



SLEEP FIX
A serious snooze is what your migraine-plagued friend needs most.

NOT YOUR TYPICAL HEADACHE

Some 27 million women suffer from the neurological condition known as migraine, and relief isn't as simple as popping an aspirin. Help a friend, mom or sister power through the pain

The throbbing one-sided head pain she complains of may sound like a simple tension headache, but if your loved one has been diagnosed with migraine, make no mistake: She needs a little extra TLC. "Migraine is a neurological condition that produces a number of associated symptoms beyond just a headache," explains Brian Grosberg, M.D., director of the Hartford Healthcare Headache Program in Connecticut. These migraine facts can help you know what to do.

IT'S NOT JUST IN HER HEAD

The headache is only one phase of a migraine. The wave of nerve cell excitement spreading across the back of the brain when a migraine hits can cause an aura that makes a migraine sufferer's vision fragment or shimmer. She may also become more sensitive to light and sound, get nauseated or vomit and feel confused and be unable to perform tasks she'd otherwise be able to do effortlessly. A tension headache might feel similar, says Dr. Grosberg, but usually is less severe, is felt on both sides of the skull and doesn't come with the other debilitating problems.

WEIRD THINGS TRIGGER IT

A standard headache often comes on when someone is sleep-deprived or dehydrated. But the brains and nervous systems of migraine sufferers are wired to process input differently, explains Dr. Grosberg, making them more vulnerable to stimuli. Aged cheese, red wine, changes in the weather and bright lights as well as hormonal shifts, stress and eyestrain can make someone with migraines want to assume the fetal position.

SHE HAS TO TREAT IT ASAP

Cut her some slack if she bails on plans and flops on her bed. "The best thing that you can do when you have a migraine is take a nap," says Dr. Grosberg. It's good to keep an NSAID with caffeine, like Excedrin, on hand, although she may have medication her doctor has prescribed. She probably knows what works for her—e.g., a magnesium supplement, coffee or ginger tea. Offer her a heat pack or a cold washcloth to help dull her pain, and lend her sunglasses or an eye mask to protect her against light sensitivity. Give her room to recover, says Dr. Grosberg: "Find a secluded area, turn off the lights and keep quiet." ♦

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-5H-imidazo[4,5-b]pyridin-2-yl]-2,2,2-trifluoroethyl-L-aminopropanoate.

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 6 weeks of age and older, weighing 4 pounds of body weight or greater, for one month.

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:
The safe use of NexGard in breeding, pregnant or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures (see **Adverse Reactions**).

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/Faiky 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.

To report suspected adverse events, for technical assistance or to obtain a copy of the MSDS, contact Meriel at 1-800-637-4251 or www.merial.com/nexgard. For additional information about adverse drug experiences reporting for animal drugs, contact FDA at 1-800-FDA-VETS or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

Mode of Action:

Afoxolaner is a member of the isoxazole 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 hyperpolarization 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 61.1% 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 (0-1 eggs and 1-17 eggs in the NexGard treated dogs, and 4-90 eggs and 0-110 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 30-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 Demarector variabilis, >94% effectiveness against Ixodes scapularis, and 93% effectiveness against Rhipicephalus sanguineus, 48 hours post-infestation for 30 days. At 12 hours post-infestation, NexGard demonstrated >97% effectiveness against Amblyomma americanum for 30 days.

Animal Safety:

In a margin of safety study, NexGard was administered orally to 8-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 chemistry, or coagulation tests), gross pathology, histopathology or organ weights. Vomiting did not occur through Day 28. On Day 28, NexGard was 61.1% effective in the treated and control groups, including one dog in the 5-mg group that vomited four hours after treatment.

In a well-controlled field study, NexGard was used concomitantly with other medications, such as vaccines, analgesics, 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

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Made in Brazil

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