Date of Approval: December 14, 2023

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-502

revolution® PLUS

(selamectin and sarolaner topical solution)

Cats

This supplement provides for the addition of the indication for the treatment and control of tick infestations with *Amblyomma americanum* (lone star tick) for one month in cats and kittens 8 weeks and older, and weighing 2.8 pounds or greater.

Sponsored by:

Zoetis Inc.

Executive Summary

revolution® PLUS (selamectin and sarolaner topical solution) is approved for the treatment and control of *Amblyomma americanum* (lone star tick) infestations for one month in cats and kittens 8 weeks and older, and weighing 2.8 pounds or greater. revolution® PLUS is an antiparasitic drug that is administered topically using the supplied applicator tubes.

revolution® PLUS is already approved to prevent heartworm disease in cats. revolution® PLUS kills adult fleas and is approved to treat and prevent flea infestations, treat and control tick infestations [*Ixodes scapularis* (black-legged tick), *Amblyomma maculatum* (Gulf Coast tick) and *Dermacentor variabilis* (American dog tick)], treat and control ear mite (*Otodectes cynotis*) infestations, and treat and control roundworm (*Toxocara cati*) and intestinal hookworm (*Ancylostoma tubaeforme*) infections for one month in cats and kittens 8 weeks and older, and weighing 2.8 pounds or greater.

Safety and Effectiveness

The sponsor conducted four laboratory studies to show that revolution® PLUS is effective against *A. americanum* tick infestations in cats. In each study, cats were experimentally infested with viable, unfed, adult ticks on Day -2 and then subsequently infested weekly through Day 33. On Day 0, cats in the treatment group were given revolution® PLUS and cats in the control group were given vehicle control. The vehicle control contained all the inactive ingredients in revolution® PLUS but contained no selamectin or sarolaner. Tick counts were performed on Day 3 (72 hours after treatment) and 72 hours after each subsequent infestation.

When the results of the four studies were averaged, revolution® PLUS was greater than 90% effective at controlling *A. americanum* tick infestations (reducing the number of live ticks) for one month. Cats in the control group remained infested with live ticks at each tick count. revolution® PLUS was also effective in treating *A. americanum* tick infestations. Compared to cats in the control group, treated cats had a higher number of dead ticks following infestation for one month. Two cats treated with revolution® PLUS had mild gastrointestinal signs that resolved without treatment.

The Freedom of Information (FOI) Summary for the original approval of revolution® PLUS, dated November 9, 2018, contains a summary of target animal safety studies for cats.

The labeling for revolution® PLUS includes safety information for people who handle the drug. People, including children, should not touch the application site for 4 hours after the dose is given.

Conclusions

Based on the data submitted by the sponsor for the approval of revolution® PLUS, the FDA determined that the drug is safe and effective when used according to the labeling.

Table of Contents

I. GENERAL INFORMATION

A. File Number

NADA 141-502

B. Sponsor

Zoetis Inc.
333 Portage St.
Kalamazoo, MI 49007

Drug Labeler Code: 054771

C. Proprietary Name

revolution® PLUS

D. Drug Product Established Name

selamectin and sarolaner topical solution

E. Pharmacological Category

Antiparasitic

F. Dosage Form

Topical Solution

G. Amount of Active Ingredient

60 mg/mL selamectin
10 mg/mL sarolaner

H. How Supplied

revolution® PLUS is available in 0.25 mL, 0.5 mL, or 1 mL applicator tubes in cartons containing 1, 3, or 6 tubes.

I. Dispensing Status

Prescription (Rx)

J. Dosage Regimen

The recommended minimum dosage is 2.7 mg selamectin per pound (6.0 mg/kg) of body weight in combination with 0.45 mg sarolaner per pound (1.0 mg/kg) of body weight administered monthly.

K. Route of Administration

Topical

L. Species/Class

Cats

M. Indication

revolution® PLUS is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis*. revolution® PLUS kills adult fleas (*Ctenocephalides felis*) and is indicated for the treatment and prevention of flea infestations, the treatment and control of tick infestations with *Amblyomma americanum* (lone star tick), *Amblyomma maculatum* (Gulf Coast tick), *Dermacentor variabilis* (American dog tick), and *Ixodes scapularis* (black-legged tick), the treatment and control of ear mite (*Otodectes cynotis*) infestations, and the treatment and control of roundworm (*Toxocara cati*) and intestinal hookworm (*Ancylostoma tubaeforme*) infections for one month in cats and kittens 8 weeks and older, and weighing 2.8 pounds or greater.

