FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

MILBEMITE™ OTIC Solution

NADA 141-163

"…indicated for the treatment of ear mite (*Otodectes cynotis*) infestations in cats and kittens four weeks of age and older."

Sponsored by:

Novartis Animal Health US, Inc.

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I. GENERAL INFORMATION:

NADA Number: NADA 141-163

Sponsor: Novartis Animal Health US, Inc.
3200 Northline Avenue
Suite 300
Greensboro, NC 27408

Generic Name: Milbemycin Oxime Solution

Trade Name: MILBEMITE™ OTIC Solution

Marketing Status: Rx

Supplement Effect: This supplement provides target animal safety study data to lower the age limitation of the product from 8 to 4 week old kittens and to allow a repeat treatment if necessary.

II. INDICATIONS FOR USE:

MILBEMITE OTIC Solution is indicated for the treatment of ear mite (*Otodectes cynotis)* infestations in cats and kittens four weeks of age and older. Effectiveness is maintained throughout the life cycle of the ear mite.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION AND DOSAGE:

MILBEMITE OTIC Solution is a 0.1% solution of milbemycin oxime. MILBEMITE OTIC Solution is recommended for use in cats and kittens four weeks of age and older.

Dosage Form: 0.1% milbemycin oxime solution

Route of Administration: Topical application into the external ear canal

Dosage and Administration: Administer one ampoule per ear followed by massaging the base of the ear to distribute the drug**.** Cleaning of the external ear canal prior to treatment may be performed, but is not necessary to provide effectiveness. Repeat the treatment one time if necessary, based upon the ear mite life cycle and the response to treatment.

IV. EFFECTIVENESS:

The effectiveness of the product is not affected by this supplement. Refer to the FOI Summary for the original approval of MILBEMITE OTIC Solution dated February 2, 2000.

V. TARGET ANIMAL SAFETY:

The supplement provides additional safety data for use on kittens. Refer to the FOI Summary for the original approval of MILBEMITE OTIC Solution dated February 2, 2000.

A. Kitten Safety Study

Title: A Study of Milbemycin Oxime Solution for the Treatment of Ear Mites (*Otodectes cynotis*) on Kittens Four Weeks of Age.

Purpose: To demonstrate the safety of 1, 3 or 5X equivalent-doses of milbemycin oxime solution administered weekly, for six treatments, in the ears of kittens (4 weeks of age).

Investigator/Study Location: Sharon A Sickles, DVM, PhD
Liberty Research, Incorporated
170 State Route 17C
Waverly, New York 14892

Animals: 32 kittens (16 males and 16 females), 4 weeks of age, 8 animals per group (4 males and 4 females).

Doage groups:

Treatment	No. of Kittens		Dose*
	Males	Females	
0X	4	4	0.2 ml control solvent (mineral oil) / ear
1X	4	4	0.2 ml 0.1% milbemycin oxime solution / ear
3X	4	4	0.2 ml 0.3% milbemycin oxime solution / ear
5X	4	4	0.2 ml 0.5% milbemycin oxime solution / ear

* The specified treatment was applied to both ears per kitten on study days 0, 7, 14, 21, 28, and 35.

Route of Administration: Topical application to both ear canals of each animal.

Frequency of Treatment: Once weekly for six applications.

Duration of Study: 42 days**.**

Parameters measured: A physical exam was performed prior to study initiation. The cats were examined daily to determine pharmacologic and/or toxicologic drug effects, and for dermal irritation in the ears. At study termination, the external ear canals were biopsied and examined histologically for dermal irritation and inflammation. Body weights and food consumption were recorded throughout the study.
Results: All cats survived to termination of the study. No test article-related changes were seen in the body weights, food consumption, physical, and macroscopic or

microscopic pathology. One female kitten in the 0.5% treatment group was lethargic 8 hours after the second treatment. The kitten was offered milk replacer and by 10 hours post-treatment it appeared normal. After subsequent treatments (3, 4, 5, and 6) no additional lethargy was noted.

Conclusions: Otic doses of 0.1% milbemycin oxime can be administered safely to kittens 4 weeks of age. Based on the duration of this study (6 treatments), the label can provide for a repeat treatment, if necessary.

VI. HUMAN SAFETY:

Data on human safety, pertaining to consumption of drug residues in food, were not required for approval of this NADA. This drug is to be labeled for use in cats which are non-food animals.

Human Warnings are provided on the product label as follows: **"**Not for human use. Keep this and all drugs out of the reach of children."

VII. AGENCY CONCLUSIONS:

The data in support of this supplemental NADA comply with the requirements of Section 512 of the Act and Section 514 of the implementing regulations. The data demonstrate that MILBEMITE OTIC Solution, when used under the labeled conditions of use, is safe and effective.

The drug is restricted to use by or on the order of a licensed veterinarian to monitor the safe use of this new product.

Under section 512(c)(2)(F)(iii) of the FFDCA, this approval for non-food producing animals qualifies for three years of marketing exclusivity beginning on the date of approval because the application contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety required for the approval of the application and conducted or sponsored by the applicant.

Novartis holds patent No. 4,547,520 which expires June 14, 2004.

VIII. LABELING (ATTACHED):

A. Veterinarian Insert
B. Foil Pouch
C. Tube Label
D. Unit Dose Carton