Date of Approval: October 7, 2024

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

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 *Haemaphysalis longicornis* (longhorned tick) infestations in dogs and puppies eight weeks of age and older, weighing four pounds of body weight or greater, for one month. This supplement also provides for the addition of label language regarding the results of a second flea field study and improvement of erythema, alopecia, papules, scales, crusts, and excoriation in dogs with flea infestations and signs of Flea Allergy Dermatitis following treatment with afoxolaner alone, as a direct result of eliminating fleas.

Sponsored by:

Boehringer Ingelheim Animal Health USA, Inc.

Executive Summary

In this supplement, NexGard® PLUS (afoxolaner, moxidectin, and pyrantel chewable tablets) is approved for the treatment and control of *Haemaphysalis longicornis* (longhorned tick) infestations in dogs and puppies 8 weeks of age and older, weighing 4 pounds of body weight or greater, for one month. The longhorned tick is a new tick species in the United States (U.S.). Not previously found in the Western Hemisphere, these ticks were reported for the first time in the U.S. in 2017.

NexGard® PLUS is already approved for the prevention of heartworm disease caused by Dirofilaria immitis. NexGard® PLUS is indicated 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) infestations for one month in dogs and puppies eight weeks of age and older, weighing four pounds of body weight or greater.

Safety and Effectiveness

The original approval of NexGard® PLUS referenced multiple studies that were conducted to demonstrate the effectiveness of afoxolaner, one of the active ingredients in NexGard® PLUS, at the dose of 2.5 mg/kg, for the treatment and control of *Ixodes scapularis*, *Rhipicephalus sanguineus*, and *Dermacentor variabilis* in support of the approval of NexGard® (afoxolaner) Chewable Tablets for Dogs in the New Animal Drug Application (NADA) 141-406. Details of these studies can be found in the Freedom of Information (FOI) Summary for NexGard® (NADA 141-406), dated September 14, 2013 (original approval), as well as May 15, 2014 and February 23, 2015 (supplemental approvals). Two laboratory studies against the least susceptible tick species for afoxolaner (in this case *Amblyomma americanum*) were conducted to demonstrate effectiveness of NexGard® PLUS against all tick species listed on the NexGard® label.

Two laboratory studies demonstrated the effectiveness of afoxolaner at the dose of 2.5 mg/kg body weight for the treatment and control of *Haemaphysalis longicornis* (longhorned tick) infestations. Refer to the FOI Summary for the supplemental approval of NexGard® (NADA 141-406), dated June 21, 2023, for details of these studies. Because *Amblyomma americanum* is also the least susceptible tick species for afoxolaner compared to *Haemaphysalis longicornis*, those studies support the effectiveness of NexGard® PLUS against *Haemaphysalis longicornis* as well.

NexGard® PLUS is already approved to kill adult fleas and treat and prevent flea infestations. In addition to the existing label language describing the effectiveness of NexGard® PLUS against fleas, this supplement provides for the inclusion of the results of an additional field study that demonstrated improvement of signs of Flea Allergy Dermatitis following treatment with afoxolaner, one of the active ingredients in NexGard® PLUS, as a direct result of eliminating fleas. Refer to the FOI Summary for NexGard® (NADA 141-406), dated June 21, 2023, for details of that study.

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 one, three, or six 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/Class

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), 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.

N. Effect of Supplement

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

This supplement also provides for the addition of label language regarding the results of a second flea field study and improvement of erythema, alopecia, papules, scales, crusts, and excoriation in dogs with flea infestations and signs of Flea Allergy Dermatitis following treatment with afoxolaner alone, as a direct result of eliminating fleas.

II. EFFECTIVENESS

A. Dosage Characterization

This supplemental approval does not change the previously approved dosage. 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

The effectiveness of NexGard® PLUS for the treatment and control of *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, was established in two laboratory studies that demonstrated the effectiveness of afoxolaner for this indication.

Two well-controlled laboratory studies demonstrated the effectiveness of afoxolaner, one of the active ingredients in NexGard® PLUS, at the dose of 2.5 mg/kg body weight, for the treatment and control of *Haemaphysalis longicornis* (longhorned tick) infestations. Refer to the FOI Summary for the supplemental approval of NexGard® (afoxolaner; NADA 141-406), dated June 21, 2023, for details of those studies. Because *Amblyomma americanum* is the less susceptible tick species for afoxolaner compared to *Haemaphysalis longicornis*, and the effectiveness of NexGard® PLUS against *Amblyomma americanum* was demonstrated by studies described in the FOI Summary for the original approval of NexGard® PLUS (NADA 141-554), dated July 19, 2023, the studies conducted under NADA 141-406 support the effectiveness of NexGard® PLUS against *Haemaphysalis longicornis*.

The addition of label language regarding the results of a second flea field study in dogs with flea infestations and the improvement of signs of Flea Allergy Dermatitis following treatment with afoxolaner alone, as a direct result of eliminating fleas, is supported by a 90-day multi-site U.S. field study that demonstrated the effectiveness of afoxolaner, one of the active ingredients in NexGard® PLUS, at the dose of 2.5 mg/kg body weight, for the flea indications. In this study, dogs with signs of Flea Allergy Dermatitis (FAD) showed improvement in erythema, alopecia, papules, scales, crusts, and excoriation following treatment, as a direct result of eliminating fleas. Refer to the FOI Summary for the supplemental approval of NexGard® (NADA 141-406), dated June 21, 2023, for details of this study.

III. TARGET ANIMAL SAFETY

The Center for Veterinary Medicine (CVM) 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 (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 *Haemaphysalis longicornis* (longhorned tick) infestations in dogs and puppies 8 weeks of age and older, weighing 4 pounds of body weight or greater, for one month and the label language regarding the results of a second flea field study and improvement of erythema, alopecia, papules, scales, crusts, and excoriation in dogs with flea infestations and signs of Flea Allergy Dermatitis following treatment with afoxolaner, as a direct result of eliminating fleas.

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.