N. Effect of Supplement

This supplement provides for the addition of the indication for the treatment and control of tick infestations with *Amblyomma americanum* (lone star tick) for one month in cats and kittens 8 weeks and older, and weighing 2.8 pounds or greater.

II. EFFECTIVENESS

The effectiveness of revolution® PLUS against *Amblyomma americanum* was demonstrated in four well-controlled laboratory studies (A186C-US-19-230, A186C-US-20-244, A186C-US-21-259, and A186C-US-22-280) described below. Study A186C-US-19-230 and Study A186C-US-21-259 demonstrated > 90% effectiveness at all timepoints, except at Day 3 (72 hours) for both studies and at Day 36 for Study A186C-US-19-230. However, when combined with Study A186C-US-20-244 and Study A186C-US-22-280, the average effectiveness against *Amblyomma americanum* at Day 3 and Day 36 is > 90% (92.5% and 96.9%, respectively). These studies demonstrated that revolution® PLUS is effective for the treatment and control of *Amblyomma americanum* (lone star tick) infestations for one month in cats and kittens 8 weeks and older, and weighing 2.8 pounds or greater.

A. Dosage Characterization

This supplemental approval does not change the previously approved dose of 2.7 mg selamectin per pound (6.0 mg/kg) of body weight in combination with 0.45 mg sarolaner per pound (1.0 mg/kg) of body weight administered monthly. The Freedom of Information (FOI) Summary for the original approval of NADA 141-502 dated November 9, 2018, contains dosage characterization information for cats.

B. Substantial Evidence

1. Laboratory Dose Confirmation Study A186C-US-19-230

   Title: Dose Confirmation of revolution® PLUS (selamectin and sarolaner topical solution) Against Induced Infestations of *Amblyomma americanum* on Cats. (Study No. A186C-US-19-230)

Study Dates: September 8, 2019, to April 22, 2020

Study Location: Turlock, CA

Study Design:

Objective: To confirm the efficacy of sarolaner (dosed at 1.0 mg/kg) in combination with selamectin (dosed at 6.0 mg/kg) applied topically against induced infestations of *Amblyomma americanum* for up to 36 days on cats.

Study Animals: Twenty domestic shorthair cats (11 males and 9 females), 16 to 34 months of age, and 2.3 to 5.8 kg body weight.

Experimental Design: This study was a vehicle-controlled, masked, randomized complete block study design. Cats were randomly assigned to the vehicle control group (10 cats) or the revolution® PLUS group (10 cats). Each cat was infested with approximately 50 unfed, wild-caught, adult *A. americanum* ticks (approximately equal numbers of males and females) on Days -2, 5, 12, 19, 26, and 33. Elizabethan collars were fitted to the cats to avoid removal of the ticks by self-grooming at infestation; the collars were temporarily removed prior to dosing on Day 0 and prior to tick counts. Ticks were counted and removed on Days 3, 8, 15, 22, 29, and 36. The study was conducted in accordance with Good Clinical Practice (GCP) guidance.

Table II.1. Treatment Groups for Study A186C-US-19-230

Treatment Group	Treatment	Day of Treatment	Cats per Group	Days of Tick Infestation	Days of Tick Count
T01	Vehicle control	Day 0	10	Days -2, 5, 12, 19, 26, and 33	Days 3, 8, 15, 22, 29, and 36
T02	revolution® PLUS	Day 0	10	Days -2, 5, 12, 19, 26, and 33	Days 3, 8, 15, 22, 29, and 36

Drug Administration: All treatments were applied topically to the skin at the base of the neck directly in front of the shoulder blades on Day 0.

Measurements and Observations: General health observations were conducted at least once daily. Clinical observations and administration site evaluations were conducted prior to treatment on Day 0 and at 1, 3, 6, and 24 hours after treatment. Administration sites were also evaluated on Days 3, 5, and 36. At each tick count, the numbers of live and dead ticks were counted and removed from the cats on Days 3, 8, 15, 22, 29, and 36.

