### Dosage Forms/Regulatory Status

**VETERINARY-LABELED PRODUCTS:** None in the USA.

**HUMAN-LABELED PRODUCTS:** None in the USA

Meglumine antimoniate may be available in several countries, including Brazil, France, Italy, Spain and Venezuela; trade names include: *Glucantime*® and *Glucantim*®. Commercially it is available as a solution containing 1.5 grams of meglumine antimoniate (425 mg pentavalent antimony) per 5 mL.

The FDA may allow legal importation of this medication for compassionate use in animals; for more information, see the *Instructions for Legally Importing Drugs for Compassionate Use in the USA* found in the appendix.

# MELARSOMINE

(mee-*lar*-soe-meen) Immiticide®

ARSENICAL ANTIPARASITIC

## Prescriber Highlights

- Organic arsenical for heartworm disease
- Contraindications: Class IV (very severe) heartworm disease; weigh risk vs. potential benefits in pregnant, lactating, or breeding dogs
- Reportedly very toxic to cats; not currently recommended
- Adverse Effects: Many possible, most common are: Injection site reactions coughing/gagging, depression/lethargy, anorexia/inappetence, excessive salivation, fever, lung congestion, vomiting, pulmonary thromboembolism
- Special IM injection technique; do not give IV or SC
- Avoid human exposure
- Calculate dosages very carefully

### Uses/Indications

Melarsomine is indicated for the treatment of stabilized class I, II, and III heartworm disease caused by immature (4 month old, stage $L_5$) to mature adult infections of *D. immitis* in dogs. When compared with thiacetarsamide, melarsomine appears to be more efficacious, less irritating to tissues, and does not cause hepatic necrosis.

Melarsomine may also be useful for treating ferrets; it has been suggested to contact the manufacturer before using the drug in this species.

### Pharmacology/Actions

While melarsomine is an arsenical compound, its exact mechanism of action is not known. Both laboratory and field studies have demonstrated that melarsomine is 90–99% effective in killing adult and $L_5$ larvae of *D. immitis* in dogs at recommended dosages.

### Pharmacokinetics

Melarsomine is reportedly rapidly absorbed after IM injection in dogs; time to peak plasma concentration is about 11 minutes. The apparent volume of distribution is about 0.7 L/kg; terminal half-life is approximately 3 hours.

### Contraindications/Precautions/Warnings

Melarsomine is contraindicated in dogs with class IV (very severe) heartworm disease. Class IV is having caval syndrome (heartworms present in venae cavae and right atrium). Melarsomine is reportedly very toxic to cats and its use cannot be recommended for this species at this time.

Older dogs (>8 years) may be more susceptible to adverse effects than younger dogs.

Do NOT give IV or SC; significant toxicity or tissue damage may occur. Administer only deep IM as directed (lumbar epaxial muscles (L3-L5). Do not administer at any other site.

While all dogs with heartworm disease are at risk for post-treatment pulmonary thromboembolism, those with severe pulmonary artery disease are at increased risk for post treatment morbidity and mortality. Dogs should be exercise restricted after treatment.

Wash hands after use or wear gloves. Avoid drug contact with animal's eyes; if exposed wash with copious amounts of water. Avoid human exposure. If human exposure occurs, contact a physician.

### Adverse Effects

Approximately ⅓ of dogs show signs of injection site reactions (pain, swelling, tenderness, reluctance to move) after receiving melarsomine. Most of these signs resolve within weeks, but, rarely, severe injection reactions can occur. Firm nodules at the injection site can persist indefinitely. SC or IV injections must be avoided. The most severe local reactions are usually seen if the drug leaks back from the injection site into subcutaneous tissues. Applying firm pressure to the injection site after administration may reduce the risk for this problem.

Other reactions reported in 5% or more dogs treated include: coughing/gagging (22% incidence; average day of onset after treatment = 10); depression/lethargy (15% incidence; average day of onset after treatment = 5); anorexia/inappetence (13% incidence; average day of onset after treatment = 5); fever (7%); lung congestion (6%); vomiting (5%). There is significant interpatient variance in both the date of onset and duration for the above effects. Dogs may also exhibit excessive salivation after dosing.

There are a plethora of other adverse effects in dogs with reported incidences less than 3%, including paresis and paralysis. Refer to the package insert for specifics.

Animals not exhibiting adverse effects after the first dose or course of therapy may demonstrate them after the second dose or course of therapy.

### Reproductive/Nursing Safety

Safety has not been established for use in pregnant, lactating, or breeding dogs. Risks versus potential benefits of therapy should be weighed before use.

### Overdosage/Acute Toxicity

There is low margin of safety with melarsomine dosages. A 3X dose (7.5 mg/kg) in healthy dogs have demonstrated respiratory inflammation and distress, excessive salivation, restlessness, panting, vomiting, edema, tremors, lethargy, ataxia, cyanosis, stupor, and death. Signs of diarrhea, excessive salivation, restlessness, panting, vomiting, and fever have been noted in infected dogs that have received inadvertent overdoses (2X).

Treatment with dimercaprol (BAL in Oil) may be considered to treat melarsomine overdoses. Clinical efficacy of melarsomine may be reduced, however.

