Date of Approval: January 20, 2026

FREEDOM OF INFORMATION (FOI) SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION (NADA)

NADA 141-554

NexGard® PLUS

(afoxolaner, moxidectin, and pyrantel chewable tablets)

Dogs

This supplement provides for the addition of the indication for the treatment and control of *Amblyomma maculatum* (Gulf Coast tick) infestations for one month in dogs and puppies eight weeks of age and older, weighing four pounds of body weight or greater.

Sponsored by:

Boehringer Ingelheim Animal Health USA, Inc.

Executive Summary

NexGard® PLUS (afoxolaner, moxidectin, and pyrantel chewable tablets) is approved for the treatment and control of *Amblyomma maculatum* (Gulf Coast tick) infestations for one month in dogs and puppies eight weeks of age and older, weighing four pounds of body weight or greater.

NexGard® PLUS is already approved for the prevention of heartworm disease caused by *Dirofilaria immitis* and for the treatment and control of adult hookworm *(Ancylostoma caninum, Ancylostoma braziliense*, and *Uncinaria stenocephala)* and roundworm *(Toxocara canis* and *Toxascaris leonina)* infections. NexGard® PLUS kills adult fleas and is indicated for the treatment and prevention of flea infestations *(Ctenocephalides felis)* and the treatment and control of *Ixodes scapularis* (black-legged tick), *Rhipicephalus sanguineus* (brown dog tick), *Dermacentor variabilis* (American dog tick), and *Amblyomma americanum* (lone star tick), and *Haemaphysalis longicornis* (longhorned tick) infestations for one month in dogs and puppies eight weeks of age and older, weighing four pounds of body weight or greater. NexGard® PLUS is indicated for the prevention of *Borrelia burgdorferi* infections as a direct result of killing *Ixodes scapularis* vector ticks.

Safety and Effectiveness

Details of the studies conducted for the original approval of NexGard® PLUS and two supplemental approvals can be found in the FOI Summaries (NADA 141-554) dated July 19, 2023, October 7, 2024, and April 23, 2025, respectively.

The sponsor conducted two laboratory studies in young, healthy, intact male and female beagles and mongrel dogs to demonstrate effectiveness against *A. maculatum*. In both studies, on Day 0, the dogs were either administered NexGard® PLUS or no treatment. Dogs were infested with approximately 50 unfed, adult *A. maculatum* ticks on Days -1, 14, and 28. Live ticks were counted and removed on Days 3, 17, and 31 (72 hours after treatment (Day 3) or infestation (Days 17 and 31)).

In both studies, NexGard® PLUS was greater than 92% effective at controlling *A. maculatum* infestations (reducing the number of live ticks) for one month, while dogs in the control group remained infested with live ticks at each tick count. NexGard® PLUS was also effective at treating *A. maculatum* infestations (increasing the number of dead ticks) for one month. Compared to dogs in the control group, treated dogs had a higher number of dead ticks. Self-limiting diarrhea was observed in two treated dogs in one of the two studies and should be considered a possible drug-related adverse reaction.

The FOI Summary for the original approval of NexGard® PLUS (NADA 141-554), dated July 19, 2023, contains a summary of target animal safety studies for dogs.

Conclusions

Based on the data submitted by the sponsor for the approval of NexGard® and NexGard® PLUS, 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 141-554

B. Sponsor

Boehringer Ingelheim Animal Health USA, Inc.
3239 Satellite Blvd.
Duluth, GA 30096

Drug Labeler Code: 000010

C. Proprietary Name

NexGard® PLUS

D. Drug Product Established Name

afoxolaner, moxidectin, and pyrantel chewable tablets

E. Pharmacological Category

Antiparasitic

F. Dosage Form

Chewable tablet

G. Amount of Active Ingredient

Each chewable contains:

9.375 mg afoxolaner, 45 mcg moxidectin, and 18.75 mg pyrantel*
18.75 mg afoxolaner, 90 mcg moxidectin, and 37.5 mg pyrantel*
37.5 mg afoxolaner, 180 mcg moxidectin, and 75 mg pyrantel*
75 mg afoxolaner, 360 mcg moxidectin, and 150 mg pyrantel*
150 mg afoxolaner, 720 mcg moxidectin, and 300 mg pyrantel*
*As pamoate salt

H. How Supplied

NexGard® PLUS is available in five strengths of beef-flavored soft chewables. Each chewable size is available in color-coded packages of 1, 3, or 6 chewables.