Statistical Methods:

Post-treatment live (free + attached) and dead (free + attached) tick counts were summarized for each individual cat at each time point and analyzed using a linear mixed model by time point. The model included the fixed effect of treatment and the random effects of block and error. Least squares mean counts were reported by treatment group at each time point. Comparison of mean live tick counts was conducted between the revolution® PLUS group and the control group using contrasts at the (two-sided) 5% significance level.

Percent effectiveness of the revolution® PLUS group with respect to the control group was calculated using least squares mean (LSM) at each time point with the formula [(C – T) / C] X 100, where C = LSM of live tick counts for the control group and T = LSM of live tick counts for the revolution® PLUS group for each time point.

Results:

The control group met the definition for adequate tick infestations throughout the study with at least 6 of the 10 cats having 12 or more ticks after each infestation.

The revolution® PLUS group had an 89.7% reduction in the initial live tick counts 72 hours after treatment, and ≥ 99.7% reduction in live tick counts 72 hours after weekly re-infestations, except for the Day 36 count which had an 88.7% reduction in live tick counts (Table II.2).

Mean live tick counts for the revolution® PLUS group were less than the control group and there was a statistically significant difference between the treated group and control group at all time points (P ≤ 0.0002).

Table II.2. LSM live tick counts and percent effectiveness for revolution® PLUS for the control of induced *Amblyomma americanum* infestations of cats, 72 hours after treatment of the initial infestation and after weekly re-infestations; Study A186C-US-19-230

Day of Tick Count	Control Group LSM Live Tick Count	revolution® PLUS LSM Live Tick Count	Percent Effectiveness
3	30.2	3.1	89.7%
8	30.2	0.0	100%
15	28.6	0.0	100%
22	29.0	0.1	99.7%
29	31.5	0.0	100%
36	27.4	3.1	88.7%

The LSM dead tick counts for the revolution® PLUS group were greater than the control group and there was a statistically significant difference between the revolution® PLUS group and control group on all post-treatment count days (P < 0.0001).

Table II.3. LSM dead tick counts for revolution® PLUS for the control of induced *Amblyomma americanum* infestations of cats, 72 hours after treatment of the initial infestation and after weekly re-infestations; Study A186C-US-19-230

Day of Tick Count	Control Group LSM Dead Tick Count	revolution® PLUS LSM Dead Tick Count
3	0.0	14.4
8	0.0	23.5
15	0.0	23.4
22	0.0	24.0
29	0.0	21.0
36	0.0	19.3

Adverse Reactions: No adverse reactions were reported in this study.

Conclusions: A single topical treatment of revolution® PLUS (1.0 mg/kg sarolaner + 6.0 mg/kg selamectin) was less than 90% effective against *A. americanum* ticks on Day 3 and Day 36, but greater than 90% effective on Days 8 through 29 when assessed 72 hours after treatment and after weekly re-infestations for one month.

2. Laboratory Dose Confirmation Study A186C-US-20-244

Title: Dose Confirmation of revolution® PLUS (selamectin and sarolaner topical solution) Against Induced Infestations of *Amblyomma americanum* on Cats. (Study No. A186C-US-20-244)

Study Dates: May 27, 2020, to November 21, 2020

Study Location: Nowata, OK

Study Design:

Objective: To confirm the efficacy of sarolaner (dosed at 1.0 mg/kg) in combination with selamectin (dosed at 6.0 mg/kg) applied topically against induced infestations of *Amblyomma americanum* for up to 36 days on cats.

Study Animals: Twenty domestic shorthair cats (9 males and 11 females), 49 to 65 months of age, and 2.5 to 4.5 kg body weight.

Experimental Design: This study was a vehicle-controlled, masked, randomized complete block study design. Cats were randomly assigned to the vehicle control group (10 cats) or the revolution® PLUS group (10 cats). Each cat was infested with approximately 50 unfed, wild-caught, adult *A. americanum* ticks (approximately equal numbers of males and females) on Days -2, 5, 12, 19, 26, and 33. Elizabethan collars were fitted to the cats to avoid removal of the ticks by self-grooming at infestation but removed prior to dosing on Day 0 and prior to tick counts. Elizabethan collars were replaced on cats on Day 1 at 24 hours after treatment, after the administration sites were completely dry. Ticks were counted and removed on Days 3, 8, 15, 22, 29, and 36. The study was conducted in accordance with GCP guidance.

