R-79} When moxidectin is administered intravenously, overall availability is unaffected by body condition; however, moxidectin is distributed and eliminated more quickly in lean animals than in fat animals.{R-79}

Effect of breed

Calves—After topical administration of moxidectin, systemic availability and peak plasma concentration were significantly lower for Aberdeen Angus calves when compared to Holstein calves.{R-145}

DORAMECTIN

Parenteral Dosage Forms

Note: Text between [EL-US] and [EL] describes uses not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses not included in Canadian product labeling.

The [EL-US] or [EL-CAN] designation may signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

DORAMECTIN INJECTION

Usual dose:

Eyeworm infection; or

Grub infection—*Cattle:* Intramuscular or subcutaneous, 0.2 mg per kg of body weight (1 mL per 50 kg of body weight).{R-24; 26}

Withdrawal times—US: Meat—35 days. Not labeled for use in female dairy cattle 20 months of age or older or in calves to be used in the production of veal.{R-24} Canada: Meat—40 days. Not labeled for use in nonlactating dairy cattle within 2 months of calving or in lactating dairy cattle.{R-26}

Note: The manufacturer recommends administration to cattle by subcutaneous injection under the loose skin in front of or behind the shoulder, or by intramuscular injection into the muscular area of the neck.{R-24} Up to 10 mL can be injected in one site.{R-26} Use of sterile equipment and disinfection of the injection site are recommended.{R-24; 26}

For the most safe and effective treatment of grubs, administration is timed to avoid killing larvae migrating through tissues and prevent serious complications due to their destruction in esophageal tissue or the vertebral canal.{R-1; 24}

Kidney worm infection—*Pigs:* Intramusuclar, 0.3 mg per kg of body weight (1 mL per 34 kg of body weight).{R-24; 26} Administration in the neck area using sterile equipment after disinfection of the injection site is recommended.{R-24; 26}

Withdrawal times—US: Meat—24 days.{R-24} Canada: Meat—62 days.{R-26}

Lungworm infection;

Mite dermatosis;

Nematode, gastrointestinal, infection; or

Pediculosis—

Cattle: Intramuscular or subcutaneous, 0.2 mg per kg of body weight (1 mL per 50 kg of body weight).{R-24; 26}

Withdrawal times—US: Meat—35 days. Not labeled for use in female dairy cattle 20 months of age or older or in calves to be used in the production of veal.{R-24} Canada: Meat—40 days. Not labeled for use in nonlactating dairy cattle within 2 months of calving or in lactating dairy cattle.{R-26}

Pigs: Intramusuclar, 0.3 mg per kg of body weight (1 mL per 34 kg of body weight).{R-24; 26} Administration in the neck area using sterile equipment after disinfection of the injection site is recommended.{R-24; 26}

Withdrawal times—US: Meat—24 days.{R-24} Canada: Meat—62 days.{R-26}

Note: In the treatment of pediculosis, lice are not immediately killed and could infect clean quarters or uninfected animals for up to one week after treatment. Also, ivermectin does not kill louse eggs, which can take up to three weeks to hatch and become susceptible; retreatment may be necessary. In controlling lice, it is recommended that sows be treated at least one week before farrowing.{R-2; 14}

Note: Mite dermatosis—[EL]US,CANFor treatment of demodicosis:

Cats—Although the safety and efficacy have not been established, a subcutaneous dose of 0.6 mg doramectin per kg of body weight, administered subcutaneously once a week, has been used in the treatment of demodicosis.{R-126} In a report of three cats, the length of treatment required to achieve negative skin scrapings was two to three injections.{R-126}

Dogs—Although the safety and efficacy have not been established, a subcutaneous dose of 0.6 mg doramectin per kg of body weight, administered once a week for at least three injections after a negative skin scraping is found, has been used in the treatment of demodicosis.[EL]{R-126}

[EL]US,CANFor treatment of notoedric mange: *Cats*—A single, subcutaneous dose of 0.2 mg doramectin per kg of body weight has been used in the treatment of notoedric mange.[EL]{R-131}

The dosages listed above should not be administered to animals known to be susceptible to macrocyclic lactone toxicity. Screening for mutation of the *MDR1* gene may be performed to predict dogs prone to toxicity.{R-155} See also the *Breed sensitivity* portion of the *Precautions* section in this monograph for more information.

Strength(s) usually available:

U.S.—{R-24}

Veterinary-labeled product(s):

10 mg per mL (OTC) [*Dectomax Injectable Solution*].

Canada—{R-26}

Veterinary-labeled product(s):

10 mg per mL (OTC) [*Dectomax Injectable Solution*].

Packaging and storage: Store below 30 °C (86 °F),{R-24; 26} unless otherwise specified by manufacturer. Protect from light.

Caution: Keep out of the reach of children and pets.{R-24}

Additional information: Environmental safety—Although doramectin tightly binds to soil and becomes inactive with time, when it enters the water, fish and other aquatic life may be harmed. Water should be prevented from running off feedlots to lakes, streams, or groundwater. Doramectin should not be directly applied to water and should be disposed of by a method that will avoid contaminating water, such as incineration or disposal in an approved landfill.{R-24; 26}

USP requirements: Not in USP.{R-42}

Topical Dosage Forms

Note: Text between [EL]US and [EL] describes uses not included in U.S. product labeling. Text between [EL]CAN and [EL] describes uses not included in Canadian product labeling.

The [EL]US or [EL]CAN designation may signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

DORAMECTIN TOPICAL SOLUTION

Usual dose:

Eyeworm infection;

Grub infection;

Horn flies;

Lungworm infection;

Mite dermatosis;

Nematode, gastrointestinal, infection; or

Pediculosis—*Cattle:* Topical, 0.5 mg per kg of body weight (1 mL per 10 kg of body weight), administered along the topline in a narrow strip from the withers to the tailhead.{R-23; 25}

Withdrawal times—US: Meat—45 days. Not labeled for use in preruminating calves or in female dairy cattle of breeding age.{R-23} Canada: Meat—55 days. Not labeled for use in nonlactating dairy cattle within 2 months of calving or in lactating dairy cows.{R-25}

Note: Simulated rainfall before, during, and forty minutes after application of doramectin topical solution on calves with induced roundworm and lungworm infection did not affect the efficacy of the treatment.{R-25} Materials, such as mud or manure, caked on the skin will reduce efficacy.{R-23; 25}

For the most safe and effective treatment of grubs, cattle are treated as soon as possible after the end of the heel fly season. Whenever it is performed, treatment should be timed to avoid killing larvae migrating through vital tissues, such as esophageal tissue or the vertebral canal.{R-23; 25}

Strength(s) usually available:

U.S.—{R-23}

Veterinary-labeled product(s):

5 mg per mL (OTC) [*Dectomax Pour-On*].

Canada—{R-}

Veterinary-labeled product(s):

5 mg per mL (OTC) [*Dectomax Pour-On*].

Packaging and storage: Store below 30 °C (86 °F),{R-25} unless otherwise specified by manufacturer. Protect from light.{R-23; 25} Protect from freezing.

Caution:

Doramectin topical solution is flammable and should be kept away from sources of ignition.{R-23; 25}

People handling this medication should be careful to avoid ivermectin contact with eyes and skin because of the risk of local irritation and of systemic absorption. Product labeling recommends covering exposed skin with long sleeves and gloves. Accidental skin exposure should be washed immediately with soap and water, eyes exposed flushed with water, and medical attention sought.{R-23}

Keep out of the reach of children and pets.{R-23; 25}

Additional information:

Doramectin topical solution is provided in a multiple dose bottle with a cup to meter the dose or "backpacks" for use with recommended applicator systems.{R-23; 25}

Environmental safety—Although doramectin tightly binds to soil and becomes inactive, when it enters the water, fish and other aquatic life may be harmed. Therefore, cattle should not enter lakes, ponds, or streams for at least six hours after being treated. Doramectin should not be directly applied to water. It should be disposed of in a way that will avoid contaminating water, such as incineration or disposal in an approved landfill.{R-23; 25}

USP requirements: Not in USP.{R-42}

EPRINOMECTIN

Topical Dosage Forms

Note: Text between EL,US and EL describes uses not included in U.S. product labeling. Text between EL,CAN and EL describes uses not included in Canadian product labeling.

