



# THE FIRST AND ONLY FELINE BROAD-SPECTRUM PARASITE PROTECTION THAT KILLS TAPEWORMS



FLEAS



TICKS



HEARTWORM  
DISEASE



ROUNDWORMS



HOOKWORMS



TAPEWORMS



## PROTECT YOUR FELINE PATIENTS WITH NexGard® COMBO (ESAFOXOLANER, EPRINOMECTIN, AND PRAZIQUANTEL TOPICAL SOLUTION)

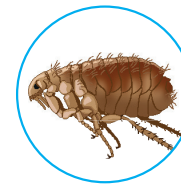
### The One You Want for One-And-Done Monthly Protection

NexGard® COMBO (esafloxolaner, eprinomectin, and praziquantel topical solution) protects your feline patients from common internal and external parasites:

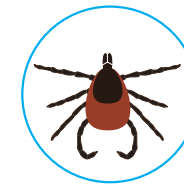
- Kills fleas and ticks
- Prevents heartworm disease
- Treats and controls roundworms and hookworms
- It's also the only feline parasiticide with broad-spectrum protection that includes tapeworm protection

## Broad-Spectrum Efficacy

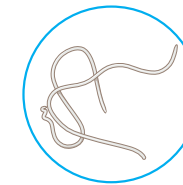
NexGard® COMBO (esafloxolaner, eprinomectin, and praziquantel topical solution) delivers powerful protection against internal and external parasites cat owners should be concerned about.



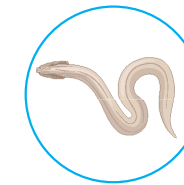
FLEAS



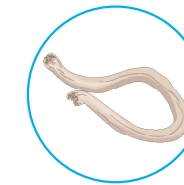
TICKS



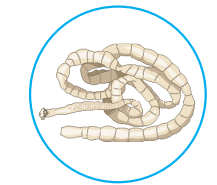
HEARTWORM  
DISEASE



ROUNDWORMS



HOOKWORMS



TAPEWORMS

## Three Active Ingredients. One Topical Solution.

NexGard COMBO topical solution features a triple-action formulation that includes esafloxolaner, the purified, active (S)-enantiomer of afoxolaner, designed specifically for cats as well as eprinomectin and praziquantel, both with a long history of safety and efficacy against heartworm disease and common intestinal parasites.



### Targeted Parasites Ectoparasites

#### Mode of Action

- Antagonist at ligand-gated chloride channels (GABA)
- Blocking pre- and post-synaptic transfer of chloride ions
  - Uncontrolled activity of the central nervous system
  - Death of insects or acarines

#### Associated Indications

- Kills adult *Ctenocephalides felis* fleas
- Treats and prevents flea infestations
- Treats and controls tick infestations:
  - Black-legged tick (*Ixodes scapularis*)
  - Lone star tick (*Amblyomma americanum*)



### Targeted Parasites Nematodes

#### Mode of Action

- High affinity to glutamate-gated chloride ion channels
- Increase in the permeability of the cell membrane to chloride ions
  - Hyperpolarization of the nerve or muscle cell
  - Flaccid paralysis and death of the parasite

#### Associated Indications

- Prevents heartworm disease caused by *Dirofilaria immitis*
- Treats and controls roundworms:
  - *Toxocara cati* (4th-stage larval and adult)
- Treats and controls hookworms:
  - *Ancylostoma tubaeforme* (4th-stage larval and adult)
  - *Ancylostoma braziliense* (adult)



### Targeted Parasites Cestodes

#### Mode of Action

- Not precisely known
- Treated tapeworms undergo muscular paralysis
  - Rapid influx of calcium ions and disruption of the tegument

#### Associated Indications

- Treats and controls tapeworms (*Dipylidium caninum*)

**IMPORTANT SAFETY INFORMATION:** NexGard COMBO is for topical use only in cats. Use with caution in cats with a history of seizures or neurologic disorders. The most frequently reported adverse reactions include vomiting, application site reactions, and anorexia. If ingested, hypersalivation may occur. Avoid direct contact with application site until visibly dry. For more information, see full prescribing information or visit NexGardCOMBOClinic.com.

# SINGLE-DOSE APPLICATOR

## Easy to Apply

NexGard® COMBO (esafoxolaner, eprinomectin, and praziquantel topical solution) is applied with an easy-to-use applicator that helps reduce stress and mess for cats and their owners.



**IMPORTANT SAFETY INFORMATION:** NexGard COMBO is for topical use only in cats. Use with caution in cats with a history of seizures or neurologic disorders. The most frequently reported adverse reactions include vomiting, application site reactions, and anorexia. If ingested, hypersalivation may occur. Avoid direct contact with application site until visibly dry. For more information, see full prescribing information or visit [NexGardCOMBOclinic.com](http://NexGardCOMBOclinic.com).



## FLEAS

NexGard® COMBO (esafoxolaner, eprinomectin, and praziquantel topical solution) kills fleas fast before they can lay eggs as well as treats and prevents flea infestations.

