

NexGard[®]

(afoxolaner) Chewables

SATISFACTION GUARANTEED.



NexGard[®] SATISFACTION GUARANTEE

Flea and tick control is an essential part of a pet's preventive healthcare, and we want pet owners to have full confidence in the choices that they make to protect their dogs. To help provide peace of mind to pet owners and to show the confidence that we have in **NexGard**, Boehringer Ingelheim, the leader in flea and tick control, is proud to offer the **NexGard** SATISFACTION GUARANTEE.

NexGard is labeled to kill adult fleas and is indicated for the treatment and prevention of flea infestations, and the treatment and control of black-legged tick, American dog tick, Lone star tick, and brown dog tick infestations in dogs and puppies 8 weeks of age and older, weighing 4 pounds of body weight or greater, for one month. It is also indicated for the prevention of *Borrelia burgdorferi* infections as a direct result of killing *Ixodes scapularis* vector ticks (black-legged ticks).

If you have questions about **NexGard**, or if you are not satisfied with **NexGard**, please call our experts on the Veterinary Technical Solutions (VeTS) team at 888-637-4251.

NexGard FLEA SATISFACTION GUARANTEE

To qualify, the affected dog must have received **NexGard**, per the label instructions, for at least 3 consecutive months. All other pets in the home must also have been treated with **NexGard** or an appropriate FRONTLINE[®] Gold product for at least 3 consecutive months prior to the report. **NexGard** is for use in dogs only.

If you are not satisfied with **NexGard** after 3 months of proper administration to the affected dog, then you may be eligible for one of the following:

- a refund of your money OR
- a product replacement OR
- a one-time free professional in-home pest control inspection and treatment, if necessary

FLEA SATISFACTION GUARANTEE GUIDELINES

- Because the flea life cycle can vary from 2 weeks to several months, it may take several monthly administrations of any flea control product to break the flea life cycle. Therefore you are required to use **NexGard** for at least 3 consecutive months in the affected dog to be eligible.
- The guarantee is available for the most recent purchase of 3 or 6 doses. **NexGard** must have been used consistently in the affected dog for the 3 months prior to the claim. You may choose to receive either one replacement package of the same **NexGard** product, a refund for the purchase price, or an in-home inspection by a professional pest control specialist. Taxes are not reimbursable. In some instances, product replacement may not be an option.

- Should you choose the in-home inspection, treatment will be provided if deemed necessary by the pest control specialist. Boehringer Ingelheim will contact the pest control service and have them schedule a service date with you. Boehringer Ingelheim will cover the cost of the visit by paying the pest control service directly. You must allow the pest control specialist into the home if an inspection is desired. One free professional in-home inspection per household.

IMPORTANT SAFETY INFORMATION

NexGard (afoxolaner) is for use in dogs only. The most frequently reported adverse reactions include vomiting, pruritus, lethargy, diarrhea, and lack of appetite. The safe use of **NexGard** in pregnant, breeding, or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures or neurologic disorders. For more information, see the full prescribing information or visit www.NexGardForDogs.com.



NexGard (afoxolaner) LYME SATISFACTION GUARANTEE

If your dog is found to be positive for *Borrelia burgdorferi* infection after consistent use of **NexGard** (*B. burgdorferi* antibody seropositive for first time since last negative test), Boehringer Ingelheim (BI) will provide financial support to your veterinarian to conduct additional testing with either the Cornell Canine Lyme Multiplex or the IDEXX® Quantitative C6® Antibody test, as well as urinalysis and urine protein: creatinine ratio, if desired. Your veterinarian should contact VeTS at 888-637-4251 to make these arrangements in advance of the testing. If a positive diagnosis is confirmed, BI will reimburse your veterinarian for treatment with appropriate antibiotics. If the dog is showing clinical signs, BI will support additional reasonable diagnostic and treatment charges up to \$5,000.