I. Dispensing Status

Prescription (Rx)

J. Dosage Regimen

NexGard® PLUS is given orally once a month at the minimum dosage of 1.14 mg/lb (2.5 mg/kg) afoxolaner, 5.45 mcg/lb (12 mcg/kg) moxidectin, and 2.27 mg/lb (5.0

mg/kg) pyrantel (as pamoate salt). **For heartworm disease prevention, give once monthly for at least six months after last exposure to mosquitoes.**

Dosing Schedule:

Body Weight (lbs.)	Afoxolaner Per Chewable (mg)	Moxidectin Per Chewable (mcg)	Pyrantel* Per Chewable (mg)	Chewables Administered
4.0-8.0	9.375	45	18.75	One
8.1-17.0	18.75	90	37.5	One
17.1-33.0	37.5	180	75	One
33.1-66.0	75	360	150	One
66.1-132.0	150	720	300	One
Over 132.0	Not Applicable	Not Applicable	Not Applicable	Administer the appropriate combination of chewables

*As pamoate salt

K. Route of Administration

Oral

L. Species

Dogs

M. Indication

NexGard® PLUS is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis* and for the treatment and control of adult hookworm (*Ancylostoma caninum*, *Ancylostoma braziliense*, and *Uncinaria stenocephala*) and roundworm (*Toxocara canis* and *Toxascaris leonina*) infections. NexGard® PLUS kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*) and the treatment and control of *Ixodes scapularis* (black-legged tick), *Rhipicephalus sanguineus* (brown dog tick), *Dermacentor variabilis* (American dog tick), *Amblyomma americanum* (lone star tick), *Amblyomma maculatum* (Gulf Coast tick), and *Haemaphysalis longicornis* (longhorned tick) infestations for one month in dogs and puppies eight weeks of age and older, weighing four pounds of body weight or greater. NexGard® PLUS 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 *Amblyomma maculatum* (Gulf Coast tick) infestations for one month in dogs and puppies eight weeks of age and older, weighing four pounds of body weight or greater.

II. EFFECTIVENESS

The effectiveness of NexGard® PLUS for the treatment and control of *Amblyomma maculatum* (Gulf Coast tick) infestations for one month in dogs and puppies eight weeks of age and older, weighing four pounds of body weight or greater, was demonstrated in two well-controlled laboratory studies described below.

A. Dosage Characterization

This supplemental approval does not change the previously approved dose of 1.14 mg/lb (2.5 mg/kg) of afoxolaner, 5.45 mcg/lb (12 mcg/kg) of moxidectin, and 2.27 mg/lb (5.0 mg/kg) of pyrantel, given orally once a month. The Freedom of Information (FOI) Summary for the original approval of NADA 141-554 dated July 19, 2023, contains dosage characterization information for dogs.

B. Substantial Evidence

1. Laboratory Dose Confirmation Study

Title: Efficacy of a Single Oral Treatment with NexGard® PLUS Against Induced Infestations of *Amblyomma maculatum* on Dogs. (Study No. 2023-3557)

Study Dates: May 9, 2024 to November 15, 2024

Study Location: Colbert, GA

Study Design:

Objective: To confirm the effectiveness of a single oral dose of NexGard® PLUS for the treatment and control of induced infestations of adult *Amblyomma maculatum* on dogs.

Study Animals: Twenty beagle dogs (11 males and 9 females), 7.9 to 10.8 months of age and weighing 6.9 to 12.2 kg.

Experimental Design: This study was a masked, negative controlled study using a completely randomized study design. Prior to allocation to treatment groups on Day -3, an initial tick infestation and count was conducted to evaluate susceptibility of each dog to induced infestation (host suitability). The dogs were randomized to treatment groups and infested with approximately 50 adult unfed *A. maculatum* ticks on Days -1, 14, and 28.

Tick counts were performed 72 hours after drug administration (Day 3) or tick infestation (Days 17 and 31). Ticks were not returned to the dog after counting. The study was conducted in accordance with Good Clinical Practice (GCP) guidelines.

Table II.1. Study 2023-3557; Treatment Groups

Treatment	Minimum Dose	Number and Sex of Dogs
Control	0 mg/kg	10 (4M, 6F)
NexGard® PLUS	2.5 mg/kg afoxolaner + 12 mcg/kg moxidectin + 5 mg/kg pyrantel	10 (7M, 3F)

Drug Administration: On Day 0, the 10 dogs in the NexGard® PLUS treated group were administered one or more chewable tablets, at afoxolaner doses as close as possible to 2.5 mg/kg without under-dosing. Afoxolaner doses ranged from 2.5 to 3.7 mg/kg per dog. Dogs were fed prior to treatment. The 10 dogs in the control group received no treatment.