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

EPRINOMECTIN TOPICAL SOLUTION

Usual dose:

Grub infection;

Horn flies;

Mite dermatosis; or

Pediculosis—*Cattle:* Topical, 0.5 mg per kg of body weight (1 mL per 10 kg of body weight), administered along the topline in a narrow strip from the withers to the tailhead.{R-27; 28}

Withdrawal times—US: Meat and milk—None.{R-27} Canada: Meat and milk—None.{R-28}

Lungworm infection; or

Nematode, gastrointestinal, infection—*Cattle* and EL,US*deer* EL: Topical, 0.5 mg per kg of body weight (1 mL per 10 kg of body weight), administered along the topline in a narrow strip from the withers to the tailhead.{R-27; 28}

Withdrawal times—*Cattle*: US—Meat and milk: None.{R-27} Canada—Meat and milk: None.{R-28} *Deer:* Canada—Meat: None.{R-28}

Note: Materials, such as mud or manure, caked on the skin will reduce efficacy, while weather conditions, including rain, should not.{R-27}

For safe and effective treatment of grubs, the timing of anthelmintic administration is important. Cattle are treated as soon as possible after the end of the heel fly season. Whenever it is performed, treatment should be timed to avoid killing larvae migrating through vital tissues, such as esophageal tissue or the vertebral canal.{R-27}

Strength(s) usually available:

U.S.—{R-27}

Veterinary-labeled product(s):

5 mg per mL (OTC) [*Eprinex Pour-On*].

Canada—{R-28}

Veterinary-labeled product(s):

5 mg per mL (OTC) [*Eprinex Pour-On*].

Packaging and storage: Store below 30 °C (86 °F),{R-27} unless otherwise specified by manufacturer. Although storage for short periods of time at temperatures up to 40 °C (104 °F) can be tolerated, such exposures should be minimized.{R-27} Protect from light.{R-28}

Stability: Canadian product labeling states that eprinomectin topical solution is stable for thirty-six months when properly stored.{R-28}

Caution:

Human handlers should be careful to avoid contact of eprinomectin with skin because of the risk of local irritation and of systemic absorption. Accidental skin exposure should be washed immediately with soap and water, and eye exposure treated by flushing with water; medical attention should be sought.{R-27; 28}

Keep out of the reach of children and pets.{R-27; 28}

Additional information:

Eprinomectin topical solution is provided in a multiple dose bottle with a cup to meter the dose or a collapsible pack for use with appropriate applicator systems.{R-27}

Environmental safety—Although eprinomectin tightly binds to soil and becomes inactive, when it enters the water, fish and other aquatic life may be harmed. Eprinomectin should not be directly applied to water. It should be disposed of in a way that will avoid contaminating water, such as incineration or disposal in an approved landfill.{R-27; 28}

USP requirements: Not in USP.{R-42}

IVERMECTIN

Oral Dosage Forms

Note: Text between EL,US and EL describes uses not included in U.S. product labeling. Text between EL,CAN and EL describes uses not included in Canadian product labeling.

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

IVERMECTIN MEDICATED FEED

Usual dose:

Kidneyworm infection;

Lungworm infection;
Mite dermatosis;
Nematode, gastrointestinal, infection; or
Pediculosis—*Pigs:*
For use in complete feed—
Starter, grower, or finisher pigs: Oral, 0.1 mg per kg of body weight, administered as 1.8 grams per ton (2 parts per million [ppm]) of complete feed, fed as the only ration for seven days.{R-4; 16}
Adult and breeding pigs: Oral, 0.1 mg per kg of body weight, administered as 9 grams per ton (10 ppm) of complete feed, if fed at one percent of body weight daily, for seven days.{R-4; 16} The concentration in the feed is adjusted if it is being fed for other percentages of body weight.{R-4}
EL CAN For use as a top dress (as described for Type C medicated feed in the United States) EL—Adult pigs: Oral, 0.1 mg per kg of body weight a day, administered to individual pigs on top of the usual daily ration.{R-4}
Withdrawal time—US and Canada: Meat—5 days.{R-4; 16}

Strength(s) usually available:
U.S.—{R-4}
Veterinary-labeled product(s):
0.2 grams per kg (182 grams per ton) of premix (OTC) [*Ivomec Premix for Swine Type C Medicated Feed 0.02%*].
Canada—{R-16}
Veterinary-labeled product(s):
6 grams per kg of premix (OTC) [*Ivomec Premix for Swine*].

Caution: Keep out of the reach of children and pets.{R-4; 16}

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

Additional information: Environmental safety—Although ivermectin binds tightly to soil and becomes inactive, when it enters the water, fish and other aquatic life may be harmed. Water runoff from swine production areas should not be allowed to directly enter lakes, streams, or ponds. Ivermectin should not be directly applied to water. It should be disposed of in a way that will avoid contaminating water, such as incineration or disposal in an approved landfill.{R-4; 16}

USP requirements: Not in USP.{R-42}

IVERMECTIN ORAL PASTE

Usual dose:
Bot infection;
Habronemiasis, cutaneous;
Lungworm infection;
Nematode, gastrointestinal, infection; or
Onchocerciasis, cutaneous—*Horses:* Oral, 0.2 mg per kg of body weight.{R-8-10; 18}
Withdrawal time—US and Canada: These products are not labeled for use in horses intended for food production.{R-8; 18}
Note: Horses with heavy loads of neck threadworm (*Onchocerca* species) microfilariae causing dermatitis may have skin swelling and itching as a reaction to treatment and death of microfilariae and may require veterinary medical attention.{R-8; 18}
Healing of significant summer sores lesions may require medical therapy in addition to anthelmintic treatment to resolve. {R-11}

Strength(s) usually available:
U.S.—{R-8; 9}
Veterinary-labeled product(s):
18.7 mg per gram of paste (1.87%) (OTC) [*Agri-Mectin Equine Paste Dewormer 1.87%; AmTech Phoenectin Paste 1.87%; Cooper's Best Ivermectin Paste 1.87%; Dealer Select Horse Care Ivermectin Paste 1.87%; Equell Paste 1.87%; Equimectrin Paste 1.87%; Eqvalan Paste 1.87%; Horse Health Equine Ivermectin Paste 1.87%; IverCare; Ivercide Equine Paste 1.87%; Parid EQ Paste 1.87%; ProMectin E Paste; Rotation 1; Zimecterin*].
Canada—{R-}
Veterinary-labeled product(s):
18.7 mg per gram of paste (1.87%) (OTC) [*Eqvalan Oral Paste; Panomec Oral Paste*].

Packaging and storage: Store below 30 °C (86 °F),{R-18} in a well-closed container, unless otherwise specified by manufacturer.

Stability: Ivermectin oral paste is expected to be stable for up to three years when properly stored.{R-18}

Caution:
It is recommended that human handlers avoid bringing medication in contact with their eyes and wash their hands after administering ivermectin oral paste.{R-8}
Keep out of the reach of children and pets.{R-8}

Additional information: Environmental safety—Although ivermectin and excreted ivermectin residues tightly bind to soil and become inactive, when ivermectin enters the water, fish and other aquatic life may be harmed. Neither ground nor surface water should be contaminated with ivermectin. Syringes should be disposed of by incineration or in an approved landfill.{R-8; 18}

USP requirements: Not in USP.{R-42}

IVERMECTIN ORAL SOLUTION

Usual dose:
Bot infection;
Lungworm infection; or
Nematode, gastrointestinal, infection—*Horses* and *sheep:* Oral, 0.2 mg per kg of body weight.{R-11; 12; 15; 17}
Withdrawal times—*Horses:* Ivermectin oral solution is not labeled for use in horses to be used in the production of food.{R-11; 17} *Sheep:* US—Meat: 11 days.{R-12} Canada—Meat: 14 days.{R-15}
Habronemiasis, cutaneous; or
Onchocerciasis, cutaneous—*Horses:* Oral, 0.2 mg per kg of body weight.{R-11; 17}
Withdrawal times—*Horses:* Ivermectin oral solution is not labeled for use in horses to be used in the production of food.{R-11; 17}
Note: Horses with heavy loads of neck threadworm (*Onchocerca* species) microfilariae causing dermatitis may have skin swelling and itching as a reaction to death of microfilariae and may require veterinary medical attention.{R-11; 17}
Healing of significant summer sore lesions may require medical therapy in addition to anthelmintic treatment to resolve. {R-11}
For horses, administration may be performed by nasogastric intubation or by oral drench. Because of the skill required to administer by nasogastric tube, it is recommended that it only be administered in this way by a veterinarian.{R-11}
For sheep, standard drenching equipment that delivers an accurate dose can be used to administer ivermectin oral solution. Some sheep may cough for several minutes after

drenching.[R-15] Salivating may indicate a lost dose and the need for a sheep to be redosed.

