Date of Approval: Jun 13 2000

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-152

REVOLUTION™
(selamectin)

"...kills adult fleas and prevents flea eggs from hatching for one month and is indicated for the prevention and control of flea infestations (*Ctenocephalides felis*), prevention of heartworm disease caused by *Dirofilaria immitis*, and the treatment and control of ear mite (*Otodectes cynotis*) infestations in cats and dogs. Revolution also is indicated for the treatment and control of sarcoptic mange (*Sarcoptes scabiei*) and for the control of tick (*Dermacentor variabilis*) infestations in dogs, and the treatment and **control of intestinal hookworm (*Ancylostoma tubaeforme*) and roundworm (*Toxocara cati*) infections in cats**. Revolution is recommended for use in dogs and cats six weeks of age and older."

Sponsored by:

PFIZER, INC

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FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

NADA Number: 141-152

Sponsor: Pfizer Inc.
235 East 42nd St.
New York, NY 10017

Generic Name: Selamectin

Trade Name: Revolution™

Marketing Status: Rx: U.S. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Effect of Supplement: Provide additional indication for control of intestinal hookworm (*Ancylostoma tubaeforme*) and roundworm (*Toxocara cati*) infections in cats. The indication for the treatment of intestinal hookworm (*Ancylostoma tubaeforme*) and roundworm (*Toxocara cati*) infections in cats was previously approved with the original approval of Revolution.

II. INDICATIONS FOR USE

Revolution kills adult fleas and prevents flea eggs from hatching for one month and is indicated for the prevention and control of flea infestations (*Ctenocephalides felis*), prevention of heartworm disease caused by *Dirofilaria immitis,* and the treatment and control of ear mite (*Otodectes cynotis*) infestations in dogs and cats. Revolution also is indicated for the treatment and control of sarcoptic mange (*Sarcoptes scabiei*) and for the control of tick (*Dermacentor variabilis*) infestations in dogs, and the treatment and control of intestinal hookworm (*Ancylostoma tubaeforme*) and roundworm (*Toxocara cati*) infections in cats. Revolution is recommended for use in dogs and cats six weeks of age and older.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND DOSAGE

The recommended minimum dose is 2.7 mg selamectin per pound (6 mg/kg) of body weight. Administer the entire contents of a single dose tube of Revolution topically in accordance with the following tables.

Cats (lb)	Package color	mg per tube	Potency (mg/mL)	Administered volume (mL)
up to 5	Mauve	15 mg	60	0.25
5.1-15	Blue	45 mg	60	0.75

For cats over 15 lbs., use the appropriate combination of tubes

Dogs (lb)	Package color	mg per tube	Potency (mg/mL)	Administered volume (mL)
up to 5	Mauve	15 mg	60	0.25
5.1-10	Purple	30 mg	120	0.25
10.1-20	Brown	60 mg	120	0.5
20.1-40	Red	120 mg	120	1.0
40.1-85	Teal	240 mg	120	2.0

For dogs over 85 lbs., use the appropriate combination of tubes

IV. EFFECTIVENESS STUDIES

Effectiveness and Safety of Selamectin in the Treatment and Control of Natural Infestations of Hookworms and Ascarids in Cats Presented as Veterinary Patients. Study #'s 1283C-60-95-156, 1283C-60-95-158, 1283C-60-95-159, 1283C-60-96-194, and 1283C-60-96-195.

Purpose: To demonstrate the effectiveness and safety of selamectin in the treatment and control of natural infections of nematodes in cats presented as veterinary patients.

Study Locations and Investigators:

Louis Burch, DVM
The Animal Medical Center
340 North 6th Street
Redland, CA 92374
1283C-60-95-158

H. Lee Butler, DVM
280 Veteran's Drive North
Huntington, TN 38344
1283C-60-96-195

Raymond L. Ewing DVM
Atglen Veterinary Hospital
150 Pine Creek Drive
Christiana, PA 17509
1283C-60-95-159

Suzanne M. Hirsch, DVM
Range Avenue Veterinary Hospital
513 North Range Avenue
Denham Springs, LA 70726
1283C-60-96-194

B. Britton Stringer, DVM
River Oaks Animal Hospital
14471 Old Hammond Highway
Baton Rouge, LA 70816
1283C-60-95-156

Animals: Eighty-three cats (36 females and 47 males), 7 weeks to 11 years of age were enrolled. Of these, 70 were considered evaluable for safety and effectiveness. Fifty-one were treated with the test article, selamectin (20 females and 31 males) and 19 (9 females and 10 males) with the control, pyrantel pamoate plus praziquantel. Of the 70 cases evaluated, 7 cats had hookworm infections only, 45 cats had roundworm infections only and 18 cats had both hookworm and roundworm infections.