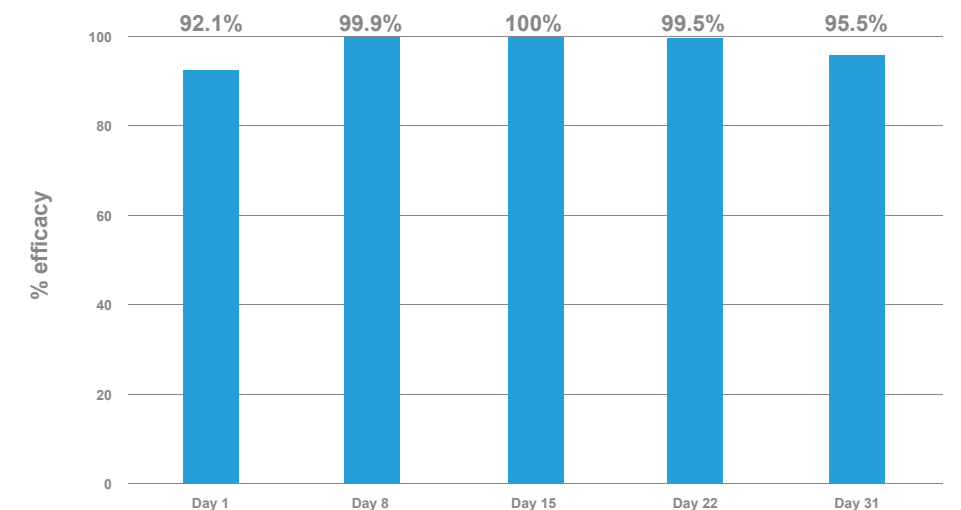
### In a well-controlled laboratory study, cats were:

- Infested with ~100 fleas on Day -1
- Treated with NexGard COMBO topical solution on Day 0
- Infested with ~100 fleas weekly on Days 7, 14, 21, and 30

## Kills Fleas All Month Long

- Killed >92% of fleas within 24 hours of treatment.
- During subsequent infestations, was over 99.5% effective through Day 22, and 95.5% effective on Day 31.

Percent efficacy\* against adult fleas 24 hours after treatment or reinfestation<sup>1</sup>

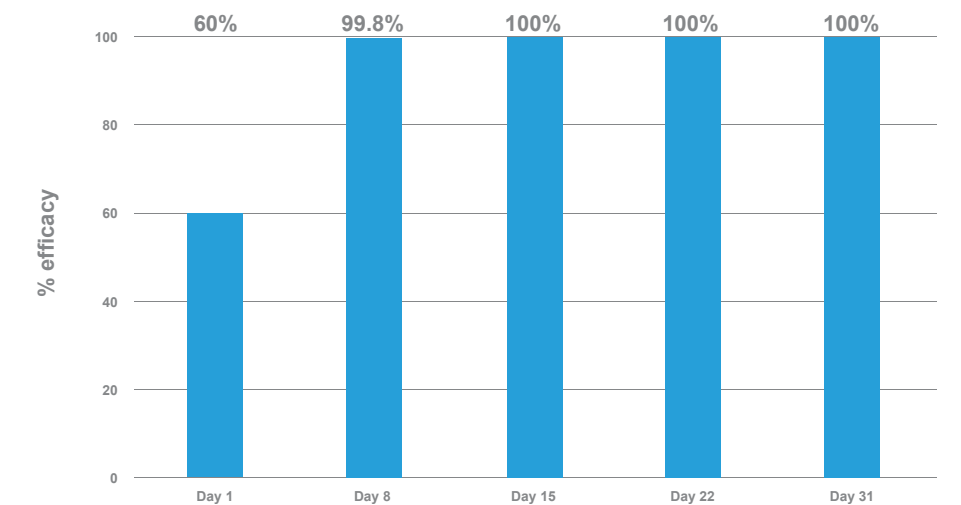


\*Percent efficacy =  $100 \times [(C-T)/C]$ , where T and C are the arithmetic mean flea counts of the treated and control groups, respectively.

## Kills Adult Fleas Before They Can Lay Eggs

- Because cats were infested with fleas on Day -1, fleas were able to produce eggs prior to exposure to NexGard COMBO topical solution
- After Day 1, inhibition of egg production was consistently  $\geq 99.8\%$

Percent efficacy\* against fleas' egg production<sup>1</sup>



\*Percent efficacy =  $100 \times [(C-T)/C]$ , where T and C are the arithmetic mean flea egg counts of the treated and control groups, respectively.



## FLEAS

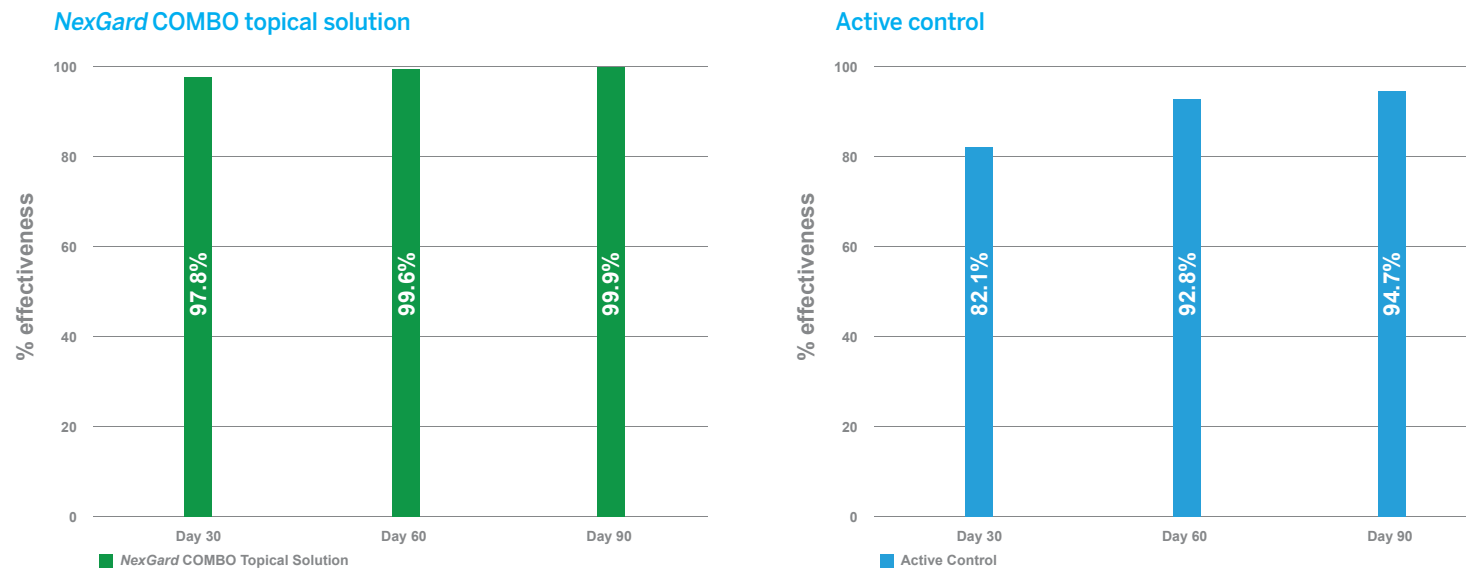
### Effectiveness of 3 monthly applications against adult fleas and flea allergy dermatitis (FAD)<sup>1</sup>