[EL][US,CAN]Mite dermatosis—For the treatment of demodicosis: *Dogs*—An oral dose of 0.3 mg per kg of body weight a day, administered for eight weeks after two consecutive negative skin scrapings, has been used.[R-122] Alternatively, an oral dose of 0.4 to 0.6 mg per kg of body weight a day has been effective when administered for up to four weeks after two consecutive negative skin scrapings have been performed.[EL][R-124; 125]

The dosages listed above should not be administered to dogs considered susceptible to macrocyclic lactone toxicity. Screening for mutation of the *MDR1* gene may be performed to predict dogs prone to toxicity.[R-155] See also the *Breed sensitivity* portion of the *Precautions* section in this monograph for more information.

Note: Nematode, gastrointestinal, infection—[EL][US,CAN]*Goats:* An oral dose of 0.4 mg per kg of body weight has been used; however, experts warn against routine administration.[R-104; 135; 136] See also the *Indications* section in this monograph.

Extra-label withdrawal information: United States—There are no established withdrawal times for goats because ivermectin is not approved for use in this species. If ivermectin is administered to goats as a single oral dose of 0.2 to 0.4 mg per kg of body weight, evidence has been compiled by the Food Animal Residue Avoidance Databank (FARAD) that suggests a meat withdrawal time of 14 days and a milk withholding time of 9 days would be sufficient to avoid residues considered potentially harmful by some national and international authorities.[R-139] Canada—There are no established withdrawal times for goats because ivermectin is not approved for use in this species. Due to the lack of established maximum residue limits for use of ivermectin in goats in Canada and the sensitivity of residue detection methods, general recommendations for withdrawal cannot be made. Contact the Canadian gFARAD (www.cgfarad.usask.ca) for more information.[EL][R-140]

Strength(s) usually available:

U.S.—[R-11; 12; 41]

Veterinary-labeled product(s):

0.8 mg per mL (OTC) [*Ivermax Drench for Sheep; Ivomec Sheep Drench; Privermectin Drench for Sheep*].

10 mg per mL (Rx) [*AmTech Phoenectin Liquid for Horses; DVMectin; Eqvalan Liquid; Ivercide Liquid for Horses; Ivermax Equine Oral Drench; Iversol Liquid for Horses; Parid EQ Liquid for Horses; Privermectin Equine Oral Liquid; ProMectin E Liquid; SparMectin-E*].

Canada—[R-15]

Veterinary-labeled product(s):

0.8 mg per mL (OTC) [*Ivomec Drench for Sheep*].

10 mg per mL (Rx) [*Eqvalan Liquid*].

Packaging and storage: Store below 30 °C (86 °F),[R-15] in a tightly closed container,[R-11; 17] unless otherwise specified by manufacturer. Protect from light.[R-11; 17] Protect from freezing.

Stability: When ivermectin oral solution for horses is diluted with tap water to a 1 to 20 or 1 to 40 dilution, it is expected to be stable for 72 hours when properly stored.[R-11]

Caution:

It is recommended that people handling this medication avoid contact of ivermectin with their eyes and wash their hands after administering the oral solution.[R-12; 17]

Keep out of the reach of children and pets.[R-12; 17]

Additional information: Environmental safety—Although ivermectin and excreted ivermectin residues tightly bind to soil and become inactive, when ivermectin enters the water, fish and other aquatic life may be harmed.[R-11; 12; 15; 17] Neither ground nor surface water should be contaminated with ivermectin; ivermectin should not be directly applied to water.[R-11; 12] Spills should be contained and soaked up with towels or mixed into loose soil.[R-12] All material collected from spills as well as used drug containers should be placed in an impervious bag and incinerated or disposed of in an approved landfill.[R-12; 15; 17]

USP requirements: Not in USP.[R-42]

IVERMECTIN TABLETS

Usual dose:

Heartworm disease (prophylaxis)—

Cats, six weeks of age or older: Oral, 0.024 mg (24 mcg) per kg of body weight every thirty days.[R-7]

Dogs, six weeks of age or older: Oral, 0.006 mg (6 mcg) per kg of body weight every 30 days.[R-5; 20]

Note: Testing for heartworm disease is recommended before beginning preventative treatment with ivermectin tablets.[R-5-7] If microfilaremic, dogs may develop a reaction to preventative treatment.[R-5] If a dog is found to be infected with heartworms, treatment before beginning preventative therapy is recommended. Cats already infected with adult heartworms can be given preventative therapy to prevent further infection.[R-7]

It is recommended that care be taken that the entire dose is swallowed.[R-5; 20] To administer the chewable tablet by hand to cats and avoid a reduction in absorption, it can broken into pieces.[R-7]

Ivermectin tablets are given during the time of year when mosquitoes are active; in some areas, year-round administration is practiced. If a cat or dog is exposed to mosquitoes before treatment, the first dose must be given within 30 days to be effective; the last dose is given within 30 days after the last exposure.[R-5]

Nematode, gastrointestinal, infection—*Cats:* For hookworm infection—Oral, 0.024 mg (24 mcg) per kg of body weight every thirty days.[R-7]

Strength(s) usually available:

U.S.—[R-5-7]

Veterinary-labeled product(s):

55 mg (Rx) [*Heartgard For Cats* (flavored chewable)].

68 mg (Rx) [*Heartgard Chewables* (flavored chewable); *Heartgard Tablets; ParaGARD* (flavored chewable)].

136 mg (Rx) [*Heartgard Chewables* (flavored chewable); *Heartgard Tablets; ParaGARD* (flavored chewable)].

165 mg (Rx) [*Heartgard For Cats* (flavored chewable)].

272 mg (Rx) [*Heartgard Chewables* (flavored chewable); *Heartgard Tablets; ParaGARD* (flavored chewable)].

Canada—[R-20]

Veterinary-labeled product(s):

55 mg (Rx) [*Heartgard-30 Chewables For Cats* (flavored chewable)].

68 mg (Rx) [*Heartgard-30 Chewables* (flavored chewable); *Heartgard-30 Tablets*].

136 mg (Rx) [*Heartgard-30 Chewables* (flavored chewable); *Heartgard-30 Tablets*].

165 mg (Rx) [*Heartgard-30 Chewables For Cats* (flavored chewable)].

272 mg (Rx) [*Heartgard-30 Chewables* (flavored chewable); *Heartgard-30 Tablets*].

Packaging and storage: Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.[R-6; 7] Protect from light.[R-6; 7]

Stability: Ivermectin tablets for cats are stable for 2 years when stored properly.{R-7}

Caution: Keep out of the reach of children and pets.{R-5; 6}

USP requirements: Not in USP.{R-42}

Parenteral Dosage Forms

Note: Text between [EL-US] and [EL] describes uses not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses not included in Canadian product labeling.

The [EL-US] or [EL-CAN] designation may signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

IVERMECTIN INJECTION

Usual dose:

Note: Ivermectin injection is administered subcutaneously to reduce the risk of clostridial infection at the injection site. Use of sterile equipment and disinfection of the injection site are also important.{R-2; 14}

In sheep, injection into the area of loose skin behind the shoulder is considered appropriate.{R-14} Similarly, in buffalo, cattle, or reindeer, injection under the loose skin in front of or behind the shoulder is recommended.{R-2} In pigs, ivermectin injection is administered subcutaneously in the neck, just behind the ear.{R-2}

[EL-US]Bot infection—*Sheep:* Subcutaneous, 0.2 mg per kg of body weight.{R-14}

Withdrawal times: Canada—Meat: 35 days. Not labeled for use in ewes when their milk is to be used for human consumption.[EL]{R-14}

[EL-US]Eyeworm infection[EL]—*Cattle:* Subcutaneous, 0.2 mg per kg of body weight.{R-14}

Withdrawal times: US and Canada—Meat: 35 days.{R-2; 14} Not labeled for use in female dairy cattle of breeding age or in calves to be used in the production of veal.{R-2}

Grub (warble) infection—[EL-CAN]*Buffalo*[EL], *cattle,* and [EL-CAN]*reindeer*[EL]: Subcutaneous, 0.2 mg per kg of body weight (1 mL per 110 pounds of body weight).{R-2}

Withdrawal times: *Buffalo* and *reindeer*—US: Meat—56 days.{R-2} *Cattle*—US and Canada: Meat—35 days.{R-2; 14} Not labeled for use in female dairy cattle of breeding age or in calves to be used in the production of veal.{R-2}

Note: For the most safe and effective treatment of grubs, cattle are treated as soon as possible after the end of the heel fly season. Whenever it is performed, treatment is timed to avoid killing larvae migrating through vulnerable tissues.{R-1}

Lungworm infection—

Cattle: Subcutaneous, 0.2 mg per kg of body weight (1 mL per 110 pounds of body weight).{R-2; 14}

Withdrawal times—US and Canada: Meat—35 days.{R-2; 14} Not labeled for use in female dairy cattle of breeding age or in calves to be used in the production of veal.{R-2}