Table II.4. Treatment Groups for Study A186C-US-20-244

Treatment Group	Treatment	Day of Treatment	Cats per Group	Days of Tick Infestation	Days of Tick Count
T01	Vehicle control	Day 0	10	Days -2, 5, 12, 19, 26, and 33	Days 3, 8, 15, 22, 29, and 36
T02	revolution® PLUS	Day 0	10	Days -2, 5, 12, 19, 26, and 33	Days 3, 8, 15, 22, 29, and 36

Drug Administration: All treatments were applied topically to the skin at the base of the neck directly in front of the shoulder blades on Day 0.

Measurements and Observations: General health observations were conducted at least once daily. Clinical observations and administration site evaluations were conducted prior to treatment on Day 0 and at 1, 3, 6, and 24 hours after treatment. Administration sites were also evaluated on Days 3, 5, and 36. At each tick count, the numbers of live and dead ticks were counted and removed from the cats on Days 3, 8, 15, 22, 29, and 36.

Statistical Methods:

Post-treatment live (free + attached) and dead (free + attached) tick counts were summarized for each individual cat at each time point and analyzed using a linear mixed model by time point. The model included the fixed effect of treatment and the random effects of block and error. Least squares mean counts were reported by treatment group at each time point. Comparison of mean live tick counts was conducted between the revolution® PLUS group and the control group using contrasts at the (two-sided) 5% significance level.

Percent effectiveness of the revolution® PLUS group with respect to the control group was calculated using LSM at each time point with the formula [(C – T) / C] X 100, where C = LSM of live tick counts for the control group and T = LSM of live tick counts for the revolution® PLUS group for each time point.

Results:

The control group met the definition for adequate tick infestations throughout the study with at least 6 of the 10 cats having 12 or more ticks after each infestation.

The revolution® PLUS group had a 93.3% reduction in the initial live tick counts 72 hours after treatment, and ≥ 98.9% reduction in live tick counts 72 hours after weekly re-infestations (Table II.5).

Mean live tick counts for the revolution® PLUS group were less than the control group and there was a statistically significant difference between the treated group and control group at all time points ($P \leq 0.0004$).

Table II.5. LSM live tick counts and percent effectiveness for revolution® PLUS for the control of induced *Amblyomma americanum* infestations of cats, 72 hours after treatment of the initial infestation and after weekly re-infestations; Study A186C-US-20-244

Day of Tick Count	Control Group LSM Live Tick Count	revolution® PLUS LSM Live Tick Count	Percent Effectiveness
3	22.5	1.5	93.3%
8	26.8	0.0	100%
15	23.4	0.0	100%
22	22.6	0.2	99.1%
29	20.5	0.0	100%
36	17.4	0.2	98.9%

The LSM dead tick counts for the revolution® PLUS group were greater than the control group and there was a statistically significant difference between the revolution® PLUS group and control group on all post-treatment count days ($P \leq 0.0002$).

Table II.6. LSM dead tick counts for revolution® PLUS for the control of induced *Amblyomma americanum* infestations of cats, 72 hours after treatment of the initial infestation and after weekly re-infestations; Study A186C-US-20-244

Day of Tick Count	Control Group LSM Dead Tick Count	revolution® PLUS LSM Dead Tick Count
3	0.1	8.9
8	0.3	15.4
15	0.6	16.8
22	0.6	11.5
29	0.6	14.7
36	1.1	9.2

Adverse Reactions: No adverse reactions were reported in this study.

Conclusions: A single topical treatment of revolution® PLUS (1.0 mg/kg sarolaner + 6.0 mg/kg selamectin) was effective against *A. americanum* ticks at 72 hours after treatment of an existing infestation and after weekly re-infestations for one month.

3. Laboratory Dose Confirmation Study A186C-US-21-259

Title: Dose Confirmation of revolution® PLUS (selamectin and sarolaner topical solution) against Induced Infestations of *Amblyomma americanum* on Cats. (Study No. A186C-US-21-259)

Study Dates: May 11, 2021, to February 8, 2022

Study Location: Turlock, CA

Study Design:

Objective: To confirm the efficacy of sarolaner (dosed at 1.0 mg/kg) in combination with selamectin (dosed at 6.0 mg/kg) applied topically against induced infestations of *Amblyomma americanum* for up to 36 days on cats.