In this multicenter clinical field study, the safety and effectiveness of NexGard<sup>®</sup> COMBO (esafoxolaner, eprinomectin, and praziquantel topical solution) was evaluated.

In the effectiveness portion of the study:

- Demonstrated  $\geq 97.8\%$  effectiveness against fleas under real-world conditions over the 3-month treatment period
- Cats treated with NexGard COMBO topical solution showed an improvement in clinical signs related to FAD, as a direct result of eliminating fleas

### Percent effectiveness\* against fleas<sup>1</sup>



\*Percent effectiveness refers to the percent reduction in flea count compared to the average baseline flea count from Day 0. Percent effectiveness =  $100 \times [(C - T)/C]$ , where T and C are the geometric mean flea counts of the treated and control groups, respectively.

**IMPORTANT SAFETY INFORMATION:** NexGard COMBO is for topical use only in cats. Use with caution in cats with a history of seizures or neurologic disorders. The most frequently reported adverse reactions include vomiting, application site reactions, and anorexia. If ingested, hypersalivation may occur. Avoid direct contact with application site until visibly dry. For more information, see full prescribing information or visit NexGardCOMBOclinic.com.



## TICKS

NexGard<sup>®</sup> COMBO (esafoxolaner, eprinomectin, and praziquantel topical solution) is effective for the treatment and control of the 2 most common tick species found on cats in the US: *Ixodes scapularis* (black-legged tick) and *Amblyomma americanum* (lone star tick).<sup>2</sup>

### Results against *I. scapularis*

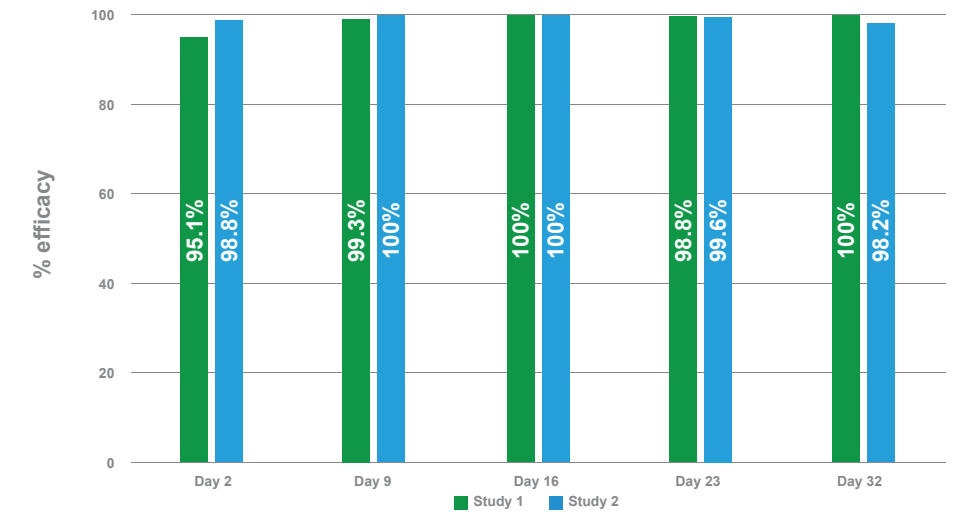
#### Day 2

At 48 hours post-treatment, NexGard COMBO topical solution showed  $\geq 95.1\%$  efficacy against *I. scapularis*.

#### Days 9, 16, 23, and 32

On subsequent days, NexGard COMBO topical solution demonstrated  $\geq 98.2\%$  efficacy against *I. scapularis* through Day 32.

Percent efficacy\* against *I. scapularis* 48 hours after treatment or reinfestation<sup>1</sup>