Pigs: Subcutaneous, 0.3 mg per kg of body weight.{R-2; 3; 14}

Withdrawal times—US: Meat—18 days (includes grower and feeder pigs){R-2} Canada: Meat—28 days.{R-14}

Note: In the United States, the 1% solution is recommended for pigs greater than 70 pounds of body weight; 1 mL administered per 75 pounds of body weight delivers 0.3 mg per kg of body weight.{R-3} For grower and feeder pigs, 1 mL of the 0.27% solution per 20 pounds of body weight delivers the same dose.{R-3} In Canada, if the 1% solution is administered to young pigs weighing less than 16 kg, a syringe that can accurately deliver as little as 0.1 mL is recommended.{R-14}

[EL-US]*Sheep*: Subcutaneous, 0.2 mg per kg of body weight.{R-14}

Withdrawal times—Canada: Meat—35 days.{R-14} Not labeled for administration to ewes when their milk is to be used for human consumption.[EL]{R-14}

Mite dermatosis—

Cattle: Subcutaneous, 0.2 mg per kg of body weight (1 mL per 110 pounds of body weight).{R-2; 14}

Withdrawal times—US and Canada: Meat—35 days.{R-2; 14} Not labeled for use in female dairy cattle of breeding age or in calves to be used in the production of veal.{R-2}

Pigs: Subcutaneous, 0.3 mg per kg of body weight.{R-2; 3; 14}

Withdrawal times—US: Meat—18 days (includes grower and feeder pigs){R-2} Canada: Meat—28 days.{R-14}

Note: In the treatment of pediculosis, lice are not immediately killed and could infect clean quarters or uninfected animals for up to one week after treatment. Also, ivermectin does not kill louse eggs, which can take up to three weeks to hatch and become susceptible; retreatment may be necessary. In controlling lice, it is recommended that sows be treated at least one week before farrowing.{R-2; 14}

[EL-US,CAN]*Cats:* For the treatment of cheyletiellosis—Subcutaneous, 0.3 mg per kg of body weight, administered twice, two weeks apart.{R-119} Alternatively, clinicians may administer this dose orally.[EL]{R-156}

[EL-US,CAN]*Dogs:*

For the treatment of cheyletiellosis—Subcutaneous, 0.3 mg per kg of body weight, administered twice, two weeks apart.{R-66} Alternatively, clinicians may administer this dose orally.{R-156}

For the treatment of demodicosis—Oral, 0.3 mg per kg of body weight a day, administered for eight weeks after two consecutive skin scrapings are found to be negative.{R-122} Alternatively, a dose of 0.4 to 0.6 mg per kg of body weight a day has been effective when administered for up to four weeks after two consecutive skin scrapings are found to be negative.{R-124; 125}

For the treatment of sarcoptic mange—

Oral, 0.2 to 0.5 mg per kg of body weight, administered twice, two to three weeks apart.{R-112-114}

Subcutaneous, 0.2 mg per kg of body weight, administered twice, two to three weeks apart.[EL]{R-113; 114}

Note: The dosages listed above should not be administered to cats or dogs considered susceptible to macrocyclic lactone toxicity. Screening for mutation of the *MDR1* gene may be performed to predict dogs prone to toxicity.{R-155} See also the *Breed sensitivity* portion of the *Precautions* section in this monograph for more information.

Mite, ear, infestation—

[EL-CAN]*Foxes,* ranch raised: Subcutaneous, 0.2 mg per kg of body weight, administered between the shoulder blades.{R-3} The dose is repeated in three weeks.[EL]{R-3}

Note: The above dosage for the treatment of foxes is included in product labeling for the 0.27% solution.{R-3}

[EL-US,CAN]*Cats* and *dogs:* Subcutaneous, 0.3 mg per kg of body weight, administered twice, fourteen days apart.{R-114; 159} Alternatively, clinicians may administer this dose orally.{R-156} Ears may be re-examined for mites at the second treatment and, if necessary, two weeks later.[EL]{R-114; 159}

Note: The dosage listed above should not be administered to animals considered susceptible to ivermectin toxicity. Screening for mutation of the *MDR1* gene may be performed to predict dogs prone to

toxicity.{R-155} See also the *Breed sensitivity* portion of the *Precautions* section in this monograph for more information.

Nematode, gastrointestinal, infection—

Cattle: Subcutaneous, 0.2 mg per kg of body weight (1 mL per 110 pounds of body weight).{R-2; 14}

Withdrawal times—US and Canada: Meat—35 days.{R-2; 14} Not labeled for use in female dairy cattle of breeding age or in calves to be used in the production of veal.{R-2}

Pigs: Subcutaneous, 0.3 mg per kg of body weight.{R-2; 3; 14}

Withdrawal times—US: Meat—18 days (includes grower and feeder pigs){R-2} Canada: Meat—28 days.{R-14}

Note: In the United States, the 1% solution is recommended for pigs greater than 70 pounds of body weight; 1 mL administered per 75 pounds of body weight delivers 0.3 mg per kg of body weight.{R-3} For grower and feeder pigs, 1 mL of the 0.27% solution per 20 pounds of body weight delivers the same dose.{R-3} In Canada, if the 1% solution is administered to young pigs weighing less than 16 kg, a syringe that can accurately deliver as little as 0.1 mL is recommended.{R-14}

EL[US] *Sheep:* Subcutaneous, 0.2 mg per kg of body weight.{R-14}

Withdrawal times—Canada: Meat—35 days.{R-14} Not labeled for use in ewes when their milk is to be used for human consumption.[EL]{R-14}

EL[US,CAN] *Dogs:* For the treatment of hookworms and whipworms—

Oral, 0.3 mg per kg of body weight.{R-134}

Subcutaneous, 0.2 mg per kg of body weight.[EL]{R-134}

Note: The dosages listed above should not be administered to dogs considered susceptible to macrocyclic lactone toxicity. Screening for mutation of the *MDR1* gene may be performed to predict dogs prone to toxicity.{R-155} See also the *Breed sensitivity* portion of the *Precautions* section in this monograph for more information.

Pediculosis—

Cattle: Subcutaneous, 0.2 mg per kg of body weight (1 mL per 110 pounds of body weight).{R-2; 14}

Withdrawal times—US and Canada: Meat—35 days.{R-2; 14} Not labeled for use in female dairy cattle of breeding age or in calves to be used in the production of veal.{R-2}

Pigs: Subcutaneous, 0.3 mg per kg of body weight.{R-2; 3; 14}

Withdrawal times—US: Meat—18 days (includes grower and feeder pigs){R-2} Canada: Meat—28 days.{R-14}

Note: In the treatment of pediculosis, lice are not immediately killed and could infect clean quarters or uninfected animals for up to one week after treatment. Also, ivermectin does not kill louse eggs, which can take up to three weeks to hatch and become susceptible; retreatment may be necessary. In controlling lice, it is recommended that sows be treated at least one week before farrowing.{R-2; 14}

Note: EL[US,CAN] Mite, nasal, infestation: *Dogs*—Although the safety and efficacy have not been established, a single subcutaneous dose of 0.2 mg per kg of body weight has been used, based on reports of four cases.[EL]{R-169; 170}

The dose listed above should not be administered to dogs considered susceptible to macrocyclic lactone toxicity. Screening for mutation of the *MDR1* gene may be performed to predict dogs prone to toxicity.{R-155} See also the *Breed sensitivity* portion of the *Precautions* section in this monograph for more information.

Strength(s) usually available:

U.S.—{R-2; 3; 41}

Veterinary-labeled product(s):

2.7 mg per mL (0.27%) (OTC) [*Ivomec Injection for Grower and Feeder Pigs*].

10 mg per mL (1%) (OTC) [*AmTech Phoenectin Injection for Cattle and Swine; Comectrin Injection for Cattle and Swine; Double Impact; Ivercide Injection for Cattle and Swine; Ivomec 1% Injection for Cattle and Swine; Ivomec 1% Injection for Swine; Produmec Injection for Cattle and Swine; Promectin Injection for Cattle and Swine; Ultramectrin Injection for Cattle and Swine*].

Canada—{R-14}

Veterinary-labeled product(s):

10 mg per mL (1%) (OTC) [*Ivomec Injection*].

Packaging and storage: Store at or below 25 °C (77 °F), unless otherwise specified by manufacturer. Protect from light.{R-2}

Stability: Ivermectin injection is stable for five years when properly stored.{R-14}

Caution: Keep out of the reach of children and pets.{R-14}

Additional information:

Ivermectin injection is available in a multiple-dose, rubber-capped bottle or in a soft, collapsible pack for use with automatic injection equipment.{R-14}

Environmental safety—Although ivermectin tightly binds to soil and becomes inactive, when it enters the water, fish and other aquatic life may be harmed. Therefore, animals should not enter lakes, ponds, or streams for at least six hours after being treated. Ivermectin should not be directly applied to water. It should be disposed of by a method that will avoid contaminating water, such as incineration or disposal in an approved landfill.{R-2; 14}

USP requirements: Not in USP.{R-42}

Topical Dosage Forms

Note: Text between EL[US] and [EL] describes uses not included in U.S. product labeling. Text between EL[CAN] and [EL] describes uses not included in Canadian product labeling.