LYME SATISFACTION GUARANTEE GUIDELINES

- To be eligible, you or your veterinarian must submit evidence of the dog's negative Lyme test within one month of the pet starting **NexGard** as well as negative annual tests thereafter. Any commercially available test indicated for the detection of exposure to *Borrelia burgdorferi* will be acceptable.
- For puppies that are started on **NexGard** prior to 4 months of age, a negative test is still recommended but not required to be eligible for the first year of coverage.
- The affected dog must have appropriate purchase history showing enough purchases of **NexGard** to have received the product consistently each month from the date of the negative test through the date of the claim. LYME SATISFACTION GUARANTEE cases are not eligible for product refund or replacement.
- While some diagnostic tests for Lyme infection can detect an infection as early as 3 weeks post-exposure, it can take up to 3 months for some currently available tests. For this reason, it is recommended (though not required for the guarantee), that dogs be tested for Lyme infection approximately 3 months after starting **NexGard** to ensure that the dog was not exposed prior to initiation of **NexGard** treatment.

LYME SATISFACTION GUARANTEE PLUS

- For any dog qualifying for the LYME SATISFACTION GUARANTEE, additional support may be possible if the dog has also been vaccinated with the RECOMBITEK® Lyme vaccine.
- To qualify, the dog must have been appropriately vaccinated with the RECOMBITEK Lyme vaccine within the 12 months preceding the claim and must meet the eligibility requirements for the **NexGard** (afoxolaner) LYME SATISFACTION GUARANTEE.
- If an affected dog had a negative Lyme test, an appropriate purchase history showing adequate purchases of **NexGard** to ensure monthly use since a negative test, and was appropriately vaccinated with the RECOMBITEK Lyme vaccine in the 12 months prior to the report, then BI will support reasonable diagnostic and treatment charges for Lyme disease up to \$10,000.

Lyme infection can lead to serious consequences in dogs. In addition to the consistent use of **NexGard**, a number of other preventive steps are recommended, including:

- Avoid areas where ticks are common, if possible.
- Reduce areas that serve as ideal tick habitat in the yard.
- Check your pets daily for ticks, and remove any that are found.
- Talk to your veterinarian about Lyme vaccination for your dog.

GENERAL ELIGIBILITY

- The guarantee is not retroactive. To qualify for any portion of the guarantee, reports must be received within 6 months of the incident in question. Please ensure that your veterinarian contacts VeTS to discuss support in advance of testing or treatment. BI will not be responsible for any diagnostic or treatment related costs that were made prior to contacting VeTS.
- An itemized receipt for the purchase of **NexGard** (afoxolaner) for the affected dog must be submitted to BI. For the FLEA SATISFACTION GUARANTEE, itemized receipts for the purchase of flea control for all pets in the home are required. The receipt must show the place of purchase, the date of purchase, the product brand name, the amount of product purchased, and the purchase price. For the LYME SATISFACTION GUARANTEE, the affected dog's medical records will be required showing Lyme testing history and **NexGard** purchase history. For the LYME SATISFACTION GUARANTEE PLUS, the records required for the LYME SATISFACTION GUARANTEE as well as documentation showing administration of RECOMBITEK Lyme within the previous twelve months must be submitted.
- **NexGard** must have been purchased from a veterinary clinic or with a written prescription via a valid veterinarian-client-patient relationship.
- BI reserves the right to request that original receipts be submitted via fax, email, or mail before a guarantee claim will be processed.
- The guarantee claim can only be processed for the individual whose name appears on the receipt.
- The guarantee is only valid for product labeled in the United States.
- Please allow 4-6 weeks for processing of refunds.
- Product that has been obtained free of charge is not eligible for the guarantee.
- This guarantee is limited to the above description. Additional costs are the responsibility of the pet owner.
- BI reserves the right to cancel or amend the guarantee program at any time.

IMPORTANT SAFETY INFORMATION

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PET-1165-NEX0119

NexGard[®]

(afoxolaner) Chewables

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description:

NexGard[®] (afoxolaner) is available in four sizes of beef-flavored, soft chewables for oral administration to dogs and puppies according to their weight. Each chewable is formulated to provide a minimum afoxolaner dosage of 1.14 mg/lb (2.5 mg/kg). Afoxolaner has the chemical composition 1-Naphthalenecarboxamide, 4-[5- [3-chloro-5-(trifluoromethyl)-phenyl]-4, 5-dihydro-5-(trifluoromethyl)-3-isoxazolyl]-N-[2-oxo-2-[(2,2,2-trifluoroethyl)amino]ethyl].

