Date of Approval: July 5, 2011

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-447

BIMECTIN Injection for Cattle and Swine
(ivermectin)

Injectable Solution

Cattle, swine, reindeer, and American bison

For the treatment and control of gastrointestinal roundworms (including inhibited *Ostertagia ostertagi* in cattle), lungworms, grubs, sucking lice, and mange mites of cattle; gastrointestinal roundworms, lungworms, lice and mange mites of swine; warbles (*Oedemagena tarandi*) in reindeer; and grubs (*Hypoderma bovis*) in American bison.

Sponsored by:

Cross Vetpharm Group Ltd.

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I. GENERAL INFORMATION:

A. File Number: ANADA 200-447

B. Sponsor: Cross Vetpharm Group Ltd.
Broomhill Rd.
Tallaght, Dublin 24, Ireland

Drug Labeler Code: 061623

U.S. Agent:
Linda M. Duple
Bimeda Inc.
2836 Dolliver Park Avenue
Lehigh, IA 50557

C. Proprietary Name: BIMECTIN Injection for Cattle and Swine

D. Established Name: Ivermectin

E. Pharmacological Category: Antiparasitic

F. Dosage Form: Injectable solution

G. Amount of Active Ingredient: 10 mg (1%) ivermectin/mL

H. How Supplied: 250 mL, 500 mL, and 1000 mL plastic bottles

I. How Dispensed: OTC

J. Dosages: Cattle: 200 mcg of ivermectin per kilogram of body weight (1 mL per 110 lb body weight).
Swine: 300 mcg of ivermectin per kilogram of body weight (1 mL per 75 lb body weight).
Reindeer: 200 mcg of ivermectin per kilogram of body weight.
American bison: 200 mcg of ivermectin per kilogram of body weight.

K. Route of Administration: Subcutaneous

L. Species/Classes: Cattle, swine, reindeer, and American bison

M. Indications:

Cattle: BIMECTIN Injection is indicated for the effective treatment and control of the following harmful species of gastrointestinal roundworms, lungworms, grubs, sucking lice, and mange mites in cattle:

Gastrointestinal Roundworms (adults and fourth-stage larvae):
Ostertagia ostertagi (including inhibited *O. ostertagi),*
O. lyrata
Haemonchus placei
Trichostrongylus axei
T. colubriformis
Cooperia oncophora
C. punctata
C. pectinata
Oesophagostomum radiatum
Bunostomum phlebotomum
Nematodirus helvetianus (adults only)
N. spathiger (adults only)

Lungworms (adults and fourth-stage larvae):
Dictyocaulus viviparus

Cattle Grubs (parasitic stages)**:**
Hypoderma bovis
H. lineatum

Sucking Lice:
Linognathus vituli
Haematopinus eurysternus
Solenopotes capillatus

Mites (scabies):
*Psoroptes ovis (*syn. *P. communis* var. *bovis)*
Sarcoptes scabiei var. *bovis.*

Persistent Activity
Ivermectin Injection has been proved to effectively control infections and to protect cattle from reinfection with *Dictyocaulus viviparus* and *Oesophagostomum radiatum* for 28 days after treatment; *Ostertagia ostertagi, Trichostrongylus axei,* and *Cooperia punctata* for 21 days after treatment; and *Haemonchus*

placei and *Cooperia oncophora* for 14 days after treatment.

Swine:
BIMECTIN Injection is indicated for the effective treatment and control of the following harmful species of gastrointestinal roundworms, lungworms, lice, and mange mites in swine:

Gastrointestinal Roundworms:
Large roundworm, *Ascaris suum* (adults and fourth-stage larvae)
Red stomach worm, *Hyostrongylus rubidus* (adults and fourth-stage larvae)
Nodular worm, *Oesophagostomum* spp. (adults and fourth-stage larvae)
Threadworm, *Strongyloides ransomi* (adults)

Somatic Roundworm Larvae:
Threadworm, *Strongyloides ransomi* (somatic larvae)
Sows must be treated at least seven days before furrowing to prevent infection in piglets.

Lungworms:
Metastrongylus spp. (adults)

Lice:
Haematopinus suis

Mange Mites:
Sarcoptes scabiei var. suis

Special Minor Use
Reindeer: For the treatment and control of warbles (*Oedemagena tarandi*).

American Bison: For the treatment and control of grubs (*Hypoderma bovis).*

N. Reference listed new animal drug: IVOMEC Injection for Cattle and Swine; ivermectin; NADA 128-409; Merial Ltd.

II. BIOEQUIVALENCE:

Under the provisions of the Federal Food, Drug and Cosmetic Act, as amended by the Generic Animal Drug and Paten 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). 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 time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an *in vivo* bioequivalence study. (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2002).

Based on the formulation characteristics of the generic product, Cross Vetpharm Group Ltd. was granted a waiver from the requirement for an *in vivo* bioequivalence study for the generic product BIMECTIN (ivermectin) Injection for Cattle and Swine. The generic product is administered subcutaneously, 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 absorption of the active ingredient. The RLNAD is IVOMAC (ivermectin), Injection for Cattle and Swine, sponsored by Merial Ltd., under NADA 128-409 and, was approved for use in cattle, swine, reindeer, and American bison on February 13, 1984.

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:

The following are assigned to this product for cattle, swine, reindeer, and American bison:

- **Tolerances for Residues:**
  The tolerances established for the pioneer product apply to the generic product. In liver (target tissue) a tolerance is established for 22,23-dihydroavermectin B1a (marker residue) as follows: (i) cattle 100 parts per billion (ppb), (ii) swine 20 ppb, (iii) reindeer 15 ppb, and (iv) American bison 15 ppb. In addition muscle residues are not indicative of the safety of other edible tissues. A tolerance is established for

22,23-dihydroavermectin B1a (marker residue) in muscle as follows: (i) swine 20 ppb and (ii) cattle 10 ppb, under 21 CFR 556.344. The acceptable daily intake (ADI) for total residues of ivermectin is 1 microgram per kilogram of body weight per day.

- **Withdrawal Times:**
  Because a waiver of the *in vivo* bioequivalence study was granted, the withdrawal times are those previously assigned to the pioneer product.

  Withdrawal periods of 35 days, 18 days, 56 days, and 56 days have been established for ivermectin in cattle, swine, reindeer, and American bison respectively.

- **Regulatory Method for Residues:**
  The official analytical methods for residues are HPLC methods with fluorescence detection. The validated regulatory analytical methods for detection and confirmation of residues of ivermectin are on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

VI. USER SAFETY:

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to BIMECTIN Injection for Cattle and Swine:

"Not For Use In Humans" and "Keep This And All Drugs Out Of The Reach Of Children."

VII. AGENCY CONCLUSIONS:

This information submitted in support of this ANADA satisfy the requirements of section 512(n) of the Federal Food, Drug, and Cosmetic Act and demonstrates that BIMECTIN Injection for Cattle and Swine, when used according to the label, is safe and effective for the treatment and control of gastrointestinal roundworms (including inhibited *Ostertagia ostertagi* in cattle), lungworms, grubs, sucking lice, and mange mites of cattle; gastrointestinal roundworms, lungworms, lice and mange mites of swine; warbles (*Oedemagena tarandi*) in reindeer; and grubs (*Hypoderma bovis*) in American bison.