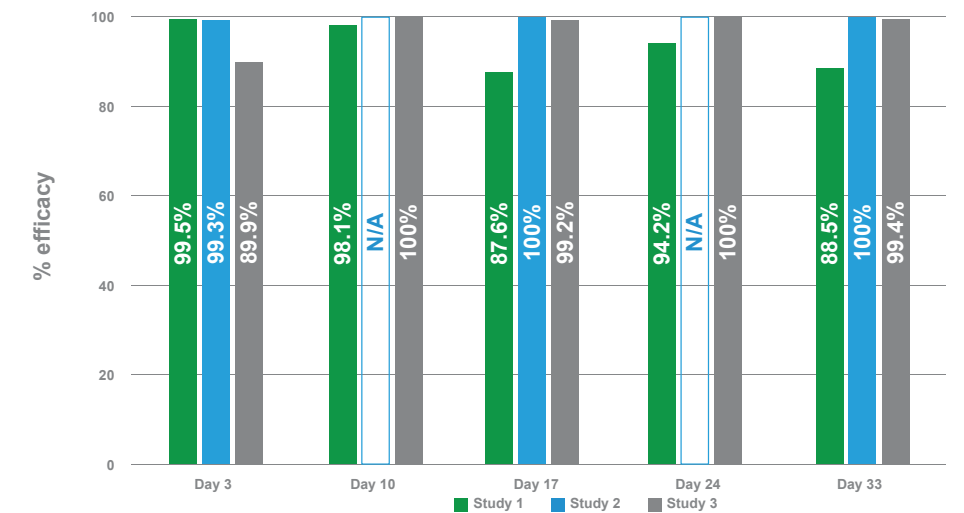


\*Percent efficacy =  $100 \times [(C - T)/C]$ , where T and C are the arithmetic mean tick counts of the treated and control groups, respectively.

### Results against *A. americanum*

On average, NexGard COMBO topical solution demonstrated **>95.6% efficacy** against *A. americanum* at all time points.

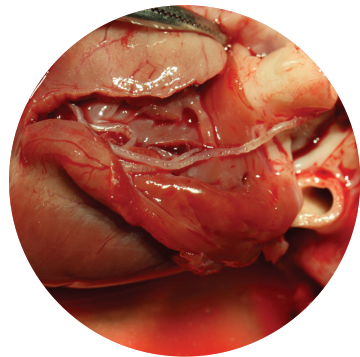
Percent efficacy\* of a single application against *A. americanum* 72 hours after treatment or reinfestation<sup>1</sup>



\*Percent efficacy =  $100 \times [(C - T)/C]$ , where T and C are the arithmetic mean tick counts of the treated and control groups, respectively.



## HEARTWORM DISEASE



### Effective in Preventing Heartworm Disease

Five studies were performed to evaluate the efficacy of NexGard® COMBO (esafoxolaner, eprinomectin, and praziquantel topical solution) against 2 heartworm isolates for the prevention of heartworm disease in cats.

In some studies, cats were treated with 1 monthly application while in other studies cats were treated monthly for 3 consecutive months.

**Result: There was 100% prevention of the development of *Dirofilaria immitis* in all groups of cats administered NexGard Combo topical solution.**

Note: For heartworm disease prevention, apply once monthly for at least 3 months after last exposure to mosquitoes



## INTESTINAL PARASITES

### Treats and Controls Intestinal Parasites

In laboratory studies, NexGard COMBO topical solution was effective against these parasites:



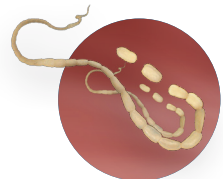
#### Roundworms (*Toxocara cati*)

Demonstrated ≥98.8% efficacy for the treatment of adult *T. cati*.



#### Hookworms (*Ancylostoma tubaeforme* and *Ancylostoma braziliense*)

In well-controlled laboratory studies using an early eprinomectin-containing formulation, the topical solution demonstrated >91% effectiveness against hookworms (adult and 4th stage larval *A. tubaeforme* and adult *A. braziliense*).<sup>3</sup>



#### Tapeworms (*Dipylidium caninum*)

Demonstrated an average 92.8% efficacy against the most common tapeworm species in cats, *D. caninum*.<sup>4</sup>

**IMPORTANT SAFETY INFORMATION:** NexGard COMBO is for topical use only in cats. Use with caution in cats with a history of seizures or neurologic disorders. The most frequently reported adverse reactions include vomiting, application site reactions, and anorexia. If ingested, hypersalivation may occur. Avoid direct contact with application site until visibly dry. For more information, see full prescribing information or visit NexGardCOMBOclinic.com.

## SAFETY AND TOLERANCE

Safe for use in cats including heartworm-positive cats, and kittens 8 weeks of age or older, weighing 1.8 pounds or more.

### Extensive Safety Testing Has Been Conducted

- Margin of safety laboratory study
  - Safe for use in cats and kittens.
- Study in heartworm positive cats
  - Safe for use in heartworm-positive cats.
- Oral administration study
  - Do not give orally. If ingested, hypersalivation may occur.

### Safety Component of the Field Flea Study

Over the course of a field study that included 244 cats treated with NexGard® COMBO (esafoxolaner, eprinomectin, and praziquantel topical solution) and 136 cats treated with an active control, there were no serious health abnormalities attributed to treatment. Concurrent administration of various medications and vaccines did not have an impact on the safety of NexGard COMBO topical solution.

### Adverse Reactions Included

The most frequently reported adverse reactions reported within any of the 3 months of observations included vomiting, application site hair change, anorexia, lethargy, skin infection, itching, and sneezing.



# SUPPORTING YOUR CLINIC

Boehringer Ingelheim, the maker of *NexGard*® COMBO (esafloxolaner, eprinomectin, and praziquantel topical solution), is committed to supporting you and your clinic's success.

## Client Education

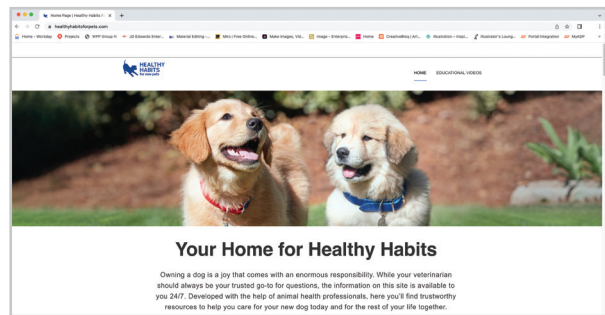
We provide complimentary resources to help you educate your clients about *NexGard* COMBO topical solution, as well as the importance of protection for their cats.



