Date of Approval: November 22, 2024

FREEDOM OF INFORMATION (FOI) SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION (NADA)

NADA 141-452

SIMPARICA®

(sarolaner)

Chewable tablet

Dogs

This supplement provides for the addition of the indication for the treatment and control of *Haemaphysalis longicornis* (Asian longhorned tick) infestations for one month in dogs 6 months of age or older and weighing 2.8 pounds or greater.

Sponsored by:

Zoetis Inc.

Executive Summary

SIMPARICA® (sarolaner) chewable tablets is approved for the treatment and control of *Haemaphysalis longicornis* (Asian longhorned tick) infestations for one month in dogs 6 months of age or older, and weighing 2.8 pounds or greater. The Asian longhorned tick is a new tick species in the United States (U.S.). Not normally found in the Western Hemisphere, these ticks were reported for the first time in the U.S. in 2017.

SIMPARICA® is already approved to 1) kill adult fleas (*Ctenocephalides felis*); 2) treat and prevent flea infestations; 3) treat and control tick infestations [*Amblyomma americanum* (lone star tick), *Amblyomma maculatum* (Gulf Coast tick), *Dermacentor variabilis* (American dog tick), *Ixodes scapularis* (black-legged tick), and *Rhipicephalus sanguineus* (brown dog tick)]; and prevent *Borrelia burgdorferi* infections as a direct result of killing *Ixodes scapularis* vector ticks for one month in dogs 6 months of age or older, and weighing 2.8 pounds or greater.

SIMPARICA® is an antiparasitic drug that is available in six strengths of chewable tablets that are given orally once a month.

Safety and Effectiveness

The sponsor conducted two laboratory studies to show that SIMPARICA® is effective against *H. longicornis* tick infestations in dogs 6 months of age or older. In each study, dogs were experimentally infested with viable, unfed, adult *H. longicornis* ticks on Day -2 and then weekly for 4 weeks. On Day 0, dogs were administered SIMPARICA® or a control tablet (a flavored vitamin and mineral supplement). Tick counts were performed on Day 2 (48 hours after treatment) and 48 hours after each weekly infestation.

In both studies, SIMPARICA® was greater than 99% effective at controlling *H. longicornis* tick infestations (reducing the number of live ticks) for 1 month, while dogs in the control group remained infested with live ticks at each tick count. SIMPARICA® was also effective at treating *H. longicornis* tick infestations (increasing the number of dead ticks). Compared to dogs in the control group, treated dogs had a higher number of dead ticks for 1 month. No adverse reactions were reported in either study.

The FOI Summary for the original approval of SIMPARICA® dated February 24, 2016, contains a summary of target animal safety studies for dogs.

Conclusions

Based on the data submitted by the sponsor for the approval of SIMPARICA®, the Food and Drug Administration (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 141-452

B. Sponsor

Zoetis Inc.
333 Portage St.
Kalamazoo, MI 49007

Drug Labeler Code: 054771

C. Proprietary Name

SIMPARICA®

D. Drug Product Established Name

sarolaner

E. Pharmacological Category

Antiparasitic

F. Dosage Form

Chewable tablet

G. Amount of Active Ingredient

Six tablet sizes: 5 mg, 10 mg, 20 mg, 40 mg, 80 mg, 120 mg.

H. How Supplied

Each tablet size is available in color-coded packages of one, three, or six tablets.

I. Dispensing Status

Prescription (Rx)

J. Dosage Regimen

SIMPARICA® is given orally, once a month, at the recommended minimum dose of 0.91 mg/lb (2 mg/kg) sarolaner.

Dosage Schedule

Dog Body Weight (lbs)	Sarolaner per Tablet (mg)	Number of tablets administered
2.8 to 5.5	5	One
5.6 to 11	10	One
11.1 to 22	20	One
22.1 to 44	40	One
44.1 to 88	80	One
88.1 to 132	120	One
>132.1	Administer the appropriate combination of tablets	

K. Route of Administration

Oral

L. Species/Class

Dogs

M. Indication

SIMPARICA® kills adult fleas, and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*), and the treatment and control of tick infestations [*Amblyomma americanum* (lone star tick), *Amblyomma maculatum* (Gulf Coast tick), *Dermacentor variabilis* (American dog tick), *Ixodes scapularis* (black-legged tick), *Rhipicephalus sanguineus* (brown dog tick), and *Haemaphysalis longicornis* (Asian longhorned tick)] for one month in dogs 6 months of age or older and weighing 2.8 pounds or greater. SIMPARICA® is indicated for the prevention of *Borrelia burgdorferi* infections as a direct result of killing *Ixodes scapularis* vector ticks.

N. Effect of Supplement

This supplement provides for the addition of the indication for the treatment and control of *Haemaphysalis longicornis* (Asian longhorned tick) infestations for one month in dogs 6 months of age or older and weighing 2.8 pounds or greater.