The EL[US] or EL[CAN] designation may signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

IVERMECTIN TOPICAL SOLUTION

Usual dose:

EL[US] Eyeworm infection[EL],{R-13}

Grub infection;

Horn flies;

Lungworm infection;

Mite dermatosis;

Nematode, gastrointestinal, infection; or

Pediculosis—*Cattle:* Topical, 0.5 mg per kg of body weight (1 mL per 10 kg of body weight), administered along the topline in a narrow strip from the withers to the tailhead.{R-1; 13}

Withdrawal times—US: Meat—48 days. Not labeled for use in female dairy cattle of breeding age.{R-1} Canada: Meat—49 days. Not labeled for use in dairy cattle within 2 months of calving.{R-13}

Note: To avoid a reduction in efficacy, product labeling recommends that cattle not be treated when their hair or hide is wet or when they are expected to become wet within six hours of treatment.{R-1; 13}

Skin lesions, dermatoses, or materials, such as mud or manure, caked on the skin will reduce efficacy.{R-1; 13}

For the most safe and effective treatment of grubs, cattle are treated as soon as possible after the end of the heel fly season. Whenever it is performed, treatment should be timed

to avoid killing larvae migrating through tissues, in particular, esophageal tissue or the vertebral canal.{R-1}

Note: Mite dermatosis—[EL US,CAN]For treatment of sarcoptic mange:

Dogs—Although the safety and efficacy have not been established, a topical dose of 0.5 mg ivermectin per kg of body weight, administered twice, fourteen days apart, has been used.[EL]{R-112}

The dose listed above should not be administered to dogs considered susceptible to macrocyclic lactone toxicity. Screening for mutation of the *MDR1* gene may be performed to predict dogs prone to toxicity.{R-155} See also the *Breed sensitivity* portion of the *Precautions* section in this monograph for more information.

Strength(s) usually available:

U.S.—{R-1}

Veterinary-labeled product(s):

5 mg per mL (OTC) [*AmTech Phoenectin Pour-On; Bimectin Pour-On; Comectrin Pour-On; Coopermec Cattle Pour-On; Ecomectin Cattle Pour-On; Ivercide Pour-On for Cattle; Iver-On; Ivomec Pour-On; Privermectin Pour-On; Produmec Pour-On; ProMectin B Pour-On; Prozap Pour-On; Top Line; Ultramectrin Pour-On*].

Canada—{R-13}

Veterinary-labeled product(s):

5 mg per mL (OTC) [*Ivomec Pour-On*].

Caution:

Ivermectin topical solution is flammable and should be kept away from sources of ignition.{R-1; 13}

People handling these medications should be careful to avoid contact of ivermectin with eyes and skin because of the risk of local irritation and of systemic absorption. Product labeling recommends covering exposed skin with long sleeves and gloves. Accidental skin exposure should be washed immediately with soap and water, eyes exposed flushed with water, and medical attention sought.{R-1; 13}

The manufacturer recommends that this product be used only in well-ventilated areas or outdoors and that the container be closed when it is not in use.{R-1; 13}

Keep out of the reach of children and pets.{R-1; 13}

Packaging and storage: Store below 40 °C (104 °F),{R-1} preferably between 15 and 30 °C (59 and 86 °F), in a tight container, unless otherwise specified by manufacturer. Protect from light.{R-1} Protect from freezing.

Additional information:

Ivermectin topical solution is provided in a multiple dose bottle with a cup to meter the dose or in collapsible packs designed for use with automatic dosing equipment.{R-1; 13}

If ivermectin topical solution is stored at temperatures less than 0 °C (32 °F), some cloudiness can occur in the solution, which clears when allowed to warm to room temperature; this change is not expected to affect efficacy.{R-1; 13} Canadian product labeling explains that it is a clear, blue solution that can have fading of color upon exposure to light, sometimes in less than 30 minutes. The loss of color does not indicate potency decline but exposure to light over weeks can cause a gradual loss of potency.{R-13}

Environmental safety—Although ivermectin tightly binds to soil and becomes inactive, when it enters the water, fish and other aquatic life may be harmed. Therefore, cattle should not enter lakes, ponds, or streams for at least six hours after being treated. Ivermectin should not be directly applied to water. It should be disposed of by a method that will avoid contaminating water, such as incineration or disposal in an approved landfill.{R-1}

USP requirements: Not in USP.{R-42}

MILBEMYCIN

Oral Dosage Forms

Note: Text between [EL US] and [EL] describes uses not included in U.S. product labeling. Text between [EL CAN] and [EL] describes uses not included in Canadian product labeling.

The [EL US] or [EL CAN] designation may signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

MILBEMYCIN OXIME TABLETS

Usual dose:

Heartworm disease (prophylaxis)—

Cats, six weeks of age or older and at least 1.5 pounds of body weight: Oral, 2 mg per kg of body weight every thirty days.{R-34}

Dogs, four weeks of age or older and at least two pounds of body weight: Oral, 0.5 mg per kg of body weight every thirty days.{R-35}

Note: Testing for heartworm disease before beginning preventative treatment with ivermectin tablets is recommended.{R-35} If microfilaremic, dogs may develop a reaction to preventative treatment.{R-35} If a dog is found to be infected with heartworms, treatment before beginning preventative therapy is recommended. For cats, studies have not been performed to demonstrate safety of administering milbemycin tablets to cats already infected with adult heartworms.{R-34}

It is recommended that care be taken that the entire dose is swallowed.{R-34; 35} If a cat or dog does not eat the entire dose within an acceptable period of time, the full dose should be readministered as soon as possible.{R-34; 35}

Milbemycin tablets are given during the time of year when mosquitoes are active. If a cat or dog is exposed to mosquitoes before treatment begins, the first dose must be given within 30 days to be effective; the last dose is given within 30 days after the last exposure.{R-34; 36} In areas where potential exposure to mosquitos is continuous, year-round administration is necessary. Even in regions where cold weather limits the mosquito season, many practitioners favor year-round heartworm disease prophylaxis, based on practical experience with dosing errors and variable owner compliance.{R-167}

Nematode, gastrointestinal, infection—

Cats: For hookworm or roundworm infection—Oral, 2 mg per kg of body weight every thirty days.{R-34}

Dogs: For hookworm, roundworm, or whipworm infection—Oral, 0.5 mg per kg of body weight every thirty days.{R-35}

Note: [EL US,CAN]Mite, nasal, infestation—*Dogs:* Although the safety and efficacy have not been established, an oral dose of 0.5 to 1 mg per kg of body weight, administered once a week for three weeks, has been used.[EL]{R-171; 172}

[EL US,CAN]Mite dermatosis—*Dogs:*

For treatment of cheyletiellosis: Although the safety and efficacy have not been established, an oral dose of 2 mg milbemycin oxime per kg of body weight, administered once a week for three doses, has been used.{R-121}

For the treatment of demodicosis: Although the safety and efficacy have not been established, an oral dose of 0.5 to 1 mg milbemycin oxime per kg of body weight every twenty-four hours, until two skin scrapings are found to be negative thirty

days apart, has been used.{R-127} Some dogs have required a higher dose (1.5 to 2 mg per kg of body weight a day) to be cleared of mites.{R-127; 128; 130} One analysis of published studies on the use of milbemycin for demodicosis noted that mean duration of treatment to negative skin scraping was eight to twenty-six weeks and mean total treatment duration was twelve to thirty weeks.{R-162}

For the treatment of sarcoptic mange: Although the safety and efficacy have not been established, an oral dose of 2 mg milbemycin oxime per kg of body weight, administered once a week for a total of four to five doses, has been used.{R-115-117} Some dogs may require a second course of treatment to eliminate infection.EL{R-115-117}

The doses listed above should not be administered to dogs considered susceptible to macrocyclic lactone toxicity. Screening for mutation of the *MDR1* gene may be performed to predict dogs prone to toxicity.{R-155} See also the *Breed sensitivity* portion of the *Precautions* section in this monograph for more information.

Strength(s) usually available:

U.S.—{R-34; 35}

Veterinary-labeled product(s):

2.3 mg (Rx) [*Interceptor Flavor Tabs* (flavored chewable)].