## Healthy Habits for Pets

With an emphasis on the importance of regular vet visits and veterinarian-prescribed parasite protection, the Healthy Habits for Pets website is designed to help you support pet owners as they develop lifelong habits to help keep their pets healthy.

**Visit [HealthyHabitsForPets.com](https://HealthyHabitsForPets.com) to learn more.**



## Pet Owner Offers

Help pet owners save money on parasite protection with rebates. Find offers on 6-month and 12-month supplies of *NexGard* COMBO topical solution at [NexGardCOMBO.com](https://NexGardCOMBO.com).

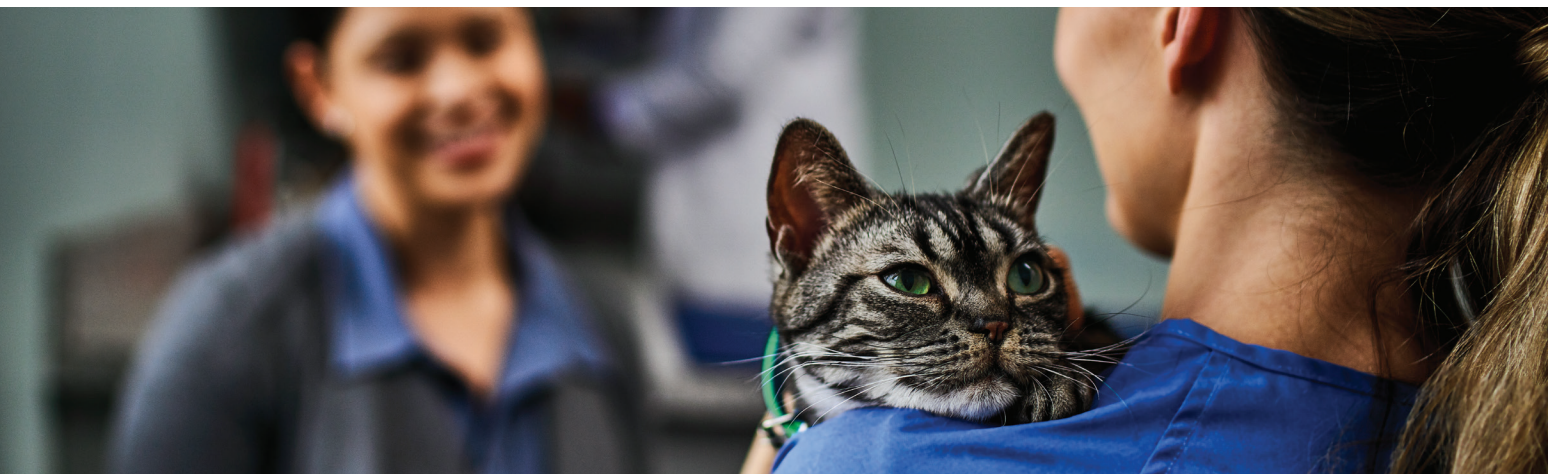
## Customer Care

Our **Customer Care Team** is ready to assist you with any product inquiries, including order placement, returns, promotion or program support, BI-CONNECT™ assistance, and more.

**They are available Monday to Friday from 8 am to 8 pm ET at 1-888-637-4251.**

Our **Veterinary Technical Solutions (VeTS) Team** is available for assistance with product label inquiries, vet-to-vet consultations, suspected adverse event reporting, and other pharmacovigilance activities.

**The VeTS Team is available Monday to Friday from 8 am to 6 pm ET at 1-888-637-4251.**



# NexGard® COMBO

(esafloxolaner, eprinomectin, and praziquantel topical solution)

**For topical use in cats only**

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

**Description:** NexGard® COMBO is a topical solution containing esafloxolaner, eprinomectin and praziquantel available in 0.3 mL and 0.9 mL unit applicators to treat cats from 1.8 lbs to 33 lbs. Each mL of NexGard® COMBO contains 12 mg of esafloxolaner, 4 mg of eprinomectin, and 83 mg of praziquantel. Inactive ingredients: dimethyl isosorbide, unstabilized glycerol formal, and butylated hydroxytoluene.

Esafloxolaner is a member of the aryl isoxazole class of compounds. Its chemical name is 4-[(5S)-5-[3-chloro-5-(trifluoromethyl)phenyl]-5-(trifluoromethyl)-4, 5-dihydro-1,2-oxazol-3-yl]-N-[2-(2,2-trifluoroethyl) aminoethyl]-1-naphthamide.

Eprinomectin belongs to the avermectin class of anthelmintics and is a mixture of homologous components referred to as eprinomectin B1a and B1b. The chemical name for eprinomectin B1a is (4'R)-acetylamino-5-O-demethyl-4'-deoxyavermectin A<sub>1</sub>. The chemical name for eprinomectin B1b is (4'R)-acetylamino-5-O-demethyl-25-de(1-methylpropyl)-4'-deoxy-25-(1-methylethyl) avermectin A<sub>1</sub>.

Praziquantel is a pyrazinoisoquinoline anthelmintic. Its chemical name is 2-(Cyclohexylcarbonyl)-1,2,3,6,7,11b-hexahydro-4H-pyrazino[2,1-a]isoquinolin-4-one.

**Indications:** NexGard® COMBO is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis* and for the treatment and control of roundworm (fourth stage larval and adult *Toxocara cati*), hookworm (fourth stage larval and adult *Ancylostoma tubaeforme*, adult *Ancylostoma braziliense*), and tapeworm (*Dipylidium caninum*) infections. NexGard® COMBO kills adult fleas (*Ctenocephalides felis*) and is indicated for the treatment and prevention of flea infestations and the treatment and control of *Ixodes scapularis* (black-legged tick) and *Amblyomma americanum* (lone star tick) infestations for one month in cats and kittens 8 weeks of age and older, and weighing 1.8 lbs or greater.