Measurements and Observations: The primary variable for effectiveness was the *A. maculatum* counts collected from the dogs. At each tick count, the ticks were removed, and the numbers of live and dead ticks were recorded. Physical examinations were conducted, and dogs were weighed on Day -7. Dogs were observed for health abnormalities at least once daily throughout the study, hourly for 6 hours after treatment, and at 8, 12, and 24 hours after treatment. Tick counts and health observations were conducted masked to treatment.

Statistical Methods: The experimental unit was the individual dog. For live tick counts at each time point, percent effectiveness of the treated groups with respect to the control groups was calculated using the formula [(C - T) / C] x 100, where C = the least squares (LS) mean of live tick counts for the control group and T = the LS mean of live tick counts for the treated groups.

On each tick count day, untransformed live tick counts were analyzed using linear mixed models, including treatment as a fixed effect. The comparisons were tested using the two-sided 5% significance level. The total counts of dead ticks recovered from each dog and from its housing enclosure were used for calculation of arithmetic means by treatment group.

Effectiveness for the control indication was determined on the basis of the percent reduction (≥90%) in live tick counts in the treated group compared to the control group. Effectiveness for the treatment indication was determined on the basis of a numerically higher value of the arithmetic mean of dead ticks in the treated group compared to the control group.

Results: At each tick count, a minimum of six dogs in the control group had an adequate tick infestation, defined as a retention rate of at least 25% (i.e., ≥12 live ticks).

The NexGard® PLUS treated group had a ≥99% reduction in live *A. maculatum* tick counts at 72 hours (Table II.2) following treatment or infestation through Day 31. On all count days following drug administration, mean live tick counts

between the NexGard® PLUS group and the control group were significantly different (p<0.0001). Dead ticks counted from the NexGard® PLUS treated group were higher compared to the control group at all post-treatment time points (Table II.3).

Table II.2. Study 2023-3557; *A. maculatum* Live Tick Counts and Percent Effectiveness 72 Hours After Administration or Infestation

Day of Tick Count	Control Group LS Mean	NexGard® PLUS Group LS Mean	Percent Effectiveness
3	40.6	0.2	99.5
17	38.5	0.4	99.0
31	34.7	0.0	100

Table II.3. Study 2023-3557; *A. maculatum* Dead Tick Counts 72 Hours After Administration or Infestation

Day of Tick Count	Control Group Arithmetic Mean	NexGard® PLUS Arithmetic Mean
3	0.2	40.6
17	0.8	24.2
31	0.9	16.7

Adverse Reactions: One dog in the NexGard® PLUS treated group had a single incidence of diarrhea noted six hours after treatment, and 1 NexGard® PLUS treated dog had diarrhea 8 and 24 hours after treatment. The diarrhea resolved without treatment and was considered minor.

Conclusions: This study demonstrated the effectiveness of NexGard® PLUS for the control (reduced live ticks) and treatment (increased dead ticks) of *A. maculatum* ticks for one month when assessed 72 hours after drug administration or infestation. Diarrhea is considered a possible drug-related adverse reaction.

2. Laboratory Dose Confirmation Study

Title: Efficacy of a Single Oral Treatment with NexGard® PLUS Against Induced Infestations of *Amblyomma maculatum* on Dogs. (Study No. 2024-4349)

Study Dates: October 15, 2024 to April 4, 2025

Study Location: Bloemfontein, South Africa

Study Design:

Objective: To confirm the effectiveness of a single oral dose of NexGard® PLUS for the treatment and control of induced infestations of adult *Amblyomma maculatum* on dogs.

Study Animals: Twenty beagle and mixed breed dogs (1 male and 19 females), 12.0 to 86.2 months of age and weighing 10.4 to 14.6 kg.

Experimental Design: This study was a masked, negative controlled study using a completely randomized study design. Prior to allocation to treatment groups on Day -4, an initial tick infestation and count was conducted to evaluate susceptibility of each dog to induced infestation (host suitability). The dogs were randomized to treatment groups and infested with approximately 50 adult unfed *A. maculatum* ticks on Days -1, 14, and 28.

