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 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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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 tick (*Dermacentor variabilis*) infestations in dogs.

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 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

1. Effectiveness Confirmation Against Adult Ticks (*Dermacentor variabilis)*: 1061E-60-98-242

   Purpose: To evaluate the effectiveness of a topical unit dose of 6 mg/kg of selamectin, administered either every 2 weeks or monthly for 3 months, against experimental infestations of adult *Dermacentor variabilis* on dogs.

   Investigator: J. A. Hair, Ph.D.

   Study Location: Nu-Era Farms
   Stillwater, Oklahoma

   Animals: 24 dogs (12 males and 12 females), 4 months to 8 years of age, 8 per treatment group.

   Tick Strain: Nu Era Farms source, wild ticks introduced every 2 years. Ticks originated from Oklahoma.

   Dosage Groups: T1: Placebo
   T2: Selamectin (≥6 mg/kg)
   T3: Selamectin (≥6 mg/kg)

   Route of Administration: Topical

   Frequency of Treatment: T1: Every 2 weeks x 6
   T2: Every 2 weeks x 6
   T3: Monthly x 3

   Duration of Study: 90 days

   Parameters measured: Each dog was infested with 50 unfed, viable adult *D. variabilis* ticks on days 2, 9, 16, 25, 32, 39, 46, 55, 62, 69, 76, and 85. The number of viable, attached adult ticks were counted on the third and fourth days post-infestation. The fifth day post-infestation, the ticks were counted, removed, and sexed. Ticks were removed and counted prior to treatment if both fell on the same day. Dogs were observed twice a day. On treatment days, dogs were observed prior to treatment, within 10 minutes post-treatment and approximately 2 and 8 hours post-treatment.
   Results: For dogs treated every two weeks or monthly with selamectin the percent reduction in mean tick counts on the fifth day post infestation were as noted in the tables below:

Percent Reduction in Mean Tick Counts on the Fifth Day After Tick Infestation Following Administration Every Two Weeks

Day of Treatment	Day of Tick Infestation	[1] Percent Reduction Five Days Post-Tick Infestation
0	2	80.8
	9	79.3
14	16	97.4
	25	98.4
30	32	99.6
	39	98.9
44	46	100
	55	100
60	62	100
	69	99.5
74	76	100
	85	98.8

[1] Percent reduction on the fifth day after tick infestation, compared to placebo.

Percent Reduction in Mean Tick Counts on the Fifth Day After Tick Infestation Following Administration Once a Month

Day of Treatment	Day of Tick Infestation	[1] Percent Reduction Five Days Post-Tick Infestation
0	2	55.9
	9	88.8
	16	77.5
	25	43.9
30	32	99.3
	39	98.1
	46	99.6
	55	97.8
60	62	99.5
	69	98.5
	76	98.5
	85	98.0

[1] Percent reduction on the fifth day after tick infestation, compared to placebo.

Conclusions: Monthly administration of selamectin providing a minimum topical dose of 6 mg/kg was effective in controlling *Dermacentor variabilis* ticks on dogs after a second dose was applied. A second dose at 14 days provided control more rapidly.

Adverse Drug Reactions: None observed

2. Effectiveness Confirmation Against Adult Ticks (*Dermacentor variabilis)*: 1061C-60-98-255

Purpose: To evaluate the effectiveness of a topical unit dose of 6 mg/kg of selamectin, administered monthly for 3 months or monthly for 3 months with an additional treatment administration 2 weeks after the first monthly treatment, against experimental infestations of adult *Dermacentor variabilis* on dogs.

Investigator: J. A. Hair, Ph.D.

Study Location: Nu-Era Farms
Stillwater, Oklahoma

Animals: 24 dogs (12 males and 12 females), 10 to 51 months of age, 8 per treatment group.

Tick Strain: EL Labs source, wild ticks have not been introduced. This strain has been in the laboratory for 7 years. Ticks originated from California.

Dosage Groups: T1: Placebo
T2: Selamectin (≥6 mg/kg)
T3: Selamectin (≥6 mg/kg)

Route of Administration: Topical

Frequency of Treatment: T1 and T2: Days 0, 14, 30 and 60
T3: Monthly x 3

Duration of Study: 90 days

Parameters measured: Each dog was infested with 50 unfed, viable adult *D. variabilis* ticks on days 2, 9, 16, 25, 32, 39, 46, 55, 62, 69, 76, and 85. The number of viable, attached adult ticks were counted on the third and fourth days post-infestation. The fifth day post-infestation, the ticks were counted, removed, and sexed. Ticks were removed and counted prior to treatment if both fell on the same day. Dogs were observed twice a day. On treatment days, dogs were observed prior to treatment, within 10 minutes post-treatment and approximately 2 and 8 hours post-treatment.

