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

INDICATIONS

Ancylostoma caninum

The Injection site observations were recorded during effectiveness and safety studies. In clinical circulating microfilariae may decrease following treatment, ProHeart 6 is not effective for microfilariae clearance.

PHARMACOLOGY

Moxidectin is a semi-synthetic methane derivative of nematicidin which is a fermentation product of Streptomycetes canyorensis subspecies noncyanogenus. Moxidectin is a pentoxylic 16-member lactone molecule.

Moxidectin has activity resulting in paralysis and death of parasitic larvae. 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. The larval and adult stages of the canine hookworm, Uncinaria stenocephala, are not susceptible.

Following injection with ProHeart 6, peak moxidectin blood levels will be observed approximately 7-14 days after treatment. At the end of the six month dosing interval, residual drug concentrations are negligible. Accordingly, little or no drug accumulation is expected to occur with repeated administrations.

INDICATIONS

ProHeart 6 is indicated for use in dogs six months of age and older for the prevention of heartworm disease caused by Dirofilaria immitis.

ProHeart 6 is indicated for the treatment of existing larval and adult hookworm (Ancylostoma caninum and Uncinaria stenocephala) infections.

DOSEAGE AND ADMINISTRATION

Owners should be given the Client Information Sheet for ProHeart 6 to read before the drug is administered and should be advised to observe their dogs for potential drug adverse events including those described in the sheet. The Client Information Sheet is attached to this package insert and available online at http://www.proheart6.com for reprinting to provide to the owner.

ProHeart 6 product information including a webcast on administration is available at https://www.zoetisus.com/products/pages/proheart6/proheart6_product_education.aspx. This website has important information on the safe and effective use of ProHeart 6 for veterinary providers and provides interactive discussions with veterinarians.

Frequency of Treatment: ProHeart 6 prevents infection by D. immitis for six months. It should be administered within one month of the dog’s first exposure to mosquitoes. Follow-up treatments may be given every six months if the dog has continued exposure to mosquitoes and continues to be at risk for heartworm infection. ProHeart 6 is not effective once the heartworm preventive product, ProHeart 6 should be given within one month of the last dose of the former medication.

ProHeart 6 eliminates the larval and adult stages of A. caninum and U. stenocephala at the time of treatment. However, persistent microfilarial infections may be established for this indication. Re-infection with A. caninum and U. stenocephala may occur sooner than 6 months.

Dose: The recommended subcutaneous dose is 0.05 mL of the constituted suspension/kg body weight (0.0227 mL/kg). This amount of suspension will provide 0.17 mg moxidectin/kg body weight (0.0737 mg/kg). To ensure accurate dosage, calculate each dose based on the dog’s weight at the time of treatment. Do not overdose growing puppies in anticipation of their adult weight. The following dosage chart may be used as a guide.

DOSAGE CHART

<table>
<thead>
<tr>
<th>Dog Wt (kg)</th>
<th>Dose Volume (mg/mL)</th>
<th>Dog Wt (kg)</th>
<th>Dose Volume (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-1.5</td>
<td>0.25</td>
<td>11-15</td>
<td>0.75</td>
</tr>
<tr>
<td>1.5-2.5</td>
<td>0.20</td>
<td>16-20</td>
<td>1.00</td>
</tr>
<tr>
<td>2.5-4.0</td>
<td>0.17</td>
<td>21-25</td>
<td>1.10</td>
</tr>
<tr>
<td>4.0-5.0</td>
<td>0.15</td>
<td>26-30</td>
<td>1.20</td>
</tr>
<tr>
<td>5.0-7.0</td>
<td>0.13</td>
<td>31-40</td>
<td>1.30</td>
</tr>
<tr>
<td>7.0-10.0</td>
<td>0.12</td>
<td>41-55</td>
<td>1.40</td>
</tr>
<tr>
<td>10.0-15.0</td>
<td>0.11</td>
<td>56-70</td>
<td>1.50</td>
</tr>
<tr>
<td>15.0-20.0</td>
<td>0.10</td>
<td>71-100</td>
<td>1.60</td>
</tr>
</tbody>
</table>

Injection Technique: The two-part sustained release product must be mixed at least 30 minutes prior to the intended time of use (see CONSTITUTION PROCEDURES for initial mixing instructions). Once constituted, swirl the bottle gently before every use to re-disperse the microspheres. Withdraw 0.05 mL of suspension/kg body weight and inject into an appropriately sized syringe fitted with an 18G or 20G hypodermic needle. Do not aspirate before injecting into the dosing syringe. If administration is delayed, gently roll the dosing syringe prior to injection to maintain a uniform suspension and accurate dosing.

Using aseptic technique, inject the product subcutaneously in the left or right side of the dorsum of the neck cranial to the scapula. No more than 3 mL should be administered in a single site. The location(s) of each injection (left or right side) should be noted so that prior injection sites can be identified and the next injection can be administered on the opposite side.