Tick counts were performed 72 hours after drug administration (Day 3) or tick infestation (Days 17 and 31). Ticks were not returned to the dog after counting. The study was conducted in accordance with GCP guidelines.

Table II.4. Study 2024-4349; Treatment Groups

Treatment	Minimum Dose	Number and Sex of Dogs
Control	0 mg/kg	10 (1M, 9F)
NexGard® PLUS	2.5 mg/kg afoxolaner + 12 mcg/kg moxidectin + 5 mg/kg pyrantel	10 (10F)

Drug Administration: On Day 0, the 10 dogs in the NexGard® PLUS treated group were administered one or more chewable tablets, at afoxolaner doses as close as possible to 2.5 mg/kg without under-dosing. Afoxolaner doses ranged from 2.6 to 3.0 mg/kg per dog. Dogs were fed prior to treatment. The 10 dogs in the control group received no treatment.

Measurements and Observations: The primary variable for effectiveness was the *A. maculatum* counts collected from the dogs. At each tick count, the ticks were removed, and the numbers of live and dead ticks were recorded. Physical examinations were conducted on Day -7, and dogs were weighed on Day -4. Dogs were observed for health abnormalities at least once daily throughout the study, hourly for 6 hours after treatment, and at 8, 12, and 24 hours after treatment. Tick counts and health observations were conducted masked to treatment.

Statistical Methods:
The experimental unit was the individual dog. For live tick counts at each time point, percent effectiveness of the treated groups with respect to the control groups was calculated using the formula [(C - T) / C] x 100, where C = the least squares (LS) mean of live tick counts for the control group and T = the LS mean of live tick counts for the treated groups.

On each tick count day, untransformed live tick counts were analyzed using linear mixed models, including treatment as a fixed effect. The comparisons were tested using the two-sided 5% significance level. The total counts of dead ticks recovered from each dog and from its housing enclosure were used for calculation of arithmetic means by treatment group.

Effectiveness for the control indication was determined on the basis of the percent reduction (≥90%) in live tick counts in the treated group compared to the control group. Effectiveness for the treatment indication was determined on the basis of a numerically higher value of the arithmetic mean of dead ticks in the treated group compared to the control group.

Results: At each tick count, a minimum of six dogs in the control group had an adequate tick infestation, defined as a retention rate of at least 25% (i.e., ≥12 live ticks).

The NexGard® PLUS treated group had a ≥92.8% reduction in live *A. maculatum* tick counts at 72 hours (Table II.5) following treatment or infestations through Day 31. On all count days following drug administration, mean live tick counts between the NexGard® PLUS group and the control group were significantly different ($p<0.0001$). Dead ticks counted from the NexGard® PLUS treated group were higher compared to the control group at all post-treatment time points (Table II.6).

Table II.5. Study 2024-4349; *A. maculatum* Live Tick Counts and Percent Effectiveness 72 Hours After Administration or Infestation

Day of Tick Count	Control Group LS Mean	NexGard® PLUS LS Mean	Percent Effectiveness
3	38.2	0.3	99.2
17	36.0	1.0	97.2
31	33.4	2.4	92.8

Table II.6. Study 2024-4349; *A. maculatum* Dead Tick Counts 72 Hours After Administration or Infestation

Day of Tick Count	Control Group Arithmetic Mean	NexGard® PLUS Arithmetic Mean
3	2.0	30.2
17	1.3	22.1
31	2.7	14.9

Adverse Reactions: No treatment-related adverse reactions were reported in the NexGard® PLUS treated dogs during the study.

Conclusions: This study demonstrated the effectiveness of NexGard® PLUS for the control (reduced live ticks) and treatment (increased dead ticks) of *A. maculatum* ticks for one month when assessed 72 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 141-554 dated July 19, 2023, 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, 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 NexGard® PLUS:

Not for use in humans. Keep this and all drugs out of the reach of children. In case of accidental ingestion, contact a physician for treatment advice.

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 NexGard® 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 the product is indicated for the prevention of heartworm infections (*Dirofilaria immitis*) in dogs, which requires veterinary examination and testing to ensure dogs are negative for adult heartworm disease prior to administration of the product to dogs.

B. Exclusivity

This supplemental approval for NexGard® 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 maculatum* (Gulf Coast tick) infestations for one month in dogs and puppies eight weeks of age and older, weighing four pounds of body weight or greater.”

C. Supplemental Applications

This supplement is a Category II supplement as defined in (21 CFR 514.106(b)(2)). This supplemental approval required 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.