**Dosage and Administration:** NexGard® COMBO is dosed at a minimum of 0.055 mL/lb (0.12 mL/kg), which delivers a minimum dose of 0.65 mg/lb (1.44 mg/kg) esafloxolaner, 0.22 mg/lb (0.48 mg/kg) eprinomectin, and 4.53 mg/lb (9.98 mg/kg) praziquantel.

**For heartworm disease prevention, apply once monthly for at least three months after last exposure to mosquitoes (see Effectiveness).**

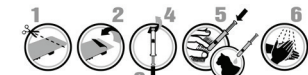
Administer the entire contents of a NexGard® COMBO unit applicator topically once a month as specified in the following table:

**Dosing Schedule:**

Cat Weight (lb)	Volume (mL)	Esafloxolaner (mg)	Eprinomectin (mg)	Praziquantel (mg)
1.8-5.5	0.3	3.6	1.2	24.9
5.6-16.5	0.9	10.8	3.6	74.7
16.6-22	0.3 + 0.9	14.4	4.8	99.6
22.1-33	0.9 + 0.9	21.6	7.2	149.4

A veterinarian or veterinary technician should demonstrate or instruct the pet owner regarding the appropriate technique for applying NexGard® COMBO topically to cats and kittens prior to first use.

Keep product in original packaging until ready to use.



**Heartworm Prevention:** For the prevention of heartworm disease, NexGard® COMBO should be administered once a month year-round. At a minimum, administration of NexGard® COMBO should start at least 1 month before the cat's first expected exposure to mosquitoes and monthly thereafter until at least 3 months after the cat's last seasonal exposure to mosquitoes (see **Effectiveness**). If a dose is missed and a 30-day interval between doses is exceeded, administer NexGard® COMBO immediately and resume the monthly dosing schedule. Treatment with fewer than 3 monthly doses may not provide complete heartworm prevention. When replacing another monthly heartworm preventive product in a heartworm prevention program, the first treatment with NexGard® COMBO should be given within one month of the last dose of the former medication. At the discretion of the veterinarian, cats older than 6 months of age may be tested to determine the presence of existing heartworm infection before treatment with NexGard® COMBO. Cats already infected with adult heartworms can be given NexGard® COMBO monthly to prevent further infections.

**Flea Treatment and Prevention:** For the treatment and prevention of flea infestations, the use of NexGard® COMBO may begin at any time of year. NexGard® COMBO should be administered year-round at monthly intervals or begin at least one month before fleas become active. However, an environmental infestation may persist for a short time after beginning treatment with NexGard® COMBO because of the development of adult fleas from eggs that were laid prior to the initiation of treatment.

**Tick Treatment and Control:** For the treatment and control of infestations with *Ixodes scapularis* and *Amblyomma americanum*, the use of NexGard® COMBO may begin at any time of year. NexGard® COMBO should be administered year-round at monthly intervals or begin at least one month before the ticks become active.

**Treatment and Control of Roundworms, Hookworms, and Tapeworms:** NexGard® COMBO provides treatment and control of roundworms (adult and fourth stage larval *Toxocara cati*), hookworms (adult and fourth stage larval *Ancylostoma tubaeforme*, adult *Ancylostoma braziliense*), and tapeworms (*Dipylidium caninum*). For the treatment of hookworm, roundworms and tapeworm infections, NexGard® COMBO should be administered once as a single dose. Monthly use of NexGard® COMBO will control any subsequent infections. Cats may be exposed to and can become infected with roundworms, hookworms, and tapeworms throughout the year, regardless of season or climate.

**Contraindications:** There are no known contraindications for the use of NexGard® COMBO.

**Human Warnings:** Not for human use. Keep this and all drugs out of sight and reach of children.

**Avoid direct contact with application site for 4 hours or until visibly dry.**

**This product may act as a mild to moderate eye irritant.**

Keep product in the original packaging until use. Wash hands after product administration. If the product accidentally gets into the eyes, rinse thoroughly with water. If wearing contact lenses, flush the eyes first with water and then remove the lenses and continue to flush thoroughly with water. In case of accidental ingestion, or if skin or eye irritation occurs, contact a poison control center or physician for treatment advice.

**Precautions:** Esafloxolaner, one of the ingredients in NexGard® COMBO, is a member of the isoxazole class. This class has been associated with neurologic adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in cats receiving isoxazole class drugs, even in cats without a history of seizures. Use with caution in cats with a history of seizures or neurologic disorders.

Do not administer orally. Cats may salivate excessively if NexGard® COMBO is accidentally administered orally or is ingested through licking/grooming the application site (see **Target Animal Safety**).

The safety of NexGard® COMBO has not been tested in breeding, pregnant, or lactating cats.

The safety of NexGard® COMBO has not been tested in kittens less than 8 weeks of age or weighing less than 1.8 lbs (0.8 kg).

**Adverse Reactions:** In a field safety and effectiveness study, which included a total of 201 households and 380 treated cats (244 cats treated with NexGard® COMBO, 136 cats treated with an active control), the safety of NexGard® COMBO was evaluated over a 90-day period through in-clinic physical examinations or through reporting of abnormalities by the owner. The most frequently reported reactions in the NexGard® COMBO and active control groups are presented in the following table.

