Date of Approval: February 17, 2017

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-609

DIROBAN™

melarsomine dihydrochloride

Sterile Powder for Injection

Dogs

For the treatment of stabilized Class 1, 2, and 3 heartworm disease caused by immature (4 month-old, stage L_5) to mature adult infections of *Dirofilaria immitis*

Sponsored by:

Anzac Animal Health, LLC

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I. GENERAL INFORMATION:

A. File Number

ANADA 200-609

B. Sponsor

Anzac Animal Health, LLC
218 Millwell Drive, Suite B
Maryland Heights, MO 63043

Drug Labeler Code: 86073

C. Proprietary Name

DIROBAN™

D. Product Established Name

melarsomine dihydrochloride

E. Pharmacological Category

Antiparasitic, Anthelminthic

F. Dosage Form

Sterile Powder for Injection

G. Amount of Active Ingredient

50 mg vial sterile powder reconstituted in 2 mL sterile water diluent (25 mg/mL)

H. How Supplied

5 x 50 mg vials of melarsomine dihydrochloride
5 x 2 mL vials of sterile water for injection

I. Dispensing Status

Rx

J. Dosage Regimen

Disease Classification*:* It is vital to classify the severity of heartworm disease to apply the appropriate dosage regime for DIROBAN.

Class 1 and 2:
If necessary, dogs should be stabilized prior to treatment. DIROBAN should be administered intramuscularly in the lumbar (L_3 - L_5) muscles at a dose of 2.5 mg/kg twice, 24 hours apart. Four months following treatment, a second treatment series (2.5 mg/kg twice, 24 hours apart) can be elected taking into consideration the response to the first DIROBAN treatment and the condition, age,

and use of the dog. 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.

Class 3:
Alternate Dosing Regime: Dogs with severe (Class 3) heartworm disease should be stabilized prior to treatment and then dosed intramuscularly in the lumbar (L_3 - L_5) muscles with a single injection of 2.5 mg/kg then approximately 1 month later with 2.5 mg/kg administered twice 24 hours apart.

***Dosing Table**:* Care must be taken to administer the proper dose. Accurately weigh the dog and calculate the volume to be injected based on the dose of **2.5 mg/kg** (1.1 mg/lb). This is equivalent to 0.1 mL/kg (0.045 mL/lb). The following table should be used as a guide to ensure that the proper volume has been calculated.

Table I.1. Dosing Table.

Weight (lb)	Weight (kg)	Volume per injection (mL)
2.2	1	0.1
4.4	2	0.2
6.6	3	0.3
8.8	4	0.4
11	5	0.5
13.2	6	0.6
15.4	7	0.7
17.6	8	0.8
19.8	9	0.9
22	10	1.0
44	20	2.0
66	30	3.0
88	40	4.0
110	50	5.0*

*Limited data were collected on the administration > 5.0 mL at a single injection site.

K. Route of Administration

DIROBAN should be administered by deep intramuscular injection ONLY in the epaxial (lumbar) muscles in the third through fifth lumbar region.
DO NOT ADMINISTER AT ANY OTHER SITE. Avoid superficial injection or leakage. Use a 23 gauge 1 inch needle for dogs equal to or less than 10 kg (22 lb) in weight. Use a 22 gauge 1½ inch needle for dogs greater than 10 kg (22 lb). Use alternating sides with each administration. If repeated administrations are warranted avoid injecting at the same lumbar location. Record the location of the first injection(s) in the patient's medical record for future reference.

L. Species/Class

Dogs

M. Indication

DIROBAN Sterile Powder for Injection is indicated for the treatment of stabilized Class 1, 2, and 3 heartworm disease caused by immature (4 month-old, stage L_5) to mature adult infections of *Dirofilaria immitis*.

N. Reference Listed New Animal Drug

IMMITICIDE®; melarsomine dihydrochloride; NADA 141-042; Merial, Inc.

II. BIOEQUIVALENCE:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an abbreviated new animal drug application (ANADA) may be submitted for a generic version of an approved new animal drug (reference listed new animal drug (RLNAD)). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA sponsor is required to show that the generic product is bioequivalent to the RLNAD, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal period for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of demonstrating bioequivalence (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2002).

Based on the formulation characteristics of the generic product, Anzac Animal Health, LLC, was granted a waiver from the requirement to demonstrate bioequivalence for the generic product DIROBAN™ (melarsomine dihydrochloride) Sterile Powder for Injection. The generic drug product is a sterile powder for injection (50 mg/vial) to be dissolved in 2 mL of sterile water for injection, contains the same active ingredient in the same concentration and dosage form as the RLNAD, and contains no inactive ingredients that may significantly affect the bioavailability of the active ingredient. The RLNAD is IMMITICIDE® (melarsomine dihydrochloride) Sterile Powder, sponsored by Merial, Inc., under NADA 141-042 and was approved for use in dogs on July 21, 1995.

III. EFFECTIVENESS:

CVM did not require effectiveness studies for this approval.

IV. TARGET ANIMAL SAFETY:

CVM did not require target animal safety studies for this approval.

V. HUMAN FOOD SAFETY:

Data on human food safety, pertaining to drug residues in food, were not required for approval of this application. This drug is approved for use in dogs, which are not food producing animals.

VI. USER SAFETY:

CVM did not require user safety studies for this approval.

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to DIROBAN™:

Keep this and all medications out of the reach of children. Avoid human exposure. Wash hands thoroughly after use or wear gloves. Potentially irritating to eyes. Rinse eyes with copious amounts of water, if exposed. Consult a physician in cases of accidental exposure by any route (dermal, oral, or by injection).

The Safety Data Sheet (SDS) contains more detailed occupational safety information. To report adverse effects, obtain a SDS or for assistance, contact Zoetis Inc. at 1-888-963-8471.

VII. AGENCY CONCLUSIONS:

This information submitted in support of this ANADA satisfies the requirements of section 512(n) of the Federal Food, Drug, and Cosmetic Act and demonstrates that DIROBAN™, when used according to the label, is safe and effective.