INFORMATION FOR DOG OWNERS

All patients should be examined and evaluated by a veterinarian immediately if signs of toxicity are observed. The vast majority of patients with drug related adverse reactions have recovered when the signs are recognized and veterinary care, if appropriate, is initiated.

CONTRAINDICATIONS

ProHeart 6 is contraindicated in animals previously found to be hypersensitive to this drug.

Caution: Not for human use. Keep this and all drugs out of the reach of children.

ADVERSE REACTIONS

In field studies, the following adverse reactions were observed in dogs treated with ProHeart 6: anaphylaxis, vomiting, diarrhea (with and without blood), listlessness, weight loss, seizures, injection site pruritus, and elevated body temperature. Dogs with clinical signs of weight loss (>10%) were more likely to develop an adverse reaction.

In a laboratory effectiveness study, dogs with 4- and 6-month-old heartworm infections experienced vomiting, lethargy and bloody diarrhea. These signs were more severe in the dogs with 4-month-old heartworm infections, including one dog that died unexpectedly 10 days after administration. In a subsequent safety study, the incidence of hypothermia was higher in dogs previously infected with dirofilarial antigen. Post-Approval Experience (Rev. 2018) The following adverse events are based on post-approval drug experience reporting. Not all adverse reactions are reported to FDA/CVM. It is not always possible to reliably estimate the adverse event incidence or relation to the drug.

In some cases, it has been reported as an outcome of the adverse events listed above. For a copy of the Safety Data Sheet (SDS) or to report suspected adverse reactions, contact Zoetis Inc. at 1-888-965-8471. For additional information about drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/AnimalVeterinary/SafetyHealth.

ANIMAL SAFETY

General Safety: ProHeart 6 has been administered to a wide variety of healthy dogs six months of age and older, including a wide variety of breeds, pregnant and lactating females, breeding males, and worm-sensitive animals. In clinical studies, two generic dogs with a history of weight loss after the initial ProHeart 6 injection died within a month of the second 6 month injection. A third dog who was overweight for its age and breed and who had a history of congenital problems experienced lethargy following the initial injection of ProHeart 6. The dog never recovered and died 3 months after the second injection. ProHeart 6 was administered at 3 times the recommended dose in dogs with patent heartworm infections and up to 5 times the recommended dose in heartworm-sensitive collies did not cause any adverse reactions. ProHeart 6 was administered at 3 times the recommended dose in dogs not previously treated for heartworm disease and did not cause any adverse reactions.

ProHeart 6 was administered in 7-8 month old puppies did not cause any systemic adverse effects.

In a 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-inflammatory drugs (NSAIDs), and analgesics and a central nervous system stimulant product. ProHeart 6 was administered with caution in dogs with pre-existing allergic disease, including food allergy, atopy, hyporesponsiveness to vaccines and other injectable products. Cardiomyopathy signs such as coughing and dyspnea may occur in heartworm positive dogs treated with ProHeart 6.

In some cases, it has been reported as an outcome of the adverse events listed above.

CONSTITUTION PROCEDURES

Dose Volume

The two-part ProHeart 6 product must be mixed at least 30 minutes prior to the intended time of use.

Items needed to constitute ProHeart 6: Microspheres, Vial 1

3. Insert the enclosed 25G needle into the microsphere vial. Slowly transfer the microsphere vial through the stopper using the stopper needle and syringe.

4. If the vehicle has been removed, re-insert the vent and transfer needle from the microsphere vial. Discard unused vehicle and needle.

5. Place the microsphere vial vigorously up to a thoroughly mixed suspension is produced.

7. Record the time and date of mixing on the microsphere vial.

9. Allow suspension to stand for at least 30 minutes to allow large air bubbles to dissipate.


STORAGE INFORMATION

The product is stable for 8 weeks stored under refrigeration at 2-8°C (36°F to 46°F).

HOW SUPPLIED

The two-part ProHeart 6 product is available in the following three package sizes.

Constitution of the 20 mL vial product:

1. Place Contents into a clean mixing container in the dark. Discard unused vehicle and needle.

2. Using an 18G or 20G needle and sterile syringe withdraw 17.0 mL of the unique vehicle from the vial. There is more vehicle supplied than the 17.0 mL required.

3. Insert the enclosed 25G needle into the microsphere vial. Slowly transfer the microsphere vial through the stopper using the stopper needle and syringe.

4. If the vehicle has been removed, re-insert the vent and transfer needle from the microsphere vial. Discard unused vehicle and needle.

5. Place the microsphere vial vigorously up to a thoroughly mixed suspension is produced.

7. Record the time and date of mixing on the microsphere vial.

9. Allow suspension to stand for at least 30 minutes to allow large air bubbles to dissipate.

Before use, gently swirl the mixture to achieve uniform suspension.

The microspheres and vehicle will gradually separate on standing.


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