**Adverse Reactions by Treatment Group**

EVENT	Treatment Group			
	NexGard COMBO		Active Control	
	n <sup>1</sup>	% (n=244)	n <sup>2</sup>	% (n=136)
Vomiting	16	6.56	8	5.88
Application Site Hair Change	9	3.69	0	0.00
Anorexia	7	2.87	4	2.94
Lethargy	6	2.46	5	3.68
Bacterial Skin Infection	4	1.64	1	0.74
Itching	4	1.64	0	0.00
Sneezing	4	1.64	5	3.68
Skin Peeling	3	1.23	2	1.47
Diarrhea	3	1.23	3	2.21
Epiphora	3	1.23	1	0.74
Hypersalivation	3	1.23	0	0.00
Hyperthermia	3	1.23	0	0.00
Alpecia	2	0.82	0	0.00
Dermal Thickening	2	0.82	0	0.00
Ear Pruritus	2	0.82	1	0.74
Application Site Redness	2	0.82	0	0.00
Conjunctivitis	1	0.41	1	0.74

<sup>1</sup>Number of cats treated with NexGard® COMBO with the identified abnormality.  
<sup>2</sup>Number of cats treated with Active Control with the identified abnormality.

**Contact Information:** To report suspected adverse events, for technical assistance or to obtain a copy of the SDS, contact [Boehringer Ingelheim Animal Health USA Inc.](https://www.boehringer-ingelheim.com) at 1-888-637-4251 or [www.nexgardforpets.com](https://www.nexgardforpets.com).

For additional information about reporting adverse drug experiences for animal drugs, contact FDA at 1-888-FDA-VETS or online at [www.fda.gov/reportanimalae](https://www.fda.gov/reportanimalae).

The Safety Data Sheet (SDS) provides additional occupational safety information. For customer service or to obtain product information, including the SDS, call 1-888-637-4251.

**Clinical Pharmacology:** Mode of Action: Esafloxolaner is a member of the isoxazole family, shown to bind at a 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 esafloxolaner-induced hyperexcitation results in uncontrolled activity of the central nervous system and death of insects and acarines. The selective toxicity of esafloxolaner between insects/acarines and mammals may be inferred by the differential sensitivity of the insects/acarines' GABA receptors versus mammalian GABA receptors.

Eprinomectin is an endectocide in the macrocyclic lactone class that binds to glutamate-gated chloride channels that are present in invertebrate nerve and muscle cells and increases the permeability of the cell membrane to chloride ions that triggers hyperpolarization of the nerve or muscle cell in susceptible parasites, resulting in paralysis and death of the parasite.

Praziquantel's mode of action is not precisely known, but treated tapeworms undergo muscular paralysis accompanied by a rapid influx of calcium ions and the disruption of the tegument.

**Pharmacokinetics:** After a single topical administration to healthy male and female cats of a combined topical formulation containing esafloxolaner (12 mg/mL), eprinomectin (4 mg/mL), and praziquantel (83 mg/mL), at dose volumes of 0.06, 0.12, or 0.24 mL/kg, there was a dose proportional increase in the exposure of each ingredient based on maximum plasma concentration (C<sub>max</sub>) and area under the plasma concentration time curve (AUC). After repeated monthly doses of the combined topical formulation at the target dose of 1.44 mg/kg esafloxolaner, 0.48 mg/kg eprinomectin, and 9.98 mg/kg praziquantel, steady state was reached by the fourth dose for esafloxolaner and after the second dose for eprinomectin and praziquantel. Additionally, modest accumulation was observed for esafloxolaner (approximately 3-fold) and praziquantel (approximately 1.5- to 2-fold) between the first and fifth dose, whereas no accumulation was observed for eprinomectin.

**Effectiveness:** Heartworm Prevention: In well-controlled laboratory studies, NexGard® COMBO (esafloxolaner, eprinomectin, and praziquantel topical solution) was 100% effective in preventing the development of heartworms in cats inoculated with infective larvae of *Dirofilaria immitis* 30 days prior to the first of three consecutive monthly treatments.

**Flea Treatment and Prevention:** In a well-controlled laboratory study, NexGard® COMBO killed >92% of fleas within 24 hours. During subsequent weekly infestations, NexGard® COMBO killed >95.5% of fleas within 24 hours through Day 31 and killed fleas before they could lay eggs. The effectiveness against adult fleas at 24 hours post-infestation in the treated cats virtually eliminated flea egg production (99.8 – 100% control of flea egg production by 24 hours) throughout the remainder of the month.

In a field safety and effectiveness study in the United States, conducted in households with existing flea infestations, the effectiveness of NexGard® COMBO against fleas was 97.8%, 99.6%, and 99.9% when assessed on Days 30, 60, and 90, respectively. Cats with signs of flea allergy dermatitis showed improvement in alopecia, dermatitis/pyodermatitis, pruritus, erythema, papules, and scaling, as a direct result of eliminating fleas.

**Tick Treatment and Control:** In well-controlled laboratory studies, NexGard® COMBO demonstrated >95.1% effectiveness against *Ixodes scapularis* 48 hours post-infestation for a month and >95.6% effectiveness against *Amblyomma americanum* 72 hours post-infestation for a month.

**Treatment and Control of Roundworms, Hookworms, and Tapeworms:** In 2 well-controlled laboratory studies, NexGard® COMBO provided 98.9% and 100% effectiveness against natural and/or induced roundworm infections with the dose-limiting gastrointestinal nematode species (adult *Toxocara cati*), respectively. Effectiveness studies against fourth stage larval *Toxocara cati* and hookworms (adult and fourth stage larval *Ancylostoma tubaeforme*, adult *Ancylostoma braziliense*) were conducted with an early formulation. The doses of eprinomectin in this early formulation are equivalent to that of the final formulation of NexGard® COMBO. In well-controlled laboratory studies, NexGard® COMBO provided on average 92.8% effectiveness against natural and/or induced infections with *Dipylidium caninum*.