Study Animals: Twenty domestic shorthair cats (8 males and 12 females), 24 to 92 months of age, and 2.4 to 5.7 kg body weight.

Experimental Design: This study was a vehicle-controlled, masked, randomized complete block study design. Cats were randomly assigned to the vehicle control group (10 cats) or the revolution® PLUS group (10 cats). Each cat was infested with approximately 50 unfed, wild-caught, adult *A. americanum* ticks (approximately equal numbers of males and females) on Days -2, 5, 12, 19, 26, and 33. Elizabethan collars were fitted to the cats to avoid removal of the ticks by self-grooming at infestation but removed prior to dosing on Day 0 and prior to tick counts. Elizabethan collars were replaced on cats on Day 1 at 24 hours after treatment, after the administration sites were completely dry. Ticks were counted and removed on Days 3, 8, 15, 22, 29, and 36. The study was conducted in accordance with GCP guidance.

Table II.7. Treatment Groups for Study A186C-US-21-259

Treatment Group	Treatment	Day of Treatment	Cats per Group	Days of Tick Infestation	Days of Tick Count
T01	Vehicle control	Day 0	10	Days -2, 5, 12, 19, 26, and 33	Days 3, 8, 15, 22, 29, and 36
T02	revolution® PLUS	Day 0	10	Days -2, 5, 12, 19, 26, and 33	Days 3, 8, 15, 22, 29, and 36

Drug Administration: All treatments were applied topically to the skin at the base of the neck directly in front of the shoulder blades on Day 0.

Measurements and Observations: General health observations were conducted at least once daily. Clinical observations and administration site evaluations were conducted prior to treatment on Day 0 and at 1, 3, 6, and 24 hours after treatment. Administration sites were also evaluated on Days 3, 5, and 36. At each tick count, the numbers of live and dead ticks were counted and removed from the cats on Days 3, 8, 15, 22, 29, and 36.

Statistical Methods:

Post-treatment live (free + attached) and dead (free + attached) tick counts were summarized for each individual cat at each time point and analyzed using a linear mixed model by time point. The model included the fixed effect of treatment and the random effects of block and error. Least squares mean counts were reported by treatment group at each time point. Comparison of mean live

tick counts was conducted between the revolution® PLUS group and the control group using contrasts at the (two-sided) 5% significance level.

Percent effectiveness of the revolution® PLUS group with respect to the control group was calculated using LSM at each time point with the formula [(C – T) / C] X 100, where C = LSM of live tick counts for the control group and T = LSM of live tick counts for the revolution® PLUS group for each time point.

Results:

The control group met the definition for adequate tick infestations throughout the study with at least 6 of the 10 cats having 12 or more ticks after each infestation.

The revolution® PLUS group had an 88.5% reduction in the initial live tick counts 72 hours after treatment, and 100% reduction in live tick counts 72 hours after weekly re-infestations (Table II.8).

Mean live tick counts for the revolution® PLUS group were less than the control group and there was a statistically significant difference between the treated group and control group at all time points ($P < 0.0001$).

Table II.8. LSM live tick counts and percent effectiveness for revolution® PLUS for the control of induced *Amblyomma americanum* infestations of cats, 72 hours after treatment of the initial infestation and after weekly re-infestations; Study A186C-US-21-259

Day of Tick Count	Control Group LSM Live Tick Count	revolution® PLUS LSM Live Tick Count	Percent Effectiveness
3	33.0	3.8	88.5%
8	35.4	0.0	100%
15	31.4	0.0	100%
22	36.0	0.0	100%
29	36.4	0.0	100%
36	26.9	0.0	100%

The LSM dead tick counts for the revolution® PLUS group were greater than the control group and there was a statistically significant difference between the revolution® PLUS group and control group on all post-treatment count days ($P < 0.0001$).

