ProHeart® 6 (moxidectin) for extended-release injectable suspension

What is ProHeart® 6?
ProHeart® 6 is a medication that prevents heartworm disease in dogs 6 months of age and older. ProHeart® 6 is given by injection by your veterinarian. One injection of ProHeart® 6 protects your dog from heartworm disease for 6 complete months. ProHeart® 6 also treats common hookworm infections that may be present at the time of injection.

PHARMACOLOGY
Moxidectin has activity resulting in paralysis and death of affected parasites. The stage of the canine heartworm affected at the recommended dose rate of 0.17 mg moxidectin/kg body weight is the tissue larval stage.

DOSAGE AND ADMINISTRATION
ProHeart® 6 (moxidectin) for extended-release injectable suspension consists of two separate vials: One vial contains 10% moxidectin sterile microspheres and the second vial contains a specifically formulated sterile vehicle for constitution with the microspheres. No other diluent should be used. A clear or translucent appearance of the vehicle is normal. Each mL of constituted drug product contains 3.4 mg moxidectin, 3.1% glyceryl tristearate, 2.4% hydroxypropyl methylcellulose, 0.87% sodium chloride, 0.17% methylparaben, 0.02% propylparaben and 0.001% butylated hydroxytoluene. Hydrochloric acid is used to adjust pH.

Injection Technique: The two part (left and right side) constituted product must be injected separately into the subcutaneous tissue of each side of the dog (left and right side). The subcutaneous area is outlined by drawing a line between the shoulder blades and the tail. The injection site is approximately 1 inch (2.5 cm) from the outlined area on each side of the dog. The needle should be inserted at a 45 degree angle and the injection should be administered over 3 seconds. The needle should be left in place until the entire injection has been given. Injection of only one part of the constituted product may result in a systemic overdose and death in some cases.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/AnimalVeterinary/SafetyHealth.

DOSAGE CHART

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<th>Species</th>
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What should I discuss with my veterinarian before using ProHeart® 6?
Talk to your veterinarian about your dog’s health, past and present:
• General health
• ProHeart® 6 should only be given to healthy dogs.
• Changes in behavior or health, including weight loss, inactivity
• Allergies
• Past problems with or reactions to medications, including food, the drug, or dye, etc.
• Problems with or reactions to vaccines or vaccinations, including:
  - Any other medications, supplements or special diets, including those you cannot afford without a prescription, if any

Heartworm disease is spread to dogs by mosquitoes and can be fatal. To help prevent the spread of heartworm disease, dogs should be treated and monitored for heartworm disease. A mosquito bites an infected animal and takes in young heartworms. Within seven months, the young heartworms grow in the animal. If this bite is to an infected animal, the young heartworms are mature by the time they arrive in the dog. If the mosquito is to a non-infected animal, the young heartworms may occur sooner than 6 months.

WARNING
Do not administer ProHeart® 6 to dogs that are sick, debilitated, or under any form of stress long enough to cause weight loss.

RECOMMENDATIONS
ProHeart® 6 is currently recommended in association with other heartworm preventive products. The current medications, including anthelmintics, have been approved by the following: Association of ProHeart® 6 and other vaccines and medications (see WARNING). For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/AnimalVeterinary/SafetyHealth.

Possible ProHeart® 6 side effects could happen to my dog?
It is important to contact your veterinarian if you do not observe any signs of illness in your dog. Some reactions require emergency treatment by your veterinarian. What you should do if you observe possible side effects:

• Allergic reaction – The most common side effects of ProHeart® 6 are allergic symptoms, including scratching of the face, rolling, gasping and/or inflamed skin. Allergic reactions have been reported with ProHeart® 6 and it is advisable to give them within 30 minutes of other vaccinations. Administer a 10 mg/kg dose of ketamine to the dog. If the reaction is severe, contact your veterinarian immediately.
• Insecticide toxicity – If the insecticide is ingested, contact your veterinarian immediately.

What happens if I give ProHeart® 6 to a dog that is not a dog?
ProHeart® 6 is a product that prevents heartworm disease in dogs 6 months of age and older. ProHeart® 6 is given by injection by your veterinarian. One injection of ProHeart® 6 protects your dog from heartworm disease for 6 complete months. ProHeart® 6 also treats common hookworm infections that may be present at the time of injection.