**Target Animal Safety:** Margin of Safety Study: NexGard® COMBO was applied topically to healthy kittens (8 to 9 weeks of age) at 1X, 3X, or 5X the maximum exposure dose six times at 28-day intervals; kittens in the control group were dosed with mineral oil. One kitten in the 5X group exhibited recumbency, tremors, hypothermia, ataxia, disorientation, and pupil dilation (responsive to light) 9 hours after the third dose. This kitten received supportive care, including washing the application site, and recovered within 48 hours post-dose. During necropsy, a dark red subcutaneous area (5 mm diameter) was observed in the treatment site area of three cats in the 5X group, but microscopic examination revealed no histologic abnormalities. No significant changes related to NexGard® COMBO were observed for physical examination, body weight, clinical pathology (hematology, coagulation, and serum chemistry), histopathology, or organ weights.

**Study in Heartworm Positive Cats:** Adult cats, 4.7 to 6.6 months of age, were experimentally infected with adult heartworms (*D. immitis*) by venous transplantation. All cats were negative for heartworm antibody, antigen and microfilariae prior to transplantation. Two weeks after transplantation, immunoserology verified positive antigen and the presence of microfilariae in all enrolled cats. A combination of fipronil, eprinomectin, praziquantel, and (S)-methoprene was applied topically to cats at 1X or 3X the maximum exposure dose once every 28 days for three consecutive treatments; cats in the control group were dosed with mineral oil. One cat in the 1X group exhibited cyanotic mucous membranes and tachypnea for 24 hours following the first treatment. The cat recovered and exhibited no abnormal signs following two subsequent treatments. There was no difference between the treatment groups in the number of adult *D. immitis* recovered at the end of the study.

**Oral Administration Study:** Oral tolerance was evaluated to assess the effects of accidental oral ingestion. Kittens (male and female) ranging in age from 7.4 to 8.9 weeks were orally administered NexGard® COMBO at 1X the maximum exposure dose; kittens in the control group were dosed with saline. Cats were observed for adverse reactions at 1, 2, 3, 4, and 8 hours following administration, then twice a day until Day 14. All 8 cats administered NexGard® COMBO immediately exhibited excessive hypersalivation after oral administration. However, all cats stopped salivating within 1 hour after exposure. No additional health-related observations were seen for the remainder of the study.

**How Supplied:** NexGard® COMBO is packaged as a single dose in 0.3 mL (for cats 1.8-5.5 lb) and 0.9 mL (for cats 5.6-16.5 lb) applicators. Each size applicator is available in cartons containing 1, 3, or 6 applications.

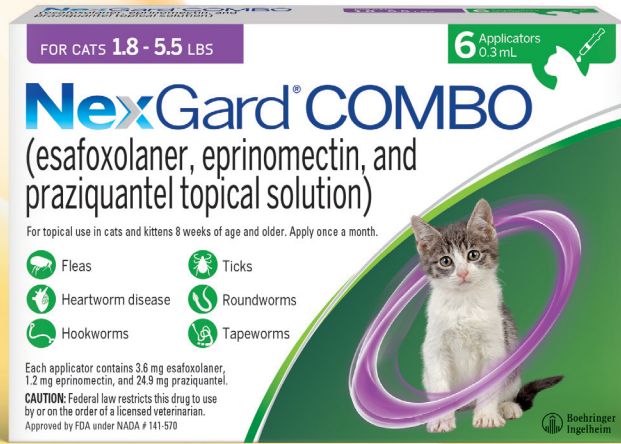
**Storage Information:** Store at 59° – 86°F (15° – 30° C). Brief periods up to 104° F (40° C) are permitted. Protect from light.

Approved by FDA under NADA # 141-570

**Marketed by:** [Boehringer Ingelheim Animal Health USA Inc.](https://www.boehringer-ingelheim.com), Duluth, GA 30096  
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FLEAS



TICKS



HEARTWORM  
DISEASE



ROUNDWORMS



HOOKWORMS



TAPEWORMS

## PROTECT YOUR FELINE PATIENTS

**NexGard® COMBO (esafoxolaner, eprinomectin, and praziquantel topical solution)** kills fleas and ticks, prevents heartworm disease, treats and controls roundworms and hookworms. And it's the only feline broad-spectrum parasiticide that includes tapeworm protection. Available in 2 convenient sizes and 3- and 6-dose presentations.

Talk to your **Boehringer Ingelheim Sales Representative** or visit [NexGardCOMBOclinic.com](https://www.NexGardCOMBOclinic.com) to learn more.



**IMPORTANT SAFETY INFORMATION:** NexGard® COMBO (esafoxolaner, eprinomectin, and praziquantel topical solution) is for topical use only in cats. Use with caution in cats with a history of seizures or neurologic disorders. The most frequently reported adverse reactions include vomiting, application site reactions, and anorexia. If ingested, hypersalivation may occur. Avoid direct contact with application site until visibly dry. For more information, see full prescribing information or visit [NexGardCOMBOclinic.com](https://www.NexGardCOMBOclinic.com).

1. Freedom of Information Summary. NADA 141-570, NexGard COMBO Topical Solution.
2. Saleh MN, Sundstrom KD, Duncan KT, et al. Show us your ticks: a survey of ticks infesting dogs and cats across the USA. *Parasit Vectors*. 2019;12:595. <https://doi.org/10.1186/s13071-019-3847-3>
3. Freedom of Information Summary. NADA 141-492, CENTRAGARD Transdermal Solution. March 8, 2018.
4. Centers for Disease Control and Prevention. Dipylidium FAQs. <https://www.cdc.gov/parasites/dipylidium/faqs.html>

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