Storage/Stability/Compatibility

Oral morphine products should be stored at in tight, light-resistant containers at room temperature unless otherwise labeled. Morphine injection should be stored at room temperature, protected from light; do not freeze.

Morphine gradually darkens in color when exposed to light; protect from prolonged exposure to bright light. Morphine does not appear to adsorb to plastic or PVC syringes, tubing or bags.

Morphine sulfate has been shown to be physically **compatible** at a concentration of 16.2 mg/L with the following intravenous fluids: Dextrose 2.5%, 5%, 10% in water; Ringer's injection and Lactated Ringer's injection; Sodium Chloride 0.45% and 0.9% for injection. The following drugs have been shown to be physically **incompatible** when mixed with morphine sulfate: aminophylline, chlorothiazide sodium, heparin sodium, meperidine, pentobarbital sodium, phenobarbital sodium, phenytoin sodium, sodium bicarbonate, and thiopental sodium. Morphine sulfate has been demonstrated to be generally physically **compatible** when mixed with the following agents: Atropine sulfate, benzquinamide HCl, butorphanol tartrate, chlorpromazine HCl, diphenhydramine HCl, dobutamine HCl, droperidol, fentanyl citrate, glycopyrrolate, hydroxyzine HCl, metoclopramide, pentazocine lactate, promazine HCl, scopolamine HBr, and succinylcholine chloride.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

The ARCI (Racing Commissioners International) has designated this drug as a class 1 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Morphine Sulfate for Injection: 0.5 mg/mL, 1 mg/mL, 2 mg/mL, 4 mg/mL, 5 mg/mL, 8 mg/mL, 10 mg/mL, 15 mg/mL, 25 mg/mL, 50 mg/mL in amps, vials, syringes, and pre-filled IV bags in sizes that range from 1 mL to 250 mL depending on manufacturer and concentration. (Rx; C-II)

Morphine Sulfate Liposomal Extended-release Injection: 15 mg/mL in 1, 1.5, & 2 mL vials; *DepoDur*® (Endo); (Rx, C-II)

Morphine Sulfate for Injection (preservative-free): 0.5 mg/mL: 2 mL amps, & 10 mL amps and vials; 1 mg/mL: 10 mL amps and vials; 10 mg/mL (200 mg) in 20 mL amps; 25 mg/mL (500 mg) in 20 mL amps; *Infumorph*® (Baxter); *Astramorph PF*® (AstraZeneca); (Rx, C-II)

Morphine Sulfate Soluble Tablets for Injection: 10 mg, 15 mg & 30 mg; generic; (Ranbaxy); (Rx, C-II)

Morphine Sulfate Tablets: 15 mg & 30 mg; generic; (Rx, C-II)

Morphine Sulfate Extended/Controlled Release Tablets: 15 mg, 30 mg, 60 mg, 100 mg & 200 mg; *MS Contin*® (Purdue Frederick); *Oramorph SR*® (aaiPharma); generic; (Rx, C-II)

Morphine Sulfate Extended/Sustained Release Capsules: 20 mg, 30 mg, 50 mg, 60 mg, 80 mg, 90 mg, 100 mg & 120 mg; *Avinza*® (Ligand); *Kadian*® (Alpharma); (Rx, C-II)

Morphine Sulfate Oral Solution: 2 mg/mL in 100 mL, 500mL and UD 5mL and 10 mL; 4 mg/mL in 100mL, 120 mL and 500 mL; 20 mg/mL (concentrate) in 15 mL, 30 mL, 120 mL and 240 mL; *MSIR*® (Purdue Frederick); Morphine Sulfate (Roxane); *Roxanol*®, *-T,* & *-100* (aaiPharma); generic; (Rx; C-II)

Morphine Sulfate Rectal Suppositories: 5 mg, 10 mg, 20 mg, and 30 mg; *RMS*® (Upsher-Smith); generic; (various); (Rx, C-II)

Note: All morphine products are Rx and a Class-II controlled substance. Very accurate record keeping is required as to use and disposition of stock.

MOXIDECTIN

(mox-i-***dek***-tin) Cydectin®

AVERMECTIN ANTIPARASITIC

Prescriber Highlights

- Avermectin antiparasitic with products approved for cattle, dogs, cats, sheep, & horses
- Contraindications: DOGS: Hypersensitive to it. CATTLE: Female dairy cattle of breeding age; HORSES: Intended for food purposes or in foals younger than 4 months of age
- Adverse Effects: DOGS (potentially): Lethargy, vomiting, ataxia, anorexia, diarrhea, nervousness, weakness, increased thirst, & itching. CATTLE: Adverse effects minimal. HORSES: At labeled doses, appear minimal.
- Apparently safe to use in mdr1 gene mutation dog breeds a recommended doses

Uses/Indications

In dogs and cats, moxidectin with lufenuron is indicated as a once a month topical preventative for the prevention of heartworm, flea adulticide, ear mites (cats) and treatment for hookworms, roundworms, and whipworms (dogs). It has also been successfully used as a treatment for generalized demodicosis.

