Date of Approval: October 28, 2005

FREEDOM OF INFORMATION SUMMARY

NADA 141-214

ZIMECTERIN Gold Paste

ivermectin/praziquantel

This supplement amends the ZIMECTERIN Gold (ivermectin/praziquantel) Paste labeling to reflect the change in the age of treatment from "5 months of age and older" to "2 months of age and older."

Sponsored by:

Merial Ltd.
3329 Satellite Blvd.
Duluth, GA 30096

Table of Contents

1. GENERAL INFORMATION:

a.	File Number:	NADA 141-214
b.	Sponsor:	Merial Ltd. 3239 Satellite Blvd. Bldg. 500 Duluth, GA 30096-4640 Drug Labeler Code: 050604
c.	Established Name:	Ivermectin/praziquantel
d.	Proprietary Name:	ZIMECTERIN Gold Paste
e.	Dosage Form:	Paste containing 1.55 % ivermectin and 7.75% praziquantel
f.	How Supplied:	Individual dose syringe contains sufficient paste to treat one 1250 lb horse orally. Each weight marking on the syringe plunger delivers enough paste to treat 250 lb of body weight.
g.	How Dispensed:	OTC
h.	Amount of Active Ingredients:	Each syringe contains 113.8 mg of ivermectin and 567.5 mg praziquantel
i.	Route of Administration:	Oral
j.	Species/Class:	Equine
k.	Recommended Dosage:	91 mcg ivermectin per lb (200 mcg/kg) and 454 mcg praziquantel per lb (1.0 mg/kg) body weight
l.	Pharmacological Category:	Anthelmintic
m.	Indications:	For treatment and control of the following parasites in horses: **Tapeworms** - *Anoplocephala perfoliata*, **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 of *Onchocerca* sp.

n. Effect of Supplement: This supplement amends the ZIMECTERIN Gold (ivermectin/praziquantel) Paste labeling to reflect the change in the age of treatment from "5 months of age and older" to "2 months of age and older."

2. EFFECTIVENESS:

No new data was required for this supplement to NADA 141-214 (original approval April 17, 2003) and this supplement did not require review of the original effectiveness data for this product.

3. TARGET ANIMAL SAFETY:

Refer to the original FOI Summary for ZIMECTERIN Gold Oral Paste for Horses (NADA 141-214) dated April 17, 2003, for safety information relative to the use of the drug in horses older than 5 months of age. To support the safety of ZIMECTERIN Gold Oral Paste in younger horses, a 1X and 3X safety study was conducted in 7-10 week old foals. The treated foals were compared with the sham dosed foals in a masked fashion.

Oral Safety Study in Juvenile Foals (PR&D 0099701)

Purpose: To determine the safety profile of a combination of ivermectin plus praziquantel when administered in an oral paste formulation to juvenile horses at 1X and 3X the target use level three times at two-week intervals.

Study Director and Study Location: Luiz Carvalho, DVM, MSc.
Merial Uruguaiana Research Center
Uruguaiana RS, Brazil

Animals: 21 foals (14 males, 7 females), ranging in age from 7 to 10 weeks.

Dosage Form: Paste

Route of Administration: Oral

Dosage and Frequency of Treatment: Foals were dosed at two-week intervals, on Days 0, 14 and 28 of the study, for a total of three administrations, at 200 mcg/kg ivermectin plus 1.0 mg/kg praziquantel or 600 mcg/kg ivermectin plus 3.0 mg/kg praziquantel (1X and 3X, respectively). There were 7 foals per group and animals were dosed based on body weight.

Controls: 7 control foals (6 males, 1 female) were sham-dosed with empty syringes in the same manner as those treated with the test article.

Duration of Study: 43-44 days

Evaluation: Mares were observed on Day -7, and then daily from Day -6 to Day 43. Foals were observed prior to dosing daily from Day -14/-12 to Day -1; prior to dosing on Days 0, 14, and 28; following dosing on Days 0, 14, and 28 at ~1, 2, 3, and 12 hours post-dosing; and once 24 hours post-dosing (Days 1, 15, and 29) and on Day 43; and twice daily on non-treatment days. Physical examinations were conducted on each foal on Day -7, -1, 4 to 10 hours after dosing on Days 0, 14 and 28 and on Day 43. Examinations of the oral cavity were conducted on each foal on study Days 0, 14 & 28 pre-dosing and on Days 1, 15 and 29 post-dosing.

Blood samples were collected for hematology and clinical chemistry evaluation on Days -14/-12, on Day 0 before dosing, ~24 hours following dosing on Days 0, 14, and 28 (Days 1, 15, and 29, respectively) and on Day 43. An additional time point, Day -6, was included for analysis of hematology variables.

Statistical Methodology: Blood chemistry, hematology and continuous physical examination variables were analyzed by repeated measures analysis of covariance, with a mean of pre-treatment values as a covariate.

Results: All foals gained weight over the course of the study. There were no treatment related adverse effects on the general health of the foals as determined by daily observations, physical examinations, and oral examinations. Although there were several hematology and clinical chemistry variables that demonstrated

statistically significant differences from the controls, there was no clinical significance to any of these statistically significant findings.

Conclusion: Ivermectin plus praziquantel is safe when administered to two-month old foals at 200 mcg/kg ivermectin plus 1.0 mg/kg praziquantel (1X) or 600 mcg/kg ivermectin plus 3.0 mg/kg praziquantel (3X) on three consecutive occasions, at two-week intervals.

4. HUMAN SAFETY:

This drug is intended for use in horses, which are non-food animals. Because this new animal drug is not intended for use in food-producing animals, data on human safety pertaining to drug residues in food were not required for approval of this supplemental NADA.

Human Warnings are provided on the product label as follows: "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. Do not use in horses intended for human consumption."

5. AGENCY CONCLUSIONS:

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that ZIMECTERIN Gold Paste is safe and effective for the labeled claim.

The drug is available over-the-counter for lay use. Routine deworming of horses is a widely accepted and recommended practice performed by the layperson. A diagnosis of parasite infection prior to deworming is not necessary. The syringe carton and package outsert contain adequate directions for use.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of approval. The three years of marketing exclusivity applies only to the change in the age of treatment from 5 months of age and older to 2 months of age and older for which this supplement is approved. A safety study was conducted in foals 2 months of age and older to support the safety of ZIMECTERIN Gold Paste.

According to the Center's supplemental approval policy (21 CFR 514.106), this is a Category II change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug. Accordingly, this approval did not require a reevaluation of the safety and effectiveness data in the parent application.

A U.S. patent for ZIMECTERIN Gold Paste is pending.

6. ATTACHMENTS:

Facsimile labeling is attached as indicated below:

Package Outsert

Syringe Label

Syringe Carton