

NexGard[®]
(afoxolaner) Chewables

Trusted for Protection

NexGard[®] (afoxolaner) is trusted flea and tick protection for canine patients. Dogs love the beef flavor,¹ and clients love the powerful protection. That's why NexGard isn't just #1 vet-recommended: it's #1 client-requested.^{2,3}



Delicious Protection

Savory beef-flavored chew that is #1 dog-preferred.⁴



Prevents Lyme Infections

FDA-approved to prevent Lyme infections by killing black-legged ticks.



Safely Protects Puppies

Safe for puppies eight weeks or older, weighing four pounds or more.



Trusted by Vets

Prescribed by vets over 270 million times, for their patients and their own dogs.⁵

Break the Cycle

NexGard kills fleas fast, disrupting the flea life cycle and killing adults before they have the chance to lay eggs. It provides powerful protection all month long, stopping current flea infestations, and preventing future infestations from occurring. After initial administration, NexGard starts killing fleas within four hours. In studies, NexGard was 100% effective against adult fleas 24 hours post-infestation for 35 days.

IMPORTANT SAFETY INFORMATION: NexGard 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 full prescribing information or visit NexGardClinic.com.



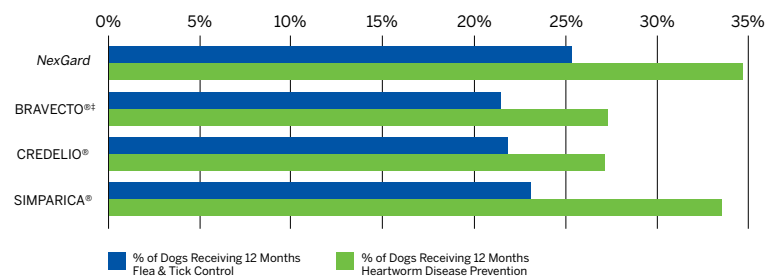
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 **Boehringer
Ingelheim**

Trusted for Compliance

NexGard® (afoxolaner), the savory, beef-flavored chew that dogs prefer, was designed with compliance in mind.⁴ An independent, third-party analysis conducted to assess the current purchase patterns of oral flea and tick products in 2020 found that NexGard was unsurpassed in average number of months of oral flea and tick product purchased per patient per year.^{*†6}

Percent of Dogs Receiving Year-Round Protection^{*†6}



- More NexGard users purchased a full 12 months of flea and tick protection than users of any of these oral flea and tick control products.^{*†6}
- Users of NexGard were also more likely to purchase a full 12 months of an additional heartworm disease prevention product.^{*†6}

Assessment Summary

In this assessment graph, for each of the flea and tick control products, the percentage of users who purchased enough product to protect their dogs for a full 12 months was determined.

- For each of the flea and tick control products evaluated, the percentage of users of a product who purchased a full 12 months of the product was calculated.
- For each of the flea and tick control products purchased (regardless of the amount purchased), the percentage of users who purchased a full 12 months of heartworm disease prevention was determined.

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* Assessment was conducted by IDEXX® and leveraged veterinary clinic PIMS transaction level data for 2020. This analysis included veterinary practices with consistent data from 2018 to 2020. To be included, patients needed to have at least one parasiticide transaction in 2019 and 2020. The analysis was limited to loyal patients, where loyalty was defined as having one flea/tick control brand during the full three-year period.

† This analysis overestimates the duration of efficacy for BRAVECTO® (fluralaner). This assessment includes BRAVECTO Chew for Dogs and BRAVECTO Topical for Dogs. For comparison purposes, each BRAVECTO dose was assessed as providing three months of flea and tick protection versus the labeled 12-week coverage for fleas and three species of ticks, and 8-week coverage for Lone Star ticks.

‡ This assessment includes BRAVECTO Chew for Dogs and BRAVECTO Topical for Dogs. In this assessment, the duration of efficacy of 4 doses of BRAVECTO is overestimated to provide year-round protection. Four doses of BRAVECTO protects against fleas and three species of ticks for 48 weeks. An additional dose would be required to provide year-round protection. Four doses of BRAVECTO would provide coverage against Lone Star ticks for only 32 weeks.

1. Data on file at Boehringer Ingelheim. 2. Data on file at Boehringer Ingelheim. 3. Data on file at Boehringer Ingelheim. 4. Data on file at Boehringer Ingelheim. 5. Data on file at Boehringer Ingelheim. 6. Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA.

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CHECK-OFF &
ECHO NOTES **byte**

Be ready to talk to your clients about the risks of fleas and ticks.

Qualify

Doctor, are you familiar with NexGard?

If **YES**, confirm and discuss benefits.

If **NO**, engage/detail the customer as the primary contact.

Confidence

Doctor, there's a reason why NexGard is the #1 client-requested, delicious beef-flavored chew^{2,3} When it comes to flea and tick control, NexGard is protection you can trust.

Neutral Invitation

Let's review some of the features of NexGard...

It's the Customer's Decision

... so that you can consider how it might fit in with your practice, and how it might serve your canine patients.

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.

Keep NexGard in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

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.

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

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

² Number 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 Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251 or www.nexgardfordogs.com.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae.

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.

Approved by FDA under NADA # 141-406

Marketed by: Frontline Vet Labs™, a Division of Boehringer Ingelheim Animal Health USA Inc. Duluth, GA 30096

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