Table II.9. LSM dead tick counts for revolution® PLUS for the control of induced *Amblyomma americanum* infestations of cats, 72 hours after treatment of the initial infestation and after weekly re-infestations; Study A186C-US-21-259

Day of Tick Count	Control Group LSM Dead Tick Count	revolution® PLUS LSM Dead Tick Count
3	0.1	26.3
8	0.0	31.5
15	0.0	24.5
22	0.0	28.3
29	0.0	20.4
36	0.0	16.6

Adverse Reactions: One cat in the revolution® PLUS group vomited once on Day 3.

Conclusions: A single topical treatment of revolution® PLUS (1.0 mg/kg sarolaner + 6.0 mg/kg selamectin) was less than 90% effective against *A. americanum* ticks on Day 3, but greater than 90% effective on Days 8 through 36 when assessed 72 hours after treatment and after weekly re-infestations for one month.

4. Laboratory Dose Confirmation Study A186C-US-22-280

Title: Dose Confirmation of revolution® PLUS (selamectin and sarolaner topical solution) against Induced Infestations of *Amblyomma americanum* on Cats. (Study No. A186C-US-22-280)

Study Dates: November 16, 2022, to June 5, 2023

Study Location: Waverly, NY

Study Design:

Objective: To confirm the efficacy of sarolaner (dosed at 1.0 mg/kg) in combination with selamectin (dosed at 6.0 mg/kg) applied topically against induced infestations of *Amblyomma americanum* for up to 36 days on cats.

Study Animals: Twenty domestic shorthair cats (12 males and 8 females), 7 to 10 months of age, and 2.5 to 6.4 kg body weight.

Experimental Design: This study was a vehicle-controlled, masked, randomized complete block study design. Cats were randomly assigned to the vehicle control group (10 cats) or the revolution® PLUS group (10 cats). Each cat was infested with approximately 50 unfed, wild-caught, adult *A. americanum* ticks (approximately equal numbers of males and females) on Days -2, 5, 12, 19, 26, and 33. Elizabethan collars were fitted to the cats to avoid removal of the ticks by self-grooming at infestation but removed prior to dosing on Day 0 and prior to tick counts. Elizabethan collars were replaced on cats on Day 1 at 24 hours after treatment, after the administration sites were completely dry. Ticks were counted

and removed on Days 3, 8, 15, 22, 29, and 36. The study was conducted in accordance with GCP guidance.

Table II.10. Treatment Groups for Study A186C-US-22-280

Treatment Group	Treatment	Day of Treatment	Cats per Group	Days of Tick Infestation	Days of Tick Count
T01	Vehicle control	Day 0	10	Days -2, 5, 12, 19, 26, and 33	Days 3, 8, 15, 22, 29, and 36
T02	revolution® PLUS	Day 0	10	Days -2, 5, 12, 19, 26, and 33	Days 3, 8, 15, 22, 29, and 36

Drug Administration: All treatments were applied topically to the skin at the base of the neck directly in front of the shoulder blades on Day 0.

Measurements and Observations: General health observations were conducted at least once daily. Clinical observations and administration site evaluations were conducted prior to treatment on Day 0 and at 1, 3, 6, and 24 hours after treatment. Administration sites were also evaluated on Days 3, 5, and 36. At each tick count, the numbers of live and dead ticks were counted and removed from the cats on Days 3, 8, 15, 22, 29, and 36.

Statistical Methods:

Post-treatment live (free + attached) and dead (free + attached) tick counts were summarized for each individual cat at each time point and analyzed using a linear mixed model by time point. The model included the fixed effect of treatment and the random effects of block and error. Least squares mean counts were reported by treatment group at each time point. Comparison of mean live tick counts was conducted between the revolution® PLUS group and the control group using contrasts at the (two-sided) 5% significance level.

Percent effectiveness of the revolution® PLUS group with respect to the control group was calculated using LSM at each time point with the formula [(C – T) / C] X 100, where C = LSM of live tick counts for the control group and T = LSM of live tick counts for the revolution® PLUS group for each time point.

Results:

The control group met the definition for adequate tick infestations throughout the study with at least 6 of the 10 cats having 12 or more ticks after each infestation.

The revolution® PLUS group had a 98.4% reduction in the initial live tick counts 72 hours after treatment, and ≥ 99.7% reduction in live tick counts 72 hours after weekly re-infestations (Table II.11).

