Date of Approval: Nov 30 2001

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

ANADA 200-270

Iverhart™ Tablets

For the prevention of canine heartworm (*Dirofilaria immitis*) disease.

Sponsored by:

Blue Ridge Pharmaceuticals, Inc.,
A Subsidiary of Idexx Laboratories, Inc.
4249 Piedmont Parkway
Greensboro, North Carolina 27410

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

ANADA:	200-270
Sponsor:	Blue Ridge Pharmaceuticals, Inc.™ 4249-105 Piedmont Parkway Greensboro, NC 27410
Generic Name:	Ivermectin Tablets
Trade Name:	Iverhart™
Dosage Form:	Tablets
How Supplied:	Three tablet sizes – 68 mcg tablet for dogs up to 25 lbs; 136 mcg tablet for dogs 26 to 50 lbs; 272 mcg tablet for dogs 51 to 100 lbs. Each tablet size packaged in blisters (6 tablets per card)
How Dispensed:	Rx
Amount of Active Ingredients:	Small tablet contains 68 mcg of ivermectin; medium tablet contains 136 mcg of ivermectin; large tablet contains 272 mcg of ivermectin
Route of Administration:	Oral
Species:	Canine
Labeled Dosage:	6 mcg/kg of body weight
Indications for Use:	Iverhart is indicated for the prevention of canine heartworm (*Dirofilaria immitis*) disease
Pioneer Product:	Heartgard™ Tablets, NADA 138-412, Merial Ltd.

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Restoration Act (53 FR 50460, December 15, 1988, First GADPTRA Policy Letter) an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). Under the Act, approval of a generic product requires a demonstration of bioequivalence to the pioneer product. Bioequivalence of the generic and pioneer products can be demonstrated by

a clinical end-point study (55 FR 24645, June 18, 1990, Fifth GADPTRA Policy Letter; Bioequivalence Guidance, October 2000). The ANADA relies on the target animal safety and drug effectiveness data in the pioneer's New Animal Drug Application (NADA).

***Effectiveness*:**

The effectiveness of ivermectin for the claim of the prevention of heartworm disease in dogs has been established by data contained in the approved NADA 138-412 for Heartgard™ Tablets, sponsored by Merial, Ltd. The following clinical end-point study establishes the bioequivalence of the generic Blue Ridge Pharmaceuticals' product to Heartgard™ Tablets.

Clinical Endpoint Bioequivalence for Canine Heartworm Disease Prevention

The following study was conducted to determine the clinical endpoint bioequivalence of the two products, Iverhart™ and Heartgard™ for the claim of heartworm prevention (*Dirofilaria immitis*) in dogs. Blood-level bioequivalence studies were not required for this approval because blood levels of ivermectin at the approved dose in dogs are too low for accurate measurement throughout the pharmacokinetic profile of the drug.

Testing Facility: TRS Labs, Inc.
295 Research Drive
Athens, GA 30605

Investigator: Dr. John W. McCall

Thirty-six beagle dogs (18 males and 18 females), ranging between 4.7 and 7.1 months of age and weighing between 16 to 33 pounds, were obtained from a USDA licensed supplier. All dogs were inoculated subcutaneously with 50 *D. immitis* L3 larvae thirty days prior to the first treatment. All of the infective larvae were from the same source, of the same age, and handled in the same manner for this study. The dogs were stratified by weight and gender, and randomly assigned to one of three treatment groups (6 males and 6 females per group). Dogs receiving the generic product (Group 1) and the pioneer product (Group 2) were treated every thirty days, for a total of four treatments. The dogs received a minimum dose of 6 mcg ivermectin/kg of body weight. The negative control group (Group 3) received no treatment. All individuals responsible for making study observations, including worm counts, were masked to the treatment groups. All dogs were necropsied 149 days post-inoculation. The heart and lungs of each dog were removed and carefully examined to collect all *D. immitis* adults or macroscopic larvae. Recovered worms were recorded as dead or alive, sexed, counted, and preserved in 10% buffered formalin for retention.

Percent efficacy was calculated using the following formula:

$$\frac{\text{mean \# of parasites in control dogs - mean \# of parasites in treated dogs}}{\text{mean \# of parasites in control dogs}} \times 100 = \% \text{ efficacy}$$

Results and Conclusions: The worm counts for both treated groups (Iverhart and Heartgard) were 0 and the mean worm count for the negative control group was 30.9, with all control animals having heartworm infections (range 22 to 43 worms). Thus, the generic product and the pioneer product were considered equivalent with efficacies of 100% for the prevention of heartworm disease, and no additional analysis was needed.

3. HUMAN SAFETY:

Human Safety Relative to Food Consumption:

None required as Iverhart is intended for use only in dogs.

Human Safety Relative to Possession, Handling, and Administration:

Labeling contains adequate caution/warning statements.

4. AGENCY CONCLUSIONS:

This is an Abbreviated New Animal Drug Application (ANADA) filed under section 512(b)(2) of the Federal, Food, Drug and Cosmetic (FFD&C) Act.

Safety and effectiveness for this generic animal drug, Iverhart™ Tablets, were established by demonstration of clinical end-point bioequivalence to the pioneer product, Heartgard™ Tablets, NADA 138-412.

The generic product and the pioneer product have identical labeling indications for use in dogs. The route and method of administration of the two drugs are identical. Both drugs are administered orally. The generic and pioneer products contain the same active ingredients.

This ANADA satisfies the requirements of section 512 of the Act and demonstrates that Iverhart™ is safe and effective for its labeled indications, when used under the proposed conditions of use.

Attachments:

1. Generic Labeling:

   Package Insert
   Blister label
   Reminder stickers
   Dispensing envelopes for bulk cards
   Box Label for 68, 136, & 272mcg tablets
   Display Carton Label for 68, 136, & 272mcg bulk tablet strips
   Shipper Label for 68, 136, & 272mcg tablets

2. Pioneer Labeling:

   Package Insert
   Box label
   Blister label