Seizures
A. caninum
Dirofilaria immitis
Ancylostoma caninum
Uncinaria stenocephala
Streptomyces cyaneogriseus

Common side effects that are possible (see the side effects table above) for dogs to heartworm disease include:

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What if ProHeart® 6 is accidentally given to a human?
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If you have any questions or concerns about ProHeart® 6, talk to your veterinarian.
In a laboratory safety study, ProHeart 6 was administered at 1, 3 and 5 times the recommended dose to 7-8 month old puppies. Injection sites were clipped to facilitate observation. Slight swelling/edema after injection. Histologically, well-defined granulomas were observed in some dogs at approximately 5 months after injection. Some dogs treated with ProHeart 6 in laboratory effectiveness studies developed transient, localized inflammatory injection site reactions. These injection site reactions were visible grossly for up to 3 weeks in one dog.

Injection site observations were recorded during effectiveness and safety studies. In clinical studies, ProHeart 6 was administered at six-month intervals to client-owned dogs under anti-inflammatory drugs (NSAIDs), anesthetics and flea control products.

In well controlled clinical field studies, ProHeart 6 was used in conjunction with a variety of veterinary products including anthelmintics, antiparasitics, antibiotics, analgesics, steroids, non-steroidal anti-inflammatories (NSAIDs), and anthelmintics.

WARNING

ProHeart 6 administered up to 5 times the recommended dose in 7-8 month old puppies did not cause any systemic adverse effects. ProHeart 6 administered at 3 times the recommended dose in dogs with patent heartworm infections and up to 5 times the recommended dose in ivermectin-sensitive collies did not cause any adverse effects. The safety and effectiveness of ProHeart 6 for use in dogs with heartworm infections were not evaluated in field conditions. There were no reports of injection site reactions in these field studies and evaluations of the injection sites revealed no abnormalities.

Post-Approval Experience (Rev. 2010)

ProHeart 6 administered up to 5 times the recommended dose in 7-8 month old puppies did not cause any systemic adverse effects. ProHeart 6 administered at 3 times the recommended dose in dogs with patent heartworm infections and up to 5 times the recommended dose in ivermectin-sensitive collies did not cause any adverse effects. The safety and effectiveness of ProHeart 6 for use in dogs with heartworm infections were not evaluated in field conditions. There were no reports of injection site reactions in these field studies and evaluations of the injection sites revealed no abnormalities.

WARNINGS

For a copy of the Safety Data Sheet (SDS) or to report suspected adverse reactions, contact Zoetis Inc. at 1-888-963-8471. For additional information about adverse drug experience reporting for animal drugs, contact the U.S. Food and Drug Administration at 1-800-FDA-VETS or http://www.fda.gov/AnimalVeterinary/SafetyHealth.

ADVERSE REACTIONS

The following adverse events have been reported after administration of ProHeart 6. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data. The following adverse events are listed in decreasing order of frequency by body system category:

General:
- depression, lethargy, anorexia, fever, weight loss, weakness

Gastrointestinal:
- vomiting, diarrhea (with and without blood), listlessness, weight loss, seizures

Hepatic:
- leukocytosis, anemia, thrombocytopenia

Respiratory:
- coughing, dyspnea

Urinary:
- hematuria

Neurological:
- seizures, ataxia, trembling, hind limb paresis

Dermatological:
- injection site pruritus/swelling, erythema multiforme

Immune:
- anaphylaxis and/or anaphylactoid reactions, urticaria, head/facial edema, pruritus, pale mucous membranes, collapse, cardiovascular shock, erythema, immune-mediated hemolytic anemia, immune-mediated thrombocytopenia and/or neutropenia, cardiopulmonary signs such as coughing and dyspnea may occur in heartworm positive dogs treated with ProHeart 6.

Cardiovascular:
- tachycardia

Hematologic:
- immune-mediated thrombocytopenia (signs reflected in other system categories could be related to allergic reactions, i.e. gastrointestinal, dermatologic, and hematologic).

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