II. EFFECTIVENESS

The effectiveness of SIMPARICA® against *Haemaphysalis longicornis* was demonstrated in two well-controlled laboratory studies, described below. Both studies included three groups of dogs (control, SIMPARICA®, and Simparica TRIO®), but only the results of the control and SIMPARICA® groups are presented. These studies demonstrated that SIMPARICA® is effective for the treatment and control of *Haemaphysalis longicornis* (Asian longhorned tick) infestations for one month in dogs 6 months of age or older and weighing 2.8 pounds or greater.

A. Dosage Characterization

This supplemental approval does not change the previously approved 2 mg/kg (0.91 mg/lb) dose, given orally once a month. The FOI Summary for the original approval of NADA 141-452 dated February 24, 2016, contains dosage characterization information for dogs.

B. Substantial Evidence

1. Laboratory Dose Confirmation Study A162C-US-22-C80

Title: Laboratory Efficacy of SIMPARICA® and Simparica TRIO® Against Induced Infestations of *Haemaphysalis longicornis* on Dogs. (Study No. A162C-US-22-C80)

Study Dates: February 7, 2023 to November 6, 2023

Study Location: Waverly, NY

Study Design:

Objective: To confirm the effectiveness of a single oral administration of SIMPARICA® against induced infestations of *H. longicornis* on dogs for one month.

Study Animals: Twenty Beagle dogs (9 males and 11 females), 10 to 15 months of age, and 5.8 to 9.9 kg body weight.

Experimental Design: This study was a negative-controlled, masked, randomized complete block study design. Dogs were randomly assigned to the control group (10 dogs) or the SIMPARICA® group (10 dogs). Each dog was sedated with dexmedetomidine hydrochloride administered intramuscularly and then infested with approximately 50 viable, unfed, adult *H. longicornis* ticks on Days -2, 7, 14, 21, and 30. Ticks were counted and removed on Days 2, 9, 16, 23, and 32. The study was conducted in accordance with Good Clinical Practice (GCP) guidance.

Table II.1. Treatment Groups (Study No. A162C-US-22-C80)

Treatment Group	Treatment	Dosage	Day of Treatment	Dogs per Group	Days of Tick Infestation	Days of Tick Counts
T01	Control*	N/A	Day 0	10	Days -2, 7, 14, 21, and 30	Days 2, 9, 16, 23, and 32
T03	SIMPARICA®	2.0 mg/kg	Day 0	10	Days -2, 7, 14, 21, and 30	Days 2, 9, 16, 23, and 32

*Pet-Tabs® chewable tablet (flavored vitamin and mineral supplement)

Drug Administration: Dogs were fasted 12 hours prior to administration and were administered SIMPARICA® or control tablet by mouth on Day 0.

Measurements and Observations: Ticks were removed, and numbers of live and dead ticks were counted at each tick count. Clinical observations were conducted at 1, 3, 6, and 24 hours after treatment. General health observations were conducted twice daily.

Statistical Methods: For live tick counts, percent effectiveness against control was calculated based on arithmetic means using the formula [(C - T)/C] x 100, where C = arithmetic mean calculated from the least squares means of live tick counts for the control group and T = arithmetic mean calculated from the least squares means of live tick counts for the treated group. Live tick counts for treated and control dogs were compared using a mixed linear model with treatment group as a fixed effect, and error and block as random effects at each time point. Testing was two-sided at the 5% significance level. For dead tick counts, the arithmetic means were calculated by treatment group and timepoint because the Least Square Means (LSMs) were not available due to model convergence issues at multiple count days.

Results: Control dogs maintained adequate tick infestations throughout the study with at least six of the ten dogs having 12 or more live ticks at each tick count.

There were no live ticks on any dog administered SIMPARICA® for 32 days after dosing. These dogs had a 100% reduction in live tick counts 48 hours after dose administration and 48 hours after weekly re-infestations for 32 days (Table II.2).

Mean live tick counts for the dogs administered SIMPARICA® were significantly different (P≤0.0001) and numerically lower than the control dogs on all days after dosing.

Table II.2. Arithmetic Mean Live Tick Count and Percent Effectiveness

Day of Tick Count	Control Group Arithmetic Mean Live Tick Count	SIMPARICA® Arithmetic Mean Live Tick Count	Percent Effectiveness
2	13.1	0.0	100%
9	15.0	0.0	100%
16	31.4	0.0	100%
23	29.7	0.0	100%
32	27.1	0.0	100%

Mean dead tick counts for the dogs administered SIMPARICA® were higher than the control dogs on all tick count days after dosing.

Table II.3. Arithmetic Mean Dead Tick Count

Day of Tick Count	Control Group Arithmetic Mean Dead Tick Count	SIMPARICA® Arithmetic Mean Dead Tick Count
2	0.1	2.4
9	0.1	2.4
16	0.1	1.5
23	0.5	3.7
32	0.0	4.2

Adverse Reactions: No adverse reactions were observed during the study.

Conclusions: This study demonstrated the effectiveness of SIMPARICA® for the control (reduced live ticks) and treatment (increased dead ticks) of *H. longicornis* for one month when assessed at 48 hours after drug administration or infestation.