Mean live tick counts for the revolution® PLUS group were less than the control group and there was a statistically significant difference between the treated group and control group at all time points ($P < 0.0001$).

Table II.11. LSM live tick counts and percent effectiveness for revolution® PLUS for the control of induced *Amblyomma americanum* infestations of cats, 72 hours after treatment of the initial infestation and after weekly re-infestations; Study A186C-US-22-280

Day of Tick Count	Control Group LSM Live Tick Count	revolution® PLUS LSM Live Tick Count	Percent Effectiveness
3	18.2	0.3	98.4%
8	25.3	0.0	100%
15	26.6	0.0	100%
22	31.5	0.1	99.7%
29	32.2	0.1	99.7%
36	35.1	0.0	100%

The LSM dead tick counts for the revolution® PLUS group were greater than the control group and there was a statistically significant difference between the revolution® PLUS group and control group on all post-treatment count days ($P \leq 0.0013$).

Table II.12. LSM dead tick counts for revolution® PLUS for the control of induced *Amblyomma americanum* infestations of cats, 72 hours after treatment of the initial infestation and after weekly re-infestations; Study A186C-US-22-280

Day of Tick Count	Control Group LSM Dead Tick Count	revolution® PLUS LSM Dead Tick Count
3	2.2	12.8
8	1.7	16.3
15	0.4	10.9
22	0.6	14.7
29	0.4	17.4
36	0.2	12.5

Adverse Reactions: One cat in the revolution® PLUS group had soft stool once on Day 3.

Conclusions: A single topical treatment of revolution® PLUS (1.0 mg/kg sarolaner + 6.0 mg/kg selamectin) was effective against *A. americanum* ticks at 72 hours after treatment of an existing infestation and after weekly re-infestations for one month.

III. TARGET ANIMAL SAFETY

CVM did not require target animal safety studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-502 dated November 9, 2018, contains a summary of target animal safety studies for cats.

IV. HUMAN FOOD SAFETY

This drug is intended for use in cats. Because this new animal drug is not intended for use in food-producing animals, CVM did not require data pertaining to drug residues in food (i.e., human food safety) for approval of this NADA.

V. USER SAFETY

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to revolution® PLUS:

Not for human use. Keep this and all drugs out of the reach of children.

Do not come into contact with or allow children to contact the application site until 4 hours post application.

In humans, REVOLUTION PLUS may be irritating to skin and eyes. REVOLUTION PLUS and selamectin topical solution contain isopropyl alcohol and the preservative butylated hydroxytoluene (BHT). Reactions such as hives, itching and skin redness have been reported in humans after accidental dermal contact with selamectin topical solution. Individuals with known hypersensitivity to selamectin topical solution should use caution or consult a health care professional before applying this product on a cat. **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; if wearing contact lenses, rinse the eyes first then remove contact lenses and continue to rinse for 5 – 10 minutes and seek medical attention. In case of ingestion by a human, contact a physician immediately. The safety data sheet (SDS) provides more detailed occupational safety information. For a copy of the SDS or to report a suspected adverse reaction, call Zoetis at 1-888-963-8471.

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

VI. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR part 514. The data demonstrate that revolution® PLUS, when used according to the label, is safe and effective for the effect of supplement in the General Information Section above.

A. Marketing Status

This product may be dispensed only by or on the lawful order of a licensed veterinarian (Rx marketing status). Adequate directions for lay use cannot be written because professional expertise is required to monitor the safe use of the product, including treatment of any adverse reactions.

B. Exclusivity

This supplemental approval for revolution® PLUS qualifies for THREE years of marketing exclusivity under section 512(c)(2)(F)(iii) of the FD&C Act because the supplemental application included effectiveness studies. This exclusivity begins as of the date of our approval letter and only applies to the indication "for the treatment and control of *Amblyomma americanum* (lone star tick) infestations for one month in cats and kittens 8 weeks and older, and weighing 2.8 pounds or greater."

C. Supplemental Applications

This supplement is a Category II supplement as defined in (21 CFR 514.106(b)(2)). This supplemental approval did not require a reevaluation of certain safety or effectiveness data in the application.

D. Patent Information

For current information on patents, see the Green Book Reports in the Animal Drugs @ FDA database.