1 Open the box and read the PROHEART 6 package insert. Remove:
   - 1 vial of moxidectin microspheres (red cap) and shake to break up any aggregates
   - 1 vial of vehicle for constitution (green cap)
   - 25G vent needle

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

3 Insert the enclosed 25G vent needle into the microsphere vial.

4 Slowly transfer the vehicle into the microsphere vial through the stopper using the transfer needle and syringe.

5 Remove the vent and transfer needles from the microsphere vial (properly dispose of all unused vehicle and needles). Shake vigorously until thoroughly mixed.

6 Record date and time of mixing on the microsphere vial. Let suspension stand for at least 30 minutes to allow large air bubbles to dissipate.

7 Before each use swirl the mixture to achieve uniform suspension. Draw up the dose using an 18G or 20G needle and a 1 mL or 3 mL syringe (refer to Dosage Chart on back).

8 If administration is delayed, gently roll the dosing syringe to maintain a uniform suspension.

9 Inject subcutaneously in the left or right side of the dorsum of the neck, cranial to the scapula. Alternate side with each treatment.
Actual dose = 0.05 mL per kg of body weight.

<table>
<thead>
<tr>
<th>DOG WEIGHT (lb)</th>
<th>DOG WEIGHT (kg)</th>
<th>DOSE VOLUME (mL/Dog)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>5</td>
<td>0.25</td>
</tr>
<tr>
<td>22</td>
<td>10</td>
<td>0.50</td>
</tr>
<tr>
<td>33</td>
<td>15</td>
<td>0.75</td>
</tr>
<tr>
<td>44</td>
<td>20</td>
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<td>2.75</td>
</tr>
<tr>
<td>132</td>
<td>60</td>
<td>3.00</td>
</tr>
</tbody>
</table>

**IMPORTANT SAFETY INFORMATION:** PROHEART 6 should be used in healthy dogs. Do not administer to sick, debilitated, underweight dogs or dogs that have a history of weight loss. Prior to administration, PROHEART 6 certified veterinarians should continue to assess patient health through a medical history, physical examination and if deemed appropriate, diagnostic testing. Continue to use caution when administering PROHEART 6 concurrently with vaccinations. Adverse events, including anaphylaxis, have been reported following the concomitant use of PROHEART 6 and vaccines. In some cases, anaphylactic reactions have resulted in death. Use with caution in dogs with pre-existing or uncontrolled allergic disease (food allergy, atopy or flea allergy dermatitis). Dogs receiving PROHEART 6 should be tested for existing heartworms as per the product label. In people, avoid PROHEART 6 contact with eyes. If contact with the eyes occurs, rinse thoroughly with water for 15 minutes and seek medical attention immediately. PROHEART 6 is available only to veterinarians through a restricted distribution program. Only certified veterinarians and staff can administer it. See full Prescribing Information, attached.

To obtain additional information, visit us at www.proheart6dvm.com or call 1-800-366-5288.
Pharmacology
Moxidectin is a semi-synthetic, monohemithioate derivative of nemadectin, which is a fermentation product of Streptomyces cyaneogriseus subspecies noncyanogenus. Moxidectin is a pentacyclic 16-membered lactone macrolide. 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 larval stage. The larval and adult stages of the canine hookworms, Ancylostoma caninum and Uncinaria stenocephala, are susceptible.

Dosage 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 toxicity described in the sheet.

Contraindications

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

Human Warnings

For human use. Keep this and all drugs out of the reach of children.

Precautions

Caution should be used when administering ProHeart 6 concurrently with vaccines. Administration, including anaphylaxis, has been reported following the concurrent administration of ProHeart 6 and vaccines (see WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS sections). Owners should be advised to contact their veterinarian immediately if signs of toxicity are observed. The vast majority of patients with drug-related adverse reactions have recovered in the sheet.

Confidentiality

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

Safety Data Sheet

Store the unconstituted product at or below 25°C (77°F). Do not expose to light extended periods of time. After constitution, the product is stable for 8 weeks stored under refrigeration at 2°C to 8°C (36°F to 46°F).

Packing List

- Microsphere vial
- Vehicle syringe
- Sterile 20 mL transfer syringe
- Transfer needle (18G)

Post-Approval Experience (Rev. 2010)

The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse reactions are reported to FDA/CVM. 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 increasing order of frequency by body system.

Immunologic: anaphylaxis, and other allergic reactions, urticaria, head, facial edema, pruritus, pale mucous membranes, collapse, cardiovascular shock, erythema, immune-mediated hemolytic anemia, immune-mediated thrombocytopenia signs reflected in other system categories could be related to allergic reactions, i.e. gastrointestinal, dermatologic, and hematologic.

Gastrointestinal: vomiting (with or without blood), diarrhea with or without blood, dysenteric reactions.

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

Dermatologic: injection site pruritus/swelling, erythema multiforme.

Neurologic: seizures, ataxia, tremoring, hind limb paraparesis.

Hematologic: leukopenia, anemia, thrombocytopenia.

Respiratory: dyspnea, tachypnea, coughing.

Hepatic: elevated liver enzymes, hyperproteinemia, hyperbilirubinemia, hepatitis.

Urinary: elevated BUN, elevated creatinine, hematuria, polydipsia, polyuria.

Cardiopulmonary: such as coughing and dyspnea may occur in heartworm-positive dogs treated with ProHeart 6.

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

A three-year repeated injection study was conducted to evaluate the safety of up to 6 injections of ProHeart 6 administered at 6-week intervals. The study was performed under field conditions. There were no reports of injection site reactions in these field studies and evaluations of the injection sites revealed no abnormalities.

Aity study, ProHeart 6 was administered at 3, 6, and 9 months respectively and the recommended dose was 7 to 8 month old puppies. In a 12-month-old dog, the vials were left to facilitate observation. Slight swelling/edema at the injection site was observed in some dogs from all treated groups. These injection site reactions appeared as quickly as 1 hour post injection and lasted up to 3 weeks. A blinded, controlled injection study was conducted to evaluate the safety of up to 6 injections of ProHeart 6 administered at the recommended dose (0.17 mg/kg) every 6 months. Mild erythema and localized deep subcuticular thickening were seen in dogs that received injections in the same area on the neck and in one dog that received two injections in the same area on the neck. Microscopic evaluation on the injection sites from all dogs 6 months after the last injection consistently showed mild granulomatous panniculitis with microvacuolation. The only adverse reaction seen that was not related to the injection site was weight loss in one dog.

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 after injection. Histologically, well defined granulomas were observed in some dogs at approximately 5 months after injection.