Indications:

NexGard kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*), and the treatment and control of Black-legged tick (*Ixodes scapularis*), American Dog tick (*Dermacentor variabilis*), Lone Star tick (*Amblyomma americanum*), and Brown dog tick (*Rhipicephalus sanguineus*) infestations in dogs and puppies 8 weeks of age and older, weighing 4 pounds of body weight or greater, for one month. NexGard is indicated for the prevention of *Borrelia burgdorferi* infections as a direct result of killing *Ixodes scapularis* vector ticks.

Dosage and Administration:

NexGard is given orally once a month, at the minimum dosage of 1.14 mg/lb (2.5 mg/kg).

Dosing Schedule:

| Body Weight | Afoxolaner Per Chewable (mg) | Chewables Administered |
|--------------------|-----------------------------------------------------|------------------------|
| 4.0 to 10.0 lbs. | 11.3 | One |
| 10.1 to 24.0 lbs. | 28.3 | One |
| 24.1 to 60.0 lbs. | 68 | One |
| 60.1 to 121.0 lbs. | 136 | One |
| Over 121.0 lbs. | Administer the appropriate combination of chewables | |

NexGard can be administered with or without food. Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes to ensure that part of the dose is not lost or refused. If it is suspected that any of the dose has been lost or if vomiting occurs within two hours of administration, redose with another full dose. If a dose is missed, administer NexGard and resume a monthly dosing schedule.

Flea Treatment and Prevention:

Treatment with NexGard may begin at any time of the year. In areas where fleas are common year-round, monthly treatment with NexGard should continue the entire year without interruption.

To minimize the likelihood of flea reinfestation, it is important to treat all animals within a household with an approved flea control product.

Tick Treatment and Control:

Treatment with NexGard may begin at any time of the year (see **Effectiveness**).

Contraindications:

There are no known contraindications for the use of NexGard.

Warnings:

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

Precautions:

Afoxolaner is a member of the isoxazoline class. This class has been associated with neurologic adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in dogs receiving isoxazoline class drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders (see **Adverse Reactions and Post-Approval Experience**).

The safe use of NexGard in breeding, pregnant or lactating dogs has not been evaluated.

Adverse Reactions:

In a well-controlled US field study, which included a total of 333 households and 615 treated dogs (415 administered afoxolaner; 200 administered active control), no serious adverse reactions were observed with NexGard.

Over the 90-day study period, all observations of potential adverse reactions were recorded. The most frequent reactions reported at an incidence of > 1% within any of the three months of observations are presented in the following table. The most frequently reported adverse reaction was vomiting. The occurrence of vomiting was generally self-limiting and of short duration and tended to decrease with subsequent doses in both groups. Five treated dogs experienced anorexia during the study, and two of those dogs experienced anorexia with the first dose but not subsequent doses.

Table 1: Dogs With Adverse Reactions.

| | Treatment Group | | | |
|-----------------------------------|-----------------|-----------|---------------------|-----------|
| | Afoxolaner | | Oral active control | |
| | N ¹ | % (n=415) | N ² | % (n=200) |
| Vomiting (with and without blood) | 17 | 4.1 | 25 | 12.5 |
| Dry/Flaky Skin | 13 | 3.1 | 2 | 1.0 |
| Diarrhea (with and without blood) | 13 | 3.1 | 7 | 3.5 |
| Lethargy | 7 | 1.7 | 4 | 2.0 |
| Anorexia | 5 | 1.2 | 9 | 4.5 |

¹Number of dogs in the afoxolaner treatment group with the identified abnormality.

²Number of dogs in the control group with the identified abnormality.

In the US field study, one dog with a history of seizures experienced a seizure on the same day after receiving the first dose and on the same day after receiving the second dose of NexGard. This dog experienced a third seizure one week after receiving the third dose. The dog remained

enrolled and completed the study. Another dog with a history of seizures had a seizure 19 days after the third dose of NexGard. The dog remained enrolled and completed the study. A third dog with a history of seizures received NexGard and experienced no seizures throughout the study.

Post-Approval Experience (July 2018):

The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse events are reported to FDA/CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data.

The following adverse events reported for dogs are listed in decreasing order of reporting frequency for NexGard:

Vomiting, pruritus, lethargy, diarrhea (with and without blood), anorexia, seizure, hyperactivity/restlessness, panting, erythema, ataxia, dermatitis (including rash, papules), allergic reactions (including hives, swelling), and tremors.

