98% of female worms were killed (total 99%). Dogs with natural and female worms 16.9% (total 51.7%). When the full regime was used 100% of male worms and with either 2.5 mg/kg once or 2.5 mg/kg once followed 1 month later with 2.5 mg/kg administered.

Laboratory Studies:
- In-office heartworm antigen test kits prior to treatment. Treatment response can be assessed best in-office heartworm antigen test kits prior to treatment. Treatment response can be assessed best.
- The efficacy of IMMITICIDE may be reduced with co-administration of BAL.
- Immunosuppressive agents are contraindicated for use with IMMITICIDE.

SAFETY
- 5 - 50 mg vials of lyophilized melarsomine dihydrochloride with accompanying 5 - 2 mL vials of sterile water for injection.
- STERILE DILUENT (sterile water for injection). Sterile water diluent is not suitable for intravascular injection. This provides 2.5 mg melarsomine dihydrochloride per 0.1 mL of injectable solution. Two 0.1 mL doses (total 0.2 mL) providing a single treatment can be administered. Two 5 mL syringes will provide 2 weeks of treatment (total 10 mL) for a large dog. Two 50 mL syringes will provide 10 weeks of treatment (total 100 mL) for a large dog.

Concomitant Therapy
- Heartworm Prophylaxis: Dogs that have been treated with IMMITICIDE should be on heartworm prophylaxis once or twice a week. Avoid exposure to heartworm infected canines.
- Treatments for heartworm disease should not be the only treatment for heartworm disease. Additionally, dogs that have been successfully treated for heartworm disease should be on heartworm prophylaxis once or twice a week.

Preparation: IMMITEC should be reconstituted with the provided 2 mL of STERILE WATER for INJECTION. (sterile water for injection). This provides 2.5 mg melarsomine dihydrochloride per 0.1 mL of injectable solution. Two 0.1 mL doses (total 0.2 mL) providing a single treatment can be administered. Two 5 mL syringes will provide 2 weeks of treatment (total 10 mL) for a large dog. Two 50 mL syringes will provide 10 weeks of treatment (total 100 mL) for a large dog.

Concomitant Therapy
- Heartworm Prophylaxis: Dogs that have been treated with IMMITICIDE should be on heartworm prophylaxis once or twice a week after treatment. Treatments for heartworm disease should not be the only treatment for heartworm disease. Additionally, dogs that have been successfully treated for heartworm disease should be on heartworm prophylaxis once or twice a week.

Key:
- 005U4020106 Rev. 04/2019
- Made in France.
- Marketed by Boehringer Ingelheim Animal Health USA Inc.
- BIAHU-003188_HGD_2023UpdatedImmiticideDetailer_17x11_r4.indd 1-2 18.2 17.6 6.6 50 110.0 1.0 0.1 2.2 44.0 0.8 1.1 0.8 8.8 9 5.0 66.0 0.6 2 0.4 0.0 2.3 0.7 40 13.2 8 0.0 31x6

Clinical Field Studies: In two well controlled clinical trials, 109 client-owned dogs, 1 to 12 years old and weighing 2.2 to 110.0 kg, with Class 1 - stabilized Class 2 heartworm disease were treated with the recommended dose of IMMITEC. In-office blood antigen tests were used prior to treatment to diagnose the 2.5 mg/kg administered twice, 24 hours apart (alternate dosing regime). Worms that were too young to be killed by the first treatment series, i.e., <4 months, may be killed by a second treatment series.

In one small (n=15), uncontrolled field study in severely ill (Class 3) dogs, 5 dogs died following administration of IMMITEC. The dog vomited once and the diarrhea resolved within 24 hours. The third dog receiving up to 3X the recommended dose included tremors, lethargy, unsteadiness/ataxia, increased respiratory rate, tachypnea, cyanosis, shock, and death. (See Table 1.)

In one of the trials described above, the Class 2 heartworm disease was the cause of death. The remaining dogs were not necropsied. All dogs were in good health at the time of treatment. Clinical signs seen in this study which were not seen in the larger studies include acute vomiting, collapse.

