Date of Approval: December 23, 2013

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-564

Ivermectin Paste 1.87%

(ivermectin)

Paste

Horses

For use in horses for treatment and control of large strongyles, small strongyles, pinworms, roundworms (ascarids), hairworms, threadworms, large-mouth stomach worms, and bots.

Sponsored by:

Merial Ltd.

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I. GENERAL INFORMATION:

A. File Number

ANADA 200-564

B. Sponsor

Merial Ltd.
3239 Satellite Blvd., Bldg. 500
Duluth, GA 30096-4640

Drug Labeler Code: 050604

Consultant Name and Address: James H. Schafer, D.V.M.
Schafer Veterinary Consultants, LLC
800 Helena Court
Fort Collins, CO 80524

C. Proprietary Name

Ivermectin Paste 1.87%

D. Established Name

ivermectin

E. Pharmacological Category

Anthelmintic and boticide

F. Dosage Form:

Paste

G. Amount of Active Ingredient

1.87% ivermectin

H. How Supplied

Individual syringe containing 6.08 g paste

I. Dispensing Status

OTC

J. Dosage Regimen

Each syringe contains sufficient paste to treat one 1250 lb horse at the recommended dose rate of 91 mcg ivermectin per lb (200 mcg/kg) body weight

K. Route of Administration

Oral

L. Species/Class

Horses

M. Indications

Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism. Ivermectin (ivermectin) Paste 1.87% provides effective treatment and control of the following parasites in horses.

- Large Strongyles (adults) - *Strongylus vulgaris* (also early forms in blood vessels), *S. edentatus* (also tissue stages), *S. equinus*, *Triodontophorus* spp. including *T. brevicauda* and *T. serratus*, and *Craterostomum acuticaudatum;*
- Small Strongyles (adults, including those resistant to some benzimidazole class compounds) - *Coronocyclus* spp. including *C. coronatus*, *C. labiatus* and *C. labratus*; *Cyathostomum* spp. including *C. catinatum* and *C. pateratum*; *Cylicocyclus* spp. including *C. insigne*, *C. leptostomum*, *C. nassatus* and *C. brevicapsulatus*, *Cylicodontophorus* spp., *Cylicostephanus* spp. including *C. calicatus*, *C. goldi*, *C. longibursatus* and *C. minutus*, and *Petrovinema poculatum;*
- Small Strongyles - Fourth-stage larvae;
- Pinworms (adults and fourth-stage larvae) - *Oxyuris equi;*
- Ascarids (adults and third- and fourth-stage larvae) - *Parascaris equorum;*
- Hairworms (adults) - *Trichostrongylus axei;*
- Large-mouth Stomach Worms (adults) - *Habronema muscae;*
- Bots (oral and gastric stages) - *Gasterophilus* spp. including *G. intestinalis* and *G. nasalis;*
- Lungworms (adults and fourth-stage larvae) - *Dictyocaulus arnfieldi;*
- Intestinal Threadworms (adults) - *Strongyloides westeri;*
- Summer Sores caused by *Habronema* and *Draschia* spp. cutaneous third-stage larvae;
- Dermatitis caused by neck threadworm microfilariae, *Onchocerca* sp.

N. Reference Listed New Animal Drug

EQVALAN Paste 1.87%; ivermectin; NADA 134-314; Merial Ltd.

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 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 or 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. Information to show that the generic version is bioequivalent to the approved RLNAD is required for approval.

For this ANADA, an *in vivo* blood-level study was conducted using the generic and RLNAD products to demonstrate product bioequivalence. Both the generic and RLNAD products are 1.87 % (ivermectin) pastes.

Blood-level Bioequivalence Study

One blood-level bioequivalence study was conducted to determine the comparative bioavailability of the generic and RLNAD formulations of ivermectin 1.87% pastes.

Testing Facility:

Ancare New Zealand, Ltd.
Takapuna, New Zealand

The name of the above facility has since changed and is currently Ancare Scientific.

Study Number:

AHSC 54897
Ancare NZ Ltd 131-4-766-601

Objective:

The objective of this study was to determine the comparative *in vivo* blood-level bioequivalence of Ancare New Zealand, LTD's 1.87% ivermectin paste (generic) and Merial Limited's 1.87 % ivermectin paste (RLNAD) in a randomized, two period, two treatment, crossover study in horses.

Study Summary:

The study was conducted as a randomized, two-period, two-treatment, crossover design with a 35 day washout between periods using 24 healthy horses consisting of 12 males and 12 intact, non-pregnant, non-lactating, female horses. Variables evaluated were area under the concentration (AUC) curve from 0 to the first value below the limit of quantitation and the observed maximum concentration (C_{MAX}). The statistical model included sequence, treatment, and period as fixed effects, and horse-within-sequence as a random effect.

The criteria for determining bioequivalence is to construct a 90% confidence interval about the difference of the two means, generic minus RLNAD, based on the log scale of AUC and C_{MAX} and then take the anti-log of the confidence limits multiplied by 100. The resulting bounds should be between 80.00% and 125.00%. As seen in the table below both AUC and C_{MAX} fall within the prescribed bounds. Time to maximum concentration (T_{MAX}) values obtained for the generic and RLNAD products indicate that these drugs will provide equivalent therapeutic results.

Table 1. Bioequivalence Evaluation

Variable	Merial Mean	Ancare Mean	Lower Bound	Upper Bound
AUC (mg/L)	0.32448*	0.34983*	97.39%	115.39%
C_{MAX} (mg/L)	−1.43335*	−1.46341*	96.68%	118.80%
T_{MAX} (hours)	7.2†	6.6†	NA	NA

*Geometric Mean
†Arithmetic Mean

Bioequivalence criteria are met for ivermectin B1a for both AUC (97% to 115%) and C_{MAX} (97% to 119%).

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 horses, which are not food producing animals.

VI. USER SAFETY:

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to Ivermectin Paste 1.87%:

Do not use in horses intended for human consumption.
Not for use in humans.
Keep this and all drugs out of the reach of children.
Refrain from smoking and eating when handling.
Wash hands after use.
Avoid contact with eyes.

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 Ivermectin Paste 1.87%, when used according to the label, is safe and effective.