5.75 mg (Rx) [*Interceptor Flavor Tabs* (flavored chewable)].

11.5 mg (Rx) [*Interceptor Flavor Tabs* (flavored chewable)].

23 mg (Rx) [*Interceptor Flavor Tabs* (flavored chewable)].

Note: In the United States, only 5.75-mg, 11.5-mg, and 23-mg tablets are labeled for cats while 2.3-mg, 5.75-mg, 11.5-mg, and 23-mg tablets are labeled for dogs.{R-34; 35}

Canada—{R-36}

Veterinary-labeled product(s):

2.3 mg (Rx) [*Interceptor Flavor Tabs* (flavored chewable)].

5.75 mg (Rx) [*Interceptor Flavor Tabs* (flavored chewable)].

11.5 mg (Rx) [*Interceptor Flavor Tabs* (flavored chewable)].

23 mg (Rx) [*Interceptor Flavor Tabs* (flavored chewable)].

Packaging and storage: Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.{R-35}

Caution: Keep out of the reach of children and pets.{R-36}

USP requirements: Not in USP.{R-42}

MOXIDECTIN

Oral Dosage Forms

Note: Text between EL,US and EL describes uses not included in U.S. product labeling. Text between EL,CAN and EL describes uses not included in Canadian product labeling.

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

MOXIDECTIN ORAL GEL

Usual dose:

Bot infection;

Nematode, gastrointestinal, infection; or

EL,USOnchocerciasis, cutaneousEL—*Horses*: Oral, 0.4 mg per kg of body weight.{R-37; 38}

Withdrawal times— Moxidectin oral gel is not labeled for use in horses that are to be slaughtered for use in food production.{R-37}

Strength(s) usually available:

U.S.—{R-37}

Veterinary-labeled product(s):

20 mg per mL (OTC) [*Quest Gel*].

Canada—{R-38}

Veterinary-labeled product(s):

20 mg per mL (OTC) [*Quest Gel*].

Caution:

Accidental skin exposure should be washed with soap and water and eyes exposed flushed with water. For accidental ingestion, induce vomiting. If symptoms develop or persist, medical attention should be sought.{R-37}

Keep out of the reach of children and pets.{R-37}

Packaging and storage: Store at or below 25 °C (77 °F), in a tight container, unless otherwise specified by manufacturer. Avoid freezing.{R-37}

Additional information:

If the product is frozen, thaw completely before use.{R-37}

Environmental safety—Moxidectin could harm aquatic life; therefore, it should not be released into ground water or free running water. It should be disposed of by a method that will avoid contaminating water, such as incineration or disposal in an approved landfill.{R-37}

USP requirements: Not in USP.{R-42}

Parenteral Dosage Forms

Note: Text between EL,US and EL describes uses not included in U.S. product labeling. Text between EL,CAN and EL describes uses not included in Canadian product labeling.

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

MOXIDECTIN INJECTION

Usual dose:

Grub infection;

Lungworm infection;

Mite dermatosis;

Nematode, gastrointestinal, infection; or

Pediculosis—*Cattle:* Subcutaneous, 0.2 mg per kg of body weight (1 mL per 110 pounds of body weight).{R-33; 174}

Withdrawal times—US: Meat—21 days.{R-174} Subcutaneous administration can cause a transient local tissue reaction that may result in trim loss of edible tissues at slaughter within 35 days of treatment.{R-174} Not labeled for use in female dairy cattle of breeding age; a milk withdrawal time has not been established. A withdrawal period has not been established for preruminating calves.{R-174} Canada: Meat—36 days.{R-33} Not labeled for use in lactating dairy cattle or in nonlactating dairy cattle within 2 months of calving.{R-33}

Note: It is recommended that moxidectin injection be administered subcutaneously in front of or behind the shoulder. Use of sterile equipment and administration of a maximum of 10 mL per injection site are also recommended.{R-33}

Animals less than 100 kg may be more susceptible to an overdose of moxidection; care when measuring the dose is recommended.{R-33}

For the most safe and effective treatment of grubs, cattle are treated as soon as possible after the end of the heel fly season. Whenever it is performed, treatment should be timed to avoid killing larvae migrating through tissues, in particular, esophageal tissue or the vertebral canal.

Strength(s) usually available:
U.S.—
Veterinary-labeled product(s):
10 mg per mL (OTC) [*Cydectin Injectable Solution*].
Canada—{R-33}
Veterinary-labeled product(s):
10 mg per mL (OTC) [*Cydectin Injection*].

Packaging and storage: Store between 4 and 25 °C (39° and 77 °F), and protect from light,{R-33; 174} unless otherwise specified by manufacturer.

Caution:
Severe adverse reactions have occurred when this product was administered to species other than cattle.{R-174}
People handling this medication should be careful to avoid contact of moxidectin with eyes and skin.{R-32} Accidental skin exposure should be washed immediately with soap and water, eyes exposed flushed with water, and medical attention sought.
Keep out of the reach of children and pets.{R-33}

Additional information:
Mixing with other medications before administration is not recommended.{R-33}
Environmental safety—Although moxidectin tightly binds to soil and becomes inactive, when free moxidectin enters the water, fish and other aquatic life may be harmed. It should be disposed of by a method that avoids direct contamination of water, such as incineration or disposal in an approved landfill.{R-33}

USP requirements: Not in USP.{R-42}

MOXIDECTIN FOR SUSTAINED-RELEASE INJECTION

Usual dose:
EL[US]Heartworm disease (prophylaxis)[EL]; or
EL[US]Nematode, gastrointestinal, infection (for treatment of hookworms)[EL]—*Dogs,* six months of age and older: Subcutaneous, 0.17 mg per kg of body weight.{R-39; 40} Moxidectin sustained-release injection is administered within one month of exposure to mosquitoes and every six months afterwards if exposure continues.{R-39} For growing dogs, the dose should be based on the average weight expected during the six-month post-injection period.{R-40}
Note: Testing and, if necessary, treating for heartworm disease before beginning preventative treatment with moxidectin sustained-release injection is recommended.{R-35; 40} Moxidectin sustained-release injection is not effective in removing adult *Dirofilaria immitis* or in clearing microfilariae.{R-39; 40}
Swirl reconstituted injection gently before drawing up each dose into a syringe with an 18- or 20-gauge needle. Once drawn into syringe, if the dose is not immediately administered, the syringe must be gently rolled to resuspend microspheres.{R-39; 40} Moxidectin sustained-release injection is administered subcutaneously on the left or right side of the dorsal neck cranial to the scapulae. A maximum of 3 mL is given in each site. The site of administration is recorded so that injections can be alternated from one side of the neck to the other{R-39} to decrease risk of adverse local tissue reactions.

Strength(s) usually available: When constituted according to manufacturer's directions—
U.S.:{R-39}
Veterinary-labeled product(s)—
Not commercially available.
Canada:{R-40}
Veterinary-labeled product(s)—
3.4 mg per mL (Rx) [*ProHeart 6*].

Packaging and storage: Store at or below 25 °C (77 °F),{R-39} unless otherwise specified by manufacturer. Protect from light.{R-39} After constitution, store under refrigeration at 2 to 8 °C (36 to 46 °F).

Preparation of dosage form: This product must be constituted by mixing the two vials provided, at least 30 minutes before administration, following manufacturer's instructions. Before drawing each dose, the vial should be swirled gently to resuspend microspheres uniformly.{R-39; 40}

Stability: After constitution, moxidectin sustained-release injection is stable for 4 weeks (U.S. product labeling) or 8 weeks (Canadian product labeling) when properly stored under refrigeration.{R-39; 40}

Caution:
People handling moxidectin sustained-release injection should be aware it is slightly irritating to eyes or to upper respiratory tract when inhaled. If accidental contact with eyes occurs, thorough rinsing with water for 15 minutes and medical attention are recommended.{R-39}
Keep out of the reach of children and pets.{R-39}

Additional information:
Mixing with other medications before administration is not recommended.{R-33}
Environmental safety—Although moxidectin tightly binds to soil and becomes inactive, when it enters the water, fish and other aquatic life may be harmed. It should be disposed of by a method that will avoid contaminating water, such as incineration or disposal in an approved landfill.{R-33}

USP requirements: Not in USP.{R-42}

Topical Dosage Forms

Note: Text between EL[US] and [EL] describes uses not included in U.S. product labeling. Text between EL[CAN] and [EL] describes uses not included in Canadian product labeling.
The EL[US] or EL[CAN] designation may signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

