NexGard SPECTRA®

NEXGARD SPECTRA 9 mg / 2 mg chewable tablets for dogs 2–3.5 kg
NEXGARD SPECTRA 19 mg / 4 mg chewable tablets for dogs >3.5–7.5 kg
NEXGARD SPECTRA 38 mg / 8 mg chewable tablets for dogs >7.5–15 kg
NEXGARD SPECTRA 75 mg / 15 mg chewable tablets for dogs >15–30 kg
NEXGARD SPECTRA 150 mg / 30 mg chewable tablets for dogs >30–60 kg

Manufactured by:
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COMPOSITION

NEXGARD SPECTRA	Afoxolaner (mg)	Milbemycin oxime (mg)
chewable tablets for dogs 2-3