Post Approval Experience:
- In the open-label study in 102 dogs, 1 to 18 years old and weighing 4.4 to 40.8 kg, with Class 1 or 2 heartworm disease. Worms that were too young to be killed by the first treatment series, i.e., <4 months, may be killed by a second treatment series. Mortality: Mortality is a possible sequelae of heartworm disease in dogs with or without treatment, especially in the Class 3 dogs. The following table shows the percentage of dogs that died in clinical trials with IMMITEC (mebolazine dihydrochloride) and the causes of death, if known.

<table>
<thead>
<tr>
<th>Disease Classification</th>
<th>Cause:</th>
<th>Undetermined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality: Disease in Dogs with Class 1, 2, and 3 Heartworm Disease Treated with IMMITEC in Clinical Field Trials</td>
<td>Death due to heartworm disease</td>
<td>1.5</td>
</tr>
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</table>

- IMMITEC should be administered empirically and the patient’s medical record for reference.
- Disease Classification: It is vital to classify the severity of heartworm infections in dogs pre-treatment to assess treatment response and to determine the appropriate dosage regimen for IMMITEC. (See INDICATIONS).

Class 1 and 2:
- If necessary, dogs should be stabilized prior to treatment. IMMITEC should be administered empirically in the tender (L-), as required, at a dose of 2.2 mg/kg twice, 24 hours apart. (See Dosing Table.)

Class 3:
- Dogs must be taken to the veterinarian for proper dose. Accurately weigh the dog and calculate the volume to be injected based on the dose of 2.5 mg/kg (1 mL/kg). This is equivalent to 0.1 mL/kg (5 mL/kg). DO NOT ADMINISTER AT ANY OTHER SITE. Avoid superficial injection or i.m. use. Use a 23 gauge, 1 inch needle for dosing up to 3X the recommended dose includes tremors, lethargy, unsteadiness/ataxia, increased respiratory rate, tachypnea, cyanosis, shock, and death. (See Table 1.)
Efficacy of the 2-DOSE PROTOCOL

Indicated for dogs with Class 1 or Class 2 heartworm disease

Admitted twice at 2.5 mg/kg, 24 hours apart

- Post-mortem reduction in worm coil (no placebo Tp)

Efficacy of the 3-DOSE PROTOCOL

Alternate dosing regimen

Indicated for dogs with Class 3 heartworm disease

Administered at 2.5 mg/kg once, followed 1 month later

- Post-mortem reduction in worm coil (no placebo Tp)

SAFETY

IMMITICIDE has a low margin of safety. A single dose of 2.5 mg/kg TP may lead to severe clinical signs in dogs with moderate heartworm disease. The clinical signs may be self-limiting, including hypotension, vomiting, diarrhea, anorexia, weight loss, and other clinical signs of thromboembolism. The death of individual dogs with severe heartworm disease may occur as a result of clinical thromboembolism. A single dose of 7.5 mg/kg TP may lead to severe clinical signs in dogs with severe heartworm disease. The clinical signs may be self-limiting, including hypotension, vomiting, diarrhea, anorexia, weight loss, and other clinical signs of thromboembolism. The death of individual dogs with severe heartworm disease may occur as a result of clinical thromboembolism. A single dose of 10 mg/kg TP may lead to severe clinical signs in dogs with very severe heartworm disease. The death of individual dogs with very severe heartworm disease may occur as a result of clinical thromboembolism. Therefore, all dogs must be clinically evaluated for severe heartworm disease and assessed for the risk of thromboembolism prior to treatment with IMMITICIDE. STERILE POWDER. DO NOT USE IN DOGS WITH MODERATE OR SEVERE HEARTWORM DISEASE.

IMPORTANT SAFETY INFORMATION:

- Do not use in dogs with severe heartworm disease.
- Do not use in dogs with moderate heartworm disease unless the patient is assessed for the risk of thromboembolism prior to treatment.
- Do not use in dogs with a history of severe heartworm disease and with signs of thromboembolism.
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