MOXIDECTIN TOPICAL SOLUTION

Usual dose:
Grub infection;
EL[CAN]Horn flies[EL];
Lungworm infection;
Mite dermatosis;
Nematode, gastrointestinal, infection; or
Pediculosis—*Cattle:* Topical, 0.5 mg per kg of body weight (1 mL per 10 kg of body weight), administered along the topline in a narrow strip from the withers to the tailhead.{R-31; 32}
Withdrawal times—US: Meat and milk—None.{R-31} Not labeled for use in calves to be processed for veal.{R-31} Canada: Meat—36 days, Milk—None.{R-32}

Note: Skin lesions, dermatoses, or caked materials, such as mud or manure, on the skin will reduce efficacy.{R-31; 32} Rainfall and varying weather conditions are not expected to affect efficacy.{R-31; 32}

For the most safe and effective treatment of grubs, cattle are treated as soon as possible after the end of the heel fly season. Whenever it is performed, treatment is timed to avoid killing larvae migrating through tissues, in particular, esophageal tissue or the vertebral canal.{R-31}

Note: Nematode, gastrointestinal, infection—[EL US,CAN]*Goats:* There are no studies specifically establishing the best dose for the oral administration of moxidectin topical solution to goats; therefore, experts warn against routine use. When administration is necessary because other parasite control methods have failed, pretreatment susceptibility testing and post-treatment assessment of efficacy are recommended.{R-157} An oral moxidectin dose of 0.4 mg per kg of body weight has been used.{R-104}

Extra-label withdrawal information: United States—There are no established withdrawal times for goats because moxidectin is not approved for use in this species. If moxidectin is administered to goats at an oral dose of 0.2 or 0.5 mg per kg of body weight as a single dose, evidence has been compiled by the Food Animal Residue Avoidance Databank (FARAD) that suggests a meat withdrawal time of 14 days for the lower dose and 23 days for the higher dose would be necessary to avoid potentially harmful residues.{R-139} There is insufficient information to recommend milk withdrawal times in lactating goats.{R-139} Canada—There are no established withdrawal times for goats because moxidectin is not approved for use in this species. Due to the lack of established maximum residue limits for use of ivermectin in goats in Canada and the sensitivity of residue detection methods, general recommendations for withdrawal cannot be made. Contact the Canadian gFARAD (www.cgfarad.usask.ca) for more information.[EL]{R-140}

Strength(s) usually available:

U.S.—{R-31}

Veterinary-labeled product(s):

5 mg per mL (OTC) [*Cydectin Pour-On*].

Canada—{R-32}

Veterinary-labeled product(s):

5 mg per mL (OTC) [*Cydectin Pour-On*].

Caution:

People handling this medication should be careful to avoid contact of moxidectin with eyes and skin.{R-32} Accidental skin exposure should be washed immediately with soap and water, eyes exposed flushed with water, and medical attention sought.

Keep out of the reach of children and pets.{R-32}

Packaging and storage: Store between 4 and 25 °C (39 and 77 °F), unless otherwise specified by the manufacturer.{R-32} Avoid prolonged exposure above 22 °C (77 °F){R-31} and avoid freezing. Protect from light.{R-32}

Additional information:

If moxidectin topical solution becomes frozen, thaw it completely and shake well before using.{R-31}

Moxidectin topical solution is provided in a multiple dose bottle with a chamber to meter the dose or containers designed for use with an appropriate applicator system.{R-31}

Environmental safety—Although moxidectin tightly binds to soil and becomes inactive, when free drug enters the water, fish and other aquatic life may be harmed. Moxidectin should not be directly applied to water and should be disposed of by a method that will avoid contaminating water, such as incineration or disposal in an approved landfill.{R-31}

USP requirements: Not in USP.{R-42}

SELAMECTIN

Oral Dosage Forms

Note: Text between [EL US] and [EL] describes uses not included in U.S. product labeling. Text between [EL CAN] and [EL] describes uses not included in Canadian product labeling.

The [EL US] or [EL CAN] designation may signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

SELAMECTIN TOPICAL SOLUTION

Usual dose:

Flea infestation;

Heartworm disease (prophylaxis); or

Mite, ear, infestation—*Cats* and *dogs*: Topical, 6 mg per kg of body weight, administered onto the skin at the base of the neck in front of the shoulders.{R-29; 30}

Mite dermatosis (specifically, sarcoptic mange); or

Tick infestation—*Dogs:* Topical, 6 mg per kg of body weight, administered onto the skin at the base of the neck in front of the shoulders.{R-29; 30}

Nematode, gastrointestinal, infection—

Cats: For treatment of hookworms or roundworms—Topical, 6 mg per kg of body weight, administered onto the skin at the base of the neck in front of the shoulders.{R-29; 30}

[EL US]*Dogs*[EL]: For treatment of roundworms—Topical, 6 mg per kg of body weight, administered onto the skin at the base of the neck in front of the shoulders.{R-29}

Note: [EL US,CAN]Mite, nasal, infestation[EL]—*Dogs:* Although the safety and efficacy have not been established, a topical dose of 6 mg per kg of body weight, administered every two weeks for a total of three doses, has been used.{R-173}

Mite dermatosis—

[EL US,CAN]For the treatment of cheyletiellosis[EL]:

Cats—Although the efficacy has not been established, a topical dose of 6 to 12 mg per kg of body weight every thirty days for three doses has been used.{R-120}

Dogs—Although the efficacy has not been established, a topical dose of 6 to 12 mg per kg of body weight every fourteen days for four doses has been used.{R-133}

[EL US,CAN]For the treatment of notoedric mange[EL]: *Cats*—Although the efficacy has not been established, a single topical dose of 6 mg per kg of body weight has been used.{R-132}

Note: Selamection should not be administered orally, as salivation and vomiting have been reported in cats.{R-57}

The labeled dose listed above is the recommended minimum dose.{R-29; 30} Medication is dispensed in application tubes with premeasured amounts of medication. Animals, depending on size, may receive up to 17 mg per kg of body weight.

Testing for heartworm disease before beginning preventative treatment is recommended.{R-29} Selamectin tablets are not an effective treatment to kill adult heartworms or clear microfilariae.{R-29}

Selamectin application is not recommended when the animal's hair is wet, but 2 hours after treatment, bathing will not affect efficacy.{R-29}

For flea control, selamectin is administered monthly, beginning one month before flea season begins.

For protection from heartworm infection, selamectin is also administered monthly, beginning within a month of first mosquito exposure. Selamectin may be administered year round.

For ear mites and for sarcopic mange in dogs, selamectin topical solution is administered as a single dose; however, a second dose a month later may be necessary in some animals.

To treat nematodes in cats, selamectin is administered as a single dose and repeated monthly if prevention is necessary. [EL][US] To aid in the treatment of roundworms in dogs, two doses of selamectin are administered, a month apart.[EL]

For tick control in dogs, selamectin must be administered monthly.{R-29; 30}

Strength(s) usually available:

U.S.—{R-29}

Veterinary-labeled product(s):

15 mg per tube [*Revolution*].
30 mg per tube [*Revolution*].
45 mg per tube [*Revolution*].
60 mg per tube [*Revolution*].
120 mg per tube [*Revolution*].
240 mg per tube [*Revolution*].

Canada—{R-30}

Veterinary-labeled product(s):

15 mg per tube [*Revolution*].
30 mg per tube [*Revolution*].
45 mg per tube [*Revolution*].
60 mg per tube [*Revolution*].
120 mg per tube [*Revolution*].
240 mg per tube [*Revolution*].

Caution:

Selamectin topical solution is flammable; prevent exposure to open flames, heat, sparks, or other sources of ignition.{R-29; 30}

People handling this medication should be aware that it may be irritating to eyes and skin, causing hives, itching, and, occasionally, skin redness. Selamectin topical solution contains isopropyl alcohol and butylated hydroxytoluene (BHT). Any skin in contact with medication should be washed immediately with soap and water. If any medication contacts eyes, they should be thoroughly flushed with water.{R-29; 30}

Keep out of the reach of children and pets.{R-29; 30}

Packaging and storage: Store below 30 °C (86 °F),{R-29; 30} unless otherwise specified by manufacturer.