2. Laboratory Dose Confirmation Study A162C-ZA-22-C81

Title: Laboratory Efficacy of SIMPARICA® and Simparica TRIO® Against Induced Infestations of *Haemaphysalis longicornis* on Dogs. (Study No. A162C-ZA-22-C81)

Study Dates: March 27, 2023 to October 31, 2023

Study Location: Bloemfontein, South Africa

Study Design:

Objective: To confirm the effectiveness of a single oral administration of SIMPARICA® against induced tick infestations of *H. longicornis* for up to one month in dogs.

Study Animals: Twenty Beagle and mongrel dogs (10 males and 10 females), 7 to 79 months of age, and 10.9 to 20 kg body weight.

Experimental Design: This study was a negative-controlled, masked, randomized complete block study design. Dogs were randomly assigned to the control group (10 dogs) or the SIMPARICA® group (10 dogs). Each dog was sedated with dexmedetomidine hydrochloride intramuscularly and then infested with approximately 50 viable, unfed, adult *H. longicornis* ticks on Days -2, 7, 14, 21, and 30. Ticks were counted and removed on Days 2, 9, 16, 23, and 32. The study was conducted in accordance with Good Clinical Practice (GCP) guidance.

Table II.4. Treatment Groups (Study No. A162C-ZA-22-C81)

Treatment Group	Treatment	Dosage	Day of Treatment	Dogs per Group	Days of Tick Infestation	Days of Tick Counts
T01	Control*	N/A	Day 0	10	Days -2, 7, 14, 21, and 30	Days 2, 9, 16, 23, and 32
T03	SIMPARICA® (sarolaner)	2 mg/kg	Day 0	10	Days -2, 7, 14, 21, and 30	Days 2, 9, 16, 23, and 32

*Pet-Tabs® chewable tablet (flavored vitamin and mineral supplement)

Drug Administration: Dogs were fasted 12 hours prior to administration and were administered SIMPARICA® or control tablet by mouth on Day 0.

Measurements and Observations: Ticks were removed, and numbers of live and dead ticks were counted at each tick count. Clinical observations were conducted 1, 3, 6, and 24 hours after treatment. General health observations were conducted twice daily.

Statistical Methods: For live tick counts, percent effectiveness against control was calculated based on arithmetic means using the formula [(C-T)/C] x 100, where C = arithmetic mean calculated from the least squares means of live tick counts for the control group and T = arithmetic mean calculated from the least squares means of live tick counts for the treated group. Live tick counts for treated and control dogs were compared using a mixed linear model with treatment group as a fixed effect, and room, block within room and error as random effects at each time point. Testing was two-sided at the 5% significance level. For dead tick counts, the arithmetic means were calculated by treatment group and timepoint because the LSMs were not available due to model convergence issues at multiple count days.

Results: Control dogs maintained adequate tick infestations throughout the study with at least six of the ten dogs having 12 or more live ticks at each tick count.

Dogs administered SIMPARICA® had a 100% reduction in live tick counts 48 hours after treatment of the existing infestation, and ≥99.7% reduction in live ticks counts 48 hours after weekly re-infestations for 32 days (Table II.5).

Mean Live tick counts for the dogs administered SIMPARICA® were significantly different ($P<0.0001$) and numerically lower than the control group on all post-treatment count days.

Table II.5. Arithmetic Mean Live Tick Count and Percent Effectiveness

Day of Tick Count	Control Group Arithmetic Mean Live Tick Count	SIMPARICA® Arithmetic Mean Live Tick Count	Percent Effectiveness
2	31.5	0.0	100%
9	24.2	0.0	100%
16	24.8	0.0	100%
23	30.3	0.0	100%
32	29.1	0.1	99.7%

Mean dead tick counts for the SIMPARICA® group were higher than the control group on all post-treatment count days.

Table II.6. Arithmetic Mean Dead Tick Count

Day of Tick Count	Control Group Arithmetic Mean Dead Tick Count	SIMPARICA® Arithmetic Mean Dead Tick Count
2	0.2	7.3
9	0.0	2.5
16	0.1	1.4
23	0.0	1.1
32	0.0	1.1

Adverse Reactions: No adverse reactions were observed during the study.

Conclusions: This study demonstrated the effectiveness of SIMPARICA® for the control (reduced live ticks) and treatment (increased dead ticks) of *H. longicornis* for one month when assessed at 48 hours after drug administration or infestation.

III. TARGET ANIMAL SAFETY

FDA did not require target animal safety studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-452 dated February 24, 2016, contains a summary of target animal safety studies for dogs.

IV. HUMAN FOOD SAFETY

This drug is intended for use in dogs. Because this new animal drug is not intended for use in food-producing animals, FDA 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 SIMPARICA®:

Not for use in humans. Keep this and all drugs out of reach of children.

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 SIMPARICA®, 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 order of a licensed veterinarian (Rx marketing status) because professional expertise is needed to monitor the safe use of the product, including treatment of any adverse reactions.

B. Exclusivity

This supplemental approval for SIMPARICA® 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 *Haemaphysalis longicornis* (Asian longhorned tick) infestations for one month in dogs 6 months of age or 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.