### Drug Interactions

The manufacturer reports that during clinical field trials, melarsomine was given to dogs receiving antiinflammatory agents, antibiotics, insecticides, heartworm prophylactic medications, and various other drugs commonly used to stabilize and support dogs with heartworm disease and that no adverse drug interactions were noted.

- **ASPIRIN:** Has been shown not to reduce adverse effects and may complicate therapy; use is not recommended
- **CNS DEPRESSANT DRUGS:** Drugs that have similar adverse effects (*e.g.*, depression caused by CNS depressants, etc.) may cause additive adverse effects or increase their incidence when used with melarsomine

### Doses

**CAUTION:** Because of the low margin of safety; calculate dosages very carefully. Do not confuse mg/lb with mg/kg!

- **DOGS:**

For treatment of dirofilariasis it is suggested to review the guidelines published by the American Heartworm Society at www.heartworm society.org for more information.

*Immiticide*® (Merial) product support phone number: 888-637-4251

For treatment of heartworm disease:

a) After diagnosis, determine the class (stage) of the disease. **Note:** The manufacturer provides worksheets that assist in the classification and treatment regime determination. It is highly recommended to use these treatment records to avoid confusion and document therapy.

Class I, & II: 2.5 mg/kg deep IM as directed (lumbar epaxial muscles (L3-L5) twice 24 hours apart and rest. Use alternating sides with each administration. In 4 months, the regimen may be repeated.

Class III: 2.5 mg/kg deep IM as directed (lumbar epaxial muscles (L3-L5). Strict rest and give all necessary systemic treatment. One month later, give 2.5 mg/kg deep IM as directed (lumbar epaxial muscles (L3-L5) twice 24 hours apart.

**Note:** Recommended needle size for dogs 10 kg or less = 23 gauge 1 inch; 10 kg or more body weight = 22 gauge 1.5 inch. (Package Insert; *Immiticide*®—Merial)

b) The three-injection alternative protocol [2.5 mg/kg deep IM as directed (lumbar epaxial muscles; L3-L5). Strict rest and give all necessary systemic treatment. One month later, give 2.5 mg/kg deep IM as directed (lumbar epaxial muscles; L3-L5) twice 24 hours apart] is the treatment of choice of the American Heartworm Society and several university teaching hospitals, regardless of stage of disease, due to the increased safety and efficacy benefits and subsequently fewer dogs that require further treatment with melarsomine. (American Heartworm Society; www.heartwormsociety.org; accessed 2007)

### Monitoring/Client Information

- Clinical efficacy
- Adverse effects; dogs should be observed for 24 hours after the last injection
- Because of the seriousness of the disease and the potential for morbidity and mortality associated with the treatment, clients should give informed consent before electing to treat.

### Chemistry/Synonyms

An organic arsenical compound, melarsomine dihydrochloride has a molecular weight of 501 and is freely soluble in water.

Melarsomine may also be known as *Immiticide*®. Its CAS registry is 128470-15-5.

### Storage/Stability/Preparation

The unreconstituted powder should be stored upright at room temperature. Once reconstituted, the solution should be kept in the original container and kept refrigerated for up to 24 hours. Do not freeze. Do not mix with any other drug.

Reconstitute with 2 mL of the diluent provided (sterile water for injection) with a resultant concentration of 25 mg/mL. Once reconstituted, the solution should be kept in the original container and kept refrigerated for up to 24 hours. Do not freeze.

### Dosage Forms/Regulatory Status

**VETERINARY-LABELED PRODUCTS:**

Melarsomine Dihydrochloride Powder for Injection: 50 mg/vial; *Immiticide*® (Merial); (Rx). Approved for use in dogs.

**HUMAN-LABELED PRODUCTS:** None

## MELATONIN

(mel-a-***tone***-in) Regulin®

HORMONE

### Prescriber Highlights

- Oral & implantable pineal gland hormone
- Potential uses include: Alopecia in dogs, sleep & behavior disorders in cats & dogs, adjust seasonally controlled fertility in sheep, goats, & horses, & adjunctive treatment for adrenal disease in ferrets
- Adverse effects appear to be minimal, but little experience
- Potential contraindications include: Pregnancy, sexually immature animals, & liver dysfunction

### Uses/Indications

Melatonin may be useful to treat Alopecia-X in Nordic breeds, canine pattern baldness, or canine recurrent flank alopecia in dogs. It has been used anecdotally for the treatment of sleep cycle disorders in cats and geriatric dogs and to treat phobias and separation anxiety in dogs. Melatonin implants are used in the mink and fox pelt industries to promote the development of luxurious hair coats. Implants are also used to improve early breeding and ovulation rates in sheep and goats. Preliminary research is being done for this purpose in horses also.

In pigs, one study (Bubenik, Ayles et al. 1998) demonstrated that 5 mg/kg in feed reduced the incidence of gastric ulcers in young pigs.

### Pharmacology/Actions

Melatonin is involved with the neuroendocrine control of photoperiod dependent molting, hair growth and pelage color. Melatonin stimulates winter coat growth and spring shedding occurs when melatonin decreases. The mechanism of how melatonin induces these effects is not well understood. It may have direct effects on the hair follicle or alter the secretion of prolactin and/or melanocyte stimulating hormone.