USP requirements: Not in USP.{R-42}

Developed: 12/23/05

Table 1. Pharmacology/Pharmacokinetics—Intravenous administration*

Species	Dose (mg/kg)	Vol_D (L/kg)	Elimination half-life (days)	Clearance (mL/min/kg)	Mean residence time (days)
DORAMECTIN					
Calves{R-99}	0.2†	1.7 ± 0.2	3.7 ± 0.5	0.22 ± 0.04	
Sheep{R-91}	0.15	Vol_{ss} = 5.07 ± 1.49	2.70 ± 0.7		
IVERMECTIN					
Cattle{R-98}	0.2	Vol_{ss} = 2.2	2.7	0.55	2.8
{R-70}	0.3	2.4	1.8		
Dogs{R-70}	0.3	1.9	2.8		
Pigs{R-79}	0.3	5.28 ± 0.22	1.33 ± 0.08	2.78 ± 0.1	0.80 ± 0.06
Sheep{R-70}	0.2	4.6	2.7		
{R-97}	0.2	Vol_{ss} = 5.32 ± 1.42		0.38 ± 0.10	
MOXIDECTIN					
Pigs{R-79}	0.3	17.9 ± 2.0	12 ± 0.63	0.78 ± 0.06	13.2 ± 0.88
SELAMECTIN					
Cats{R-90}	0.05 to 0.2	Vol_{ss} = 2.19 ± 0.05	2.88‡	0.47 ± 0.04	4.01 ± 0.68
Dogs{R-90}	0.05 to 0.2	Vol_{ss} = 1.24 ± 0.26	0.58‡	1.18 ± 0.31	0.80 ± 0.33

*Abbreviations: Vol_D = Volume of distribution, Vol_{ss} = Volume of distribution at steady state
†Administered as an aqueous micelle formulation
‡Harmonic mean

Table 2. Pharmacology/Pharmacokinetics—Other routes of administration*

Species	Dose (mg/kg); Route	Absorption half-life (days)	C_{max} (nanograms/mL)	T_{max} (days)	Terminal half-life (days)	Mean residence time (days)
DORAMECTIN						
Calves, 7-month-old{R-68}	0.5; TOP		12.2 ± 4.8	4.3 ± 1.6	9.8 ± 2.6	12.8 ± 1.9
Calves, 7-month-old{R-142}	0.2; SC		32.0 ± 9.34	3.86 ± 1.77		9.19 ± 1.29
Calves, 10-month-old{R-67}	0.2; SC	2.35 ± 0.76	37.5 ± 3.89	6.00 ± 1.35	6.25 ± 0.16	9.09 ± 0.23
Cattle{R-89}	0.2; IM		33.1 ± 9.0	4.7	6.5†	
	0.2; SC		27.8 ± 7.9	5.9	7.5†	
{R-52}	0.2; SC	5.39 ± 0.36	32.6 ± 1.45	5.31 ± 0.35	3.00 ± 0.33	
Goats{R-86}	0.2; SC	0.69 ± 0.22	16.5 ± 1.2	1.71 ± 0.23	2.6 ± 0.2	4.9 ± 0.1
Horses{R-72}	0.2; PO		21.3	0.33		3.0
{R-73}	0.2; PO	0.06†	51.62 ± 22.2	0.20 ± 0.07		7.72 ± 0.93

Pigs[R-69]	0.3; SC		39.6 ± 3.84	0.94 ± 0.16		5.78 ± 0.18
Sheep[R-91]	0.15; PO		6.81 ± 1.38	1.12 ± 0.20	5.37 ± 0.17	
[R-85]	0.2; SC	2.71 ± 1.95	22.7 ± 1.75	5.4 ± 0.89	11.4 ± 2.02	
[R-81]	0.2; SC	0.67 ± 0.31	34.91 ± 10.50	1.79 ± 0.65	2.77 ± 0.80	
Sheep, lactating[R-94]	0.2; SC	1.17 ± 0.27	25.0 ± 4.03	2.20 ± 0.37	4.06 ± 0.75	7.00 ± 0.87
EPRINOMECTIN						
Cattle[R-75]	0.5; TOP		43.76 ± 18.23	2.05 ± 0.32		4.16 ± 0.61
Goats[R-87]	0.5; TOP	0.66 ± 0.36	5.60 ± 1.01	2.55 ± 0.85	7.47 ± 0.54	9.42 ± 0.43
Goats, lactating[R-92]	0.5; TOP	0.18 ± 0.04	2.2 ± 0.52	0.75 ± 0.13	2.44 ± 1.11	2.67 ± 0.60
	1; TOP	0.26 ± 0.21	2.98 ± 1.37	0.99 ± 0.48	3.04 ± 0.76	3.69 ± 0.90
IVERMECTIN						
Calves, 100 to 120 kg of body weight[R-69]	0.2; SC		46.4 ± 3.88	2.12 ± 0.14		5.39 ± 0.25
Calves, 7-month-old[R-68]	0.5; TOP		12.2 ± 6.0	3.4 ± 0.8	5.3 ± 1.8	8.4 ± 1.5
Calves, 10-month-old[R-67]	0.2; SC	1.63 ± 0.93	42.8 ± 3.83	4.00 ± 0.94	17.2 ± 4.26	7.35 ± 0.21
Cattle[R-52]	0.2; SC	4.32 ± 0.25	31.7 ± 2.45	3.98 ± 0.28	2.02 ± 0.23	
[R-51]	0.2; SC		54.58 ± 16.95	1.45 ± 1.02		
Goats[R-95]	0.2; SC	1.21 ± 0.58	6.12 ± 1.15	2.85 ± 0.89	4.03 ± 0.94	7.85 ± 1.42
Horses[R-72]	0.2; PO		21.4	0.32		2.3
[R-74]	0.2; PO	0.07 ± 0.09	44.0 ± 23,1	0.38 ± 0.24	4.25 ± 0.29	4.78 ± 0.65
[R-73]	0.2; PO	0.04†	51.32 ± 16.1	0.15 ± 0.04	2.89	4.20 ± 0.43
[R-71]	0.2; PO		82.3 ± 12.4	0.13 ± 0.03		
Sheep[R-80]	0.2; PO	0.29 ± 0.05	6.88 ± 0.59	0.86 ± 0.12	2.14 ± 0.23	2.85 ± 0.32
[R-82]	0.2; PO	0.43 ± 0.21	11.28 ± 7.43	1.33 ± 0.52	3.63 ± 0.76	3.45 ± 1.36
[R-71]	0.2; PO		22.0 ± 1.8	0.68 ± 0.15	2.55 ± 0.10	
[R-85]	0.2; SC	1.21 ± 0.16	16.3 ± 2.15	2.6 ± 0.55	7.02 ± 2.05	5.88 ± 0.41
[R-84]	0.2; SC	0.85 ± 0.62	24.09 ± 6.57	2.67 ± 0.52	5.57 ± 1.25	8.61 ± 0.68
[R-81]	0.2; SC	0.50 ± 0.05	25.76 ± 7.61	1.24 ± 0.14	1.67 ± 0.40	
[R-71]	0.2; SC		30.8 ± 3.4	2.5 ± 0.71	1.47 ± 0.43	
Sheep, lactating[R-83]	0.2; SC	0.73 ± 0.55	11.88 ± 6.96	1.70 ± 0.65	2.85 ± 1.97	5.16 ± 2.79
MOXIDECTIN						
Calves, 10-month-old[R-67]	0.2; SC	0.06 ± 0.02	39.4 ± 3.4	0.32 ± 0.00	14.5 ± 1.20	14.6 ± 0.67
Goats[R-86]	0.2; PO	0.13 ± 0.02	15.5 ± 1.3	0.38 ± 0.02	12.0 ± 0.6	10.3 ± 0.8
	0.2; SC	0.12 ± 0.06	24.3 ± 2.0	0.36 ± 0.06	9.9 ± 1.1	12.4 ± 1.3
Horses[R-72]	0.2; PO		30.1	0.32		17.5
[R-74]	0.4; PO	0.05 ± 0.09	70.4 ± 10.7	0.37 ± 0.19	23.11 ± 11.90	18.42 ± 4.38
Sheep[R-80]	0.2; PO	0.20 ± 0.04	17.2 ± 2.61	0.79 ± 0.19	15.4 ± 1.98	17.7 ± 2.56
[R-81]	0.2; SC	0.03 ± 0.03	65.12 ± 18.48	0.15 ± 0.10	7.96 ± 2.22	
[R-93]	0.2; PO		28.07 ± 10.06	0.22 ± 0.04	21.04 ± 2.01	12.55 ± 1.45
	0.2; SC		8.29 ± 3.14	0.88 ± 0.24	29.94 ± 9.00	16.80 ± 1.80
SELAMECTIN						
Cats[R-90]	24; PO		11929 ± 5922	0.29 ± 0.25	4.07†	5.7 ± 2.3
	24; TOP		5513 ± 2173	0.63 ± 0.5	8.25†	9.14 ± 3.59
Dogs[R-90]	24; PO		7630 ± 3140	0.33 ± 0.21	1.9†	1.30 ± 0.49
	24; TOP		86.5 ± 34.0	3 ± 2	11.1†	11.26 ± 2.51

*Abbreviations: C_{max} = Peak serum concentration, T_{max} = Time to peak serum concentration, IM = Intramuscular, SC = Subcutaneous, TOP = Topical

†Harmonic mean

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