Contact Information:

For a copy of the Safety Data Sheet (SDS) or to report suspected adverse drug events, contact Merial at 1-888-FDA-VETS or www.nexgardfordogs.com.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

Mode of Action:

Afoxolaner is a member of the isoxazoline family, shown to bind at a binding site to inhibit insect and acarine ligand-gated chloride channels, in particular those gated by the neurotransmitter gamma-aminobutyric acid (GABA), thereby blocking pre- and post-synaptic transfer of chloride ions across cell membranes. Prolonged afoxolaner-induced hyperexcitation results in uncontrolled activity of the central nervous system and death of insects and acarines. The selective toxicity of afoxolaner between insects and acarines and mammals may be inferred by the differential sensitivity of the insects and acarines' GABA receptors versus mammalian GABA receptors.

Effectiveness:

In a well-controlled laboratory study, NexGard began to kill fleas four hours after initial administration and demonstrated >99% effectiveness at eight hours. In a separate well-controlled laboratory study, NexGard demonstrated 100% effectiveness against adult fleas 24 hours post-infestation for 35 days, and was ≥93% effective at 12 hours post-infestation through Day 21, and on Day 35. On Day 28, NexGard was 81.1% effective 12 hours post-infestation. Dogs in both the treated and control groups that were infested with fleas on Day -1 generated flea eggs at 12- and 24-hours post-treatment (0-11 eggs and 1-17 eggs in the NexGard treated dogs, and 4-90 eggs and 0-118 eggs in the control dogs, at 12- and 24-hours, respectively). At subsequent evaluations post-infestation, fleas from dogs in the treated group were essentially unable to produce any eggs (0-1 eggs) while fleas from dogs in the control group continued to produce eggs (1-141 eggs).

In a 90-day US field study conducted in households with existing flea infestations of varying severity, the effectiveness of NexGard against fleas on the Day 30, 60 and 90 visits compared with baseline was 98.0%, 99.7%, and 99.9%, respectively.

Collectively, the data from the three studies (two laboratory and one field) demonstrate that NexGard kills fleas before they can lay eggs, thus preventing subsequent flea infestations after the start of treatment of existing flea infestations.

In well-controlled laboratory studies, NexGard demonstrated >97% effectiveness against *Dermacentor variabilis*, >94% effectiveness against *Ixodes scapularis*, and >93% effectiveness against *Rhipicephalus sanguineus*, 48 hours post-infestation for 30 days. At 72 hours post-infestation, NexGard demonstrated >97% effectiveness against *Amblyomma americanum* for 30 days. In two separate, well-controlled laboratory studies, NexGard was effective at preventing *Borrelia burgdorferi* infections after dogs were infested with *Ixodes scapularis* vector ticks 28 days post-treatment.

Animal Safety:

In a margin of safety study, NexGard was administered orally to 8 to 9-week-old Beagle puppies at 1, 3, and 5 times the maximum exposure dose (6.3 mg/kg) for three treatments every 28 days, followed by three treatments every 14 days, for a total of six treatments. Dogs in the control group were sham-dosed. There were no clinically-relevant effects related to treatment on physical examination, body weight, food consumption, clinical pathology (hematology, clinical chemistries, or coagulation tests), gross pathology, histopathology or organ weights. Vomiting occurred throughout the study, with a similar incidence in the treated and control groups, including one dog in the 5x group that vomited four hours after treatment.

In a well-controlled field study, NexGard was used concomitantly with other medications, such as vaccines, anthelmintics, antibiotics (including topicals), steroids, NSAIDs, anesthetics, and antihistamines. No adverse reactions were observed from the concomitant use of NexGard with other medications.

Storage Information:

Store at or below 30°C (86°F) with excursions permitted up to 40°C (104°F).

How Supplied:

NexGard is available in four sizes of beef-flavored soft chewables: 11.3, 28.3, 68 or 136 mg afoxolaner. Each chewable size is available in color-coded packages of 1, 3 or 6 beef-flavored chewables.

NADA 141-406, Approved by FDA

Marketed by: Frontline Vet Labs[™], a Division of Merial, Inc.
Duluth, GA 30096-4640 USA

Made in Brazil.

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