In cattle, moxidectin is indicated for the treatment and control of the following internal [adult and fourth stage larvae (L4)] and external parasites: Gastrointestinal roundworms: *Ostertagia ostertagi* (adult and L4, including inhibited larvae), *Haemonchus placei* (adult), *Trichostrongylus axei* (adult and L4), *Trichostrongylus colubriformis* (adult), *Cooperia oncophora* (adult), *Cooperia punctata* (adult), *Bunostomum phlebotomum* (adult), *Oesophagostomum radiatum* (adult), *Nematodirus helvetianus* (adult); Lungworm: *Dictyocaulus viviparus* (adult and L4); Cattle Grubs: *Hypoderma bovis*, *Hypoderma lineatum* Mites: *Chorioptes bovis*, *Psoroptes ovis* (*Psoroptes communis var. bovis*); Lice: *Linognathus vituli*, *Haematopinus eurysternus*, *Solenopotes capillatus*, *Damalinia bovis*; Horn flies: *Haematobia irritans*. To control infections and to protect from reinfection from *Ostertagia ostertagi* for 28 days after treatment and from *Dictyocaulus viviparus* for 42 days after treatment.

In sheep, oral moxidectin is indicated for the control of *Haemonchus contortus* (adult and L4), *Teladosrsagia circumcincta & trifurcata* (adult and L4), *Trichostrongylus colubriformis, axei,* & *vitrinius* (adult & L4), *Cooperia curticei* & *oncophora* (adult and L4), *Oesophagostomum columbianum* & *venolosum* (adult & L4), and *Nematodirus battus, filicollis,* & *spathiger* (adult & L4).

In horses and ponies, moxidectin is indicated for the treatment and control of the following stages of gastrointestinal parasites: Large strongyles: *Strongylus vulgaris* (adults and L4L5 arterial stages); *Strongylus edentatus* (adults and tissue stages); *Triodontophorus brevicauda* (adults); *Triodontophorus serratus* (adults); Small strongyles (adults and larvae): *Cyathostomum* spp. *(adults); Cylicocyclus* spp. (adults); *Cylicostephanus* spp. (adults); *Gyalocephalus capitatus* (adults); undifferentiated lumenal larvae; Encysted cyathostomes: late L3 and L4 mucosal cyathostome larvae; Ascarids: *Parascaris equorum* (adults and L4 larval stages); Pin worms: *Oxyuris equi* (adults and L4 larval stages); Hair worms: Trich*ostrongylus axei* (adults); Large-mouth stomach worms: *Habronema muscae* (adults); Horse stomach bots: *Gasterophilus intestinalis* (2nd and 3rd instars). When combined with praziquantel, additional coverage against *Anoplocephala* spp. occurs.

Pharmacology/Actions

The primary mode of action of avermectins like moxidectin is to affect chloride ion channel activity in the nervous system of nematodes and arthropods. The drug binds to receptors that increase membrane permeability to chloride ions. This inhibits the electrical activity of nerve cells in nematodes and muscle cells in arthropods and causes paralysis and death of the parasites. Avermectins also enhance the release of gamma amino butyric acid (GABA) at presynaptic neurons. GABA acts as an inhibitory neurotransmitter and blocks the post-synaptic stimulation of the adjacent neuron in nematodes or the muscle fiber in arthropods. Avermectins are generally not toxic to mammals, since they do not have glutamate-gated chloride channels and these compounds do not readily cross the blood-brain barrier where mammalian GABA receptors occur.

Pharmacokinetics

Minimal information was located. In cattle, the drug apparently has a long duration of plasma residence (14–15 days). After SC injection, approximately 5% of the dose given to the cow can be passed to the suckling calf.

Contraindications/Precautions/Warnings

Dogs: Contraindicated in dogs hypersensitive to it. The manufacturer warns to only use the oral product in dogs tested negative for heartworm infection. Adult heartworms and microfilaria should be removed prior to therapy. If more than two months pass between dosages of this or other once a month heartworm preventative medications, the dog should be tested for heartworm infection before receiving the next dose.

Cattle: Not for use in female dairy cattle of breeding age.

Horses: Not for horses intended for food purposes and is not labeled for use in foals younger than 4 months of age.