Results: The percent reduction in mean tick counts for dogs treated with selamectin either monthly or monthly with an additional treatment 2 weeks after the first monthly treatment are noted in the tables below:

Percent Reduction in Mean Tick Counts on the Fifth Day After Tick Infestation Following Administration Once a Month with an Additional Treatment on Day 14

Day of Treatment	Day of Tick Infestation	[1] Percent Reduction Five Days Post-Tick Infestation

0	2	99.5
	9	97.6
14	16	98.2
	25	97.1
30	32	99.3
	39	99.3
	46	94.5
	55	94.5
60	62	99.6
	69	99.6
	76	98.7
	85	94.8

[1] Percent reduction on the fifth day after tick infestation, compared to placebo.

Percent Reduction in Mean Tick Counts on the Fifth Day After Tick Infestation Following Administration Once a Month

Day of Treatment	Day of Tick Infestation	[1] Percent Reduction Five Days Post-Tick Infestation
0	2	99.0
	9	94.5
	16	96.0
	25	94.5
30	32	99.6
	39	98.5
	46	92.0
	55	99.2
60	62	100
	69	97.6
	76	99.0
	85	89.6

[1] Percent reduction on the fifth day after tick infestation, compared to placebo.

Conclusions: Administration of selamectin providing a minimum topical dose of 6 mg/kg was effective in controlling *Dermacentor variabilis* on dogs when used either monthly or monthly with an additional treatment 2 weeks after the first treatment.

Adverse Drug Reactions: None observed

3. Effectiveness Confirmation Against Adult Ticks (*Dermacentor variabilis)*:
1061C-60-98-256

Purpose: To evaluate the effectiveness of a topical unit dose of 6 mg/kg of selamectin, administered monthly for 3 months or monthly for 3 months with an additional treatment administration 2 weeks after the first monthly treatment, against experimental infestations of adult *Dermacentor variabilis* on dogs.

Investigator: D. R. Young, Ph.D.

Study Location: Young Veterinary Research Services
Turlock, California

Animals: 24 dogs (12 males and 12 females), 10 to 21 months of age, 8 per treatment group.

Tick Strain: Oklahoma State University source, wild ticks introduced every 3 years. Ticks originally collected from around Oklahoma State University.

Dosage Groups: T1: Placebo
T2: Selamectin (≥6 mg/kg)
T3: Selamectin (≥6 mg/kg)

Route of Administration: Topical

Frequency of Treatment: T1 and T2: Days 0, 14, 30 and 60
T3: Monthly x 3

Duration of Study: 90 days

Parameters measured: Each dog was infested with 50 unfed, viable adult *D. variabilis* ticks on days 2, 9, 16, 25, 32, 39, 46, 55, 62, 69, 76, and 85. The number of viable, attached adult ticks were counted on the third and fourth days post-infestation. The fifth day post-infestation, the ticks were counted, removed, and sexed. Ticks were removed and counted prior to treatment if both fell on the same day. Dogs were observed twice a day. On treatment days, dogs were observed prior to treatment, within 10 minutes post-treatment and approximately 2 and 8 hours post-treatment.

Results: The percent reduction in mean tick counts for dogs treated with selamectin either monthly or monthly with an additional treatment 2 weeks after the first monthly treatment are noted in the tables below:

Percent Reduction in Mean Tick Counts on the Fifth Day After Tick Infestation Following Administration Once a Month with an Additional Treatment on Day 14

Day of Treatment	Day of Tick Infestation	[1] Percent Reduction Five Days Post-Tick Infestation
0	2	97.3
	9	82.5
14	16	98.4
	25	81.6

30	32	96.3
	39	96.1
	46	50.8
	55	23.1
60	62	98.8
	69	95.0
	76	40.5
	85	(2.6)

[1] Percent reduction on the fifth day after tick infestation, compared to placebo.

Percent Reduction in Mean Tick Counts on the Fifth Day After Tick Infestation Following Administration Once a Month

Day of Treatment	Day of Tick Infestation	[1] Percent Reduction Five Days Post-Tick Infestation
0	2	97.8
	9	92.4
	16	30.5
	25	16.3
30	32	93.8
	39	87.4
	46	56.6
	55	34.0
60	62	97.6
	69	96.5
	76	51.4
	85	29.2

[1] Percent reduction on the fifth day after tick infestation, compared to placebo.

Conclusions: In this study monthly administration of selamectin providing a minimum topical dose of 6 mg/kg was effective in controlling *Dermacentor variabilis* on dogs for two weeks after each treatment administration. One additional dose on Day 14 provided additional control for two more weeks.

Adverse Drug Reactions: None observed

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 dogs, when used under labeled conditions of use, is effective against tick (*Dermacentor variabilis*) infestations.

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 tick (*Dermacentor variabilis*) infestations for which the supplemental application was approved.

Pfizer, Inc. patent pending in the U.S.

VIII. Labeling (Attached)

A. Package Insert
B. Carton Label