Dosage Groups: T1: selamectin ≥6 mg/kg

T2: pyrantel pamoate (20 mg/kg) plus praziquantel (5 mg/kg) Drontal™

Route of Administration: T1: Topical
T2: Oral tablet

Frequency of Administration: Monthly for 2 months

Duration of Study: 60 days

Parameters measured: Effectiveness was assessed on the basis of a reduction in the number of hookworm and/or roundworm eggs in fecal samples collected from each cat on days 30 and 60, as compared to eggs in fecal samples collected prior to treatment on day 0.

Results: Effectiveness of 6 mg/kg selamectin against *A. tubaeforme* and *T. cati* in cats is shown in the table 1:

Table 1: Geometric Mean Fecal Egg Counts for both Roundworm and Hookworm Infections Prior to Treatment and 30 Days After Each Treatment with % Effectiveness in parenthesis

Treatment[a]	**Geometric Mean Roundworm/Hookworm Egg Counts and % Effectiveness**[d]		
Selamectin	Day 0	Day 30	Day 60
Roundworms[b]	101.3	0.5[e] (99.5%)	0.0[f] (100%)
Hookworms[c]	70.9	0.8[e] (98.8%)	0.0[f] (100%)
Drontal			
Roundworms[b]	89.6	0.5[e] (99.4%)	0[f] (100%)
Hookworms[c]	57.4	1.1[e] (98.0%)	0.3[f] (99.5%)

[a] Treatments were administered on days 0 and 30
[b] There were 49 selamectin-treated cats and 14 Drontal-treated cats.
[c] There were 17 selamectin-treated cats and 8 Drontal-treated cats.
[d] Day 30 as compared to day 0, day 60 as compared to day 0
[e] Day 30 was significantly different from day 0 (P=0.0001)
[f] Day 60 was significantly different from day 0 (P=0.0001)

The 95% confidence intervals for the differences in fecal egg counts between treatment groups on each day are presented in Table 2 and 3 for each species.

Table 2: 95% Confidence Intervals for Hookworms

Day	95% Lower Limit	95% Upper Limit
0	-0.57	2.50
30	-0.70	1.43
60	-0.74	1.07

Table 3: 95% Confidence Intervals for Roundworms

Day	95% Lower Limit	95% Upper Limit

0	-0.58	2.06
30	-0.53	1.05
60	-0.09	0.18

The confidence intervals for the treatment differences indicate that cats in each treatment group had similar fecal egg counts on Day 0 and differed by fewer than 2 eggs per gram of feces on Day 30 onwards.

Conclusions: Selamectin administered topically at monthly intervals at a minimum dose of 6 mg/kg was safe and effective in the control of natural infections of *T. cati* and *A. tubaeforme*.

Adverse Drug Reactions: Two cats treated with selamectin were observed to be drowsy or lethargic following administration of the drug.

V. Animal Safety Studies

Target animal safety studies in support of this supplement are referenced in the FOI Summary for the original NADA 141-152 approval dated May 26, 1999. Additional safety studies were not necessary for this supplemental application.

VI. Human Safety

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

Human warnings are provided on the product label as follows: "May be irritating to skin and eyes. Wash hands after use and wash off any product in contact with the skin immediately with soap and water. If contact with eyes occurs, then flush eyes copiously with water. In case of ingestion by a human, contact a physician immediately. The material safety data sheet (MSDS) provides more detailed occupational safety information. For a copy of the MSDS or to report adverse reactions attributable to exposure to this product, call 1-800-366-5288

Flammable – Keep away from heat, sparks, open flames or other sources of ignition."

VII. Agency Conclusions

The data in support of this NADA comply with the requirements of Section 512 of the Act and Section 514 of the implementing regulations. The data demonstrate that Revolution (selamectin) topical for cats, when used under labeled conditions of use, is effective against hookworm (*Ancylostoma tubaeforme*) and roundworm (*Toxocara cati*) infections.

The drug is restricted to use by or on the order of a licensed veterinarian because professional expertise and proper diagnosis are required to determine the existence of heartworm infections and sarcoptic mange infestations and to monitor the safe use of the 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 supplemental application contains substantial evidence of the effectiveness of the drug involved,

or any studies of animal safety, required for the approval of the application and conducted or sponsored by the applicant. The three years of marketing exclusivity applies to only the indication for the control of hookworm (*Ancylostoma tubaeforme*) and roundworm (*Toxocara cati*) infections for which the supplemental application was approved.

Pfizer, Inc. Patent No. 5,981,500

VIII. Labeling (Attached)

A. Package Insert
B. Carton Label for cats (15 mg and 45 mg)