Adverse Effects

Dogs: While adverse reactions to this medication apparently occur infrequently, after the injectable product (*ProHeart®6*) was administered to heartworm positive dogs, a low number experienced coughing or cardiopulmonary signs and deaths have occurred (very rarely; 2.5 per 100,000 doses). Additionally, the following adverse reactions may be seen: lethargy, vomiting, ataxia, anorexia, diarrhea, nervousness, weakness, increased thirst, and itching. Studies done in Collies (up to 20X) demonstrated no notable adverse effects. One Collie receiving doses of 30X demonstrated mild signs of depression, ataxia, and salivation.

Cattle: Thus far at labeled doses, adverse effects appear to nonexistent or minimal.

Horses: Thus far at labeled doses, adverse effects appear to be nonexistent or minimal. A case report where three foals developed CNS depression and coma after receiving high dosages has been reported. Two of these three animals were less than 2 weeks of age and all received much higher than labeled dosages.

Reproductive/Nursing Safety

Dogs, Cats: Reproductive studies have demonstrated no evidence of adverse effects on fertility, reproductive performance, or offspring.

Cattle & Horses: Reproductive studies performed thus far have demonstrated no evidence of adverse effects on fertility, reproductive performance, or offspring in cattle or horses treated.

Overdosage/Acute Toxicity

Dogs: The drug apparently has a very wide margin of safety in dogs when administered orally. Dosages of up to 300X (1120 mcg/kg) demonstrated little or no effects. Dogs administered inadvertent overdoses during a clinical study treating demodicosis showed signs of dysorexia, hypersalivation, mydriasis, and fasiculations and ataxia of the pelvic limbs.

There were 172 exposures to moxidectin reported to the ASPCA Animal Poison Control Center (APCC; www.apcc.aspca.org) during 2005–2006. In these cases, 171 were dogs with 42 showing clinical signs and the remaining case was 1 cat that showed clinical signs. Common findings in dogs recorded in decreasing frequency included tremors, ataxia, seizures, vomiting and hyperesthesia. Common findings in cats recorded included recumbency.

Cattle: In studies done on cattle, application of the pour-on solution at 5X the recommended dose for five consecutive days, 10X for two consecutive days and 25X for one day did not produce any significant adverse clinical or pathological effects.

Horses: In one study, three of eight foals given the 3X dose became depressed or ataxic after one treatment. The author has received an anecdotal report of a miniature horse developing seizures after receiving a full tube of *Quest®*.

Drug Interactions

While no specific drug interactions for moxidectin have been reported, the following drug interactions have either been reported or are theoretical in humans or animals receiving ivermectin (a related compound) and may be of significance in veterinary patients:

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

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

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

Doses

- **DOGS:**
  a) For labeled indications (prevention of heartworm disease, adult fleas, adult and immature hookworms, adult roundworms, and adult whipworms): Recommended minimum dose is 10 mg/kg imidacloprid/2.5 mg/kg moxidectin once a month by topical administration (**Note:** See package insert for specific instructions on application and safety). For dogs 3–9 lb = 0.4 mL; 9.1–20 lb = 1 mL; 20.1–55 lb = 2.5 mL, 55.1–88 lb = 4 mL; dogs over 88 lb should be treated with appropriate combination for their weight. (Label directions; *Advantage Multi® for Dogs*—Bayer)
  b) For scabiocidal therapy: Where *Cydectin®* is available for injection: 0.25 mg/kg SC every 7 days for three treatments. If using oral therapy 0.4 mg/kg PO every 3–4 days for 3–6 weeks. (Foil 2003c)
  c) For generalized demodicosis: 0.2–0.4 mg/kg PO once a day. Clinical cure averages 75 days; parasitic cure averages 112 days. (Merchant 2000)

■ **CATS:**

a) For labeled indications (prevention of heartworm disease, adult fleas, ear mites, adult and immature hookworms, and adult roundworms: Recommended minimum dose is 10 mg/kg imidacloprid/1 mg/kg moxidectin once a month by topical administration (**Note:** See package insert for specific instructions on application and safety). For cats 2–5 lb = 0.23 mL; 5.1–9 lb = 0.4 mL; 9.1–18 lb = 0.8 mL; cats over 18 lb should be treated with appropriate combination for their weight. (Label directions; *Advantage Multi® for Cats*—Bayer)

■ **CATTLE:**

a) For labeled indications: 1 mL (5 mg)/10 kg (22 lb) bodyweight applied directly to the hair and skin along the top of the back from the withers to the base of the tail. Application should be made to healthy skin avoiding mange scabs, skin lesions or extraneous foreign matter. (Label Directions; *Cydectin® Pour-On*—Fort Dodge)

b) 0.2 mg/kg [1 mL for each 110 lb (50 kg) of bodyweight] subcutaneously under the loose skin in front of or behind the shoulder. Needles 1/2–3/4 inch in length and 16–18 gauge are recommended. (Label Directions; *Cydectin® Injection*—Fort Dodge)

■ **SHEEP:**

a) For labeled indications: 0.2 mg/kg [1 mL per 11 lb (1 mL per 5 kg) bodyweight] PO (drench); *Cydectin® Oral Drench for Sheep*—Fort Dodge)

■ **HORSES:**

a) For labeled indications using the combination oral gel with praziquantel: Dial in the weight of the animal on the syringe. Administer gel by inserting the syringe applicator into the animal's mouth through the interdental space and depositing the gel in the back of the mouth near the base of the tongue. Once the syringe is removed, the animal's head should be raised to insure proper swallowing of the gel. Horses weighing more than 1250 lb require additional gel from a second syringe. (Label Directions; *Quest® Plus*—Fort Dodge)

b) For mucosal stages of small strongyles: 400 mcg/kg PO (Lyons and Drudge 2000)

Chemistry/Synonyms

An avermectin-class antiparasitic agent, moxidectin is a semi-synthetic methoxime derivative of nemadectin.

Moxidectin may also be known as CL-301423, *Advantage Multi®*, *ComboCare®*, *Cydectin®*, and *Quest®*.

Storage/Stability

The commercially available injection and the oral drench for sheep should be stored at, or below 77°F (25°C) and protected from light.

The topical solution for cattle should be stored at or below room temperature. Do not allow prolonged exposure to temperatures above 77°F. If product becomes frozen, thaw completely and shake well before using.

The oral gel for horses should be stored at or near room temperature (59°F–86°F); avoid freezing. If product becomes frozen, thaw completely before using. Partially used syringes should have the cap tightly secured.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Moxidectin 0.5% (5 mg/mL) Pour-On for Cattle in 500 mL, 1 L, 2.5 L, 5 L, and 10 L containers; *Cydectin®* (Fort Dodge); (OTC). Approved for use in cattle; not to be used in veal calves. No meat or milk withdrawal times required, but FDA has established tolerances of 50 ppb and 200 ppb for parent moxidectin in muscle and liver, respectively, for cattle.

Moxidectin 10 mg/mL Injectable Solution in 200 mL and 500 mL; *Cydectin® Injectable Solution* (Fort Dodge); (OTC). Approved for cattle. Not to be used in female dairy cattle of breeding age, veal calves, and calves less than 8 weeks of age. Meat withdrawal = 21 days.

Moxidectin 1 mg/mL Injectable Solution in 1 L and 4 L; *Cydectin® Oral Drench for Sheep* (Fort Dodge); (OTC). Approved for sheep. Not to be used in female sheep providing milk for human consumption. Meat withdrawal = 7 days.

Moxidectin Oral Gel containing 20 mg/mL in 11.3 g syringes (sufficient to treat one 1150 lb horse); *Quest®* (Fort Dodge); (OTC). Approved for use in horse or ponies not intended for food purposes.

Oral Gel containing 20 mg/mL moxidectin and 125 mg/mL of praziquantel in 11.6 g syringes (sufficient to treat one 1150 lb horse); *Quest Plus®* (Fort Dodge), *ComboCare® Equine Oral Gel* (Farnam); (OTC). Approved for use in horse or ponies not intended for food purposes.

Moxidectin 1% (10 mg/mL) and Imidacloprid 10% (100 mg/mL) Topical Solution in 3—0.23mL tubes, 6—0.4mL tubes & 6—0.8mL tubes; *Advantage Multi® for Cats* (Bayer); (Rx). Approved for use on cats 9 weeks of age or greater, and more than 2 lb body weight.

Moxidectin 2.5% (25 mg/mL) and Imidacloprid 10% (100 mg/mL) Topical Solution in 6—0.4mL tubes, 6—1mL tubes, 6—2.5 mL tubes, & 6—4mL tubes; *Advantage Multi® for Dogs* (Bayer); (Rx). Approved for use on dogs 7 weeks of age or greater, and more than 3 lb body weight.

HUMAN-LABELED PRODUCTS: None

MYCOBACTERIAL CELL WALL FRACTION IMMUNOMODULATOR

(my-koe-bak-*tear*-ee-al) Regressin®-V, Equimune® I.V.

IMMUNOSTIMULANT

Prescriber Highlights

- **Biologic used as a locally infiltrated injection for immunotherapy treatment of mixed mammary tumor & mammary adenocarcinomas in dogs**
- **In horses, used for immunotherapy treatment of sarcoids (local infiltration), ERCD (IV) or as an aid in the treatment of equine metritis caused by *Streptococcus zooepidemicus* (IV, IU)**
- **Adverse effects include: Transient fever, depression, decreased appetite, localized pain. Hypersensitivity & systemic inflammatory reactions possible.**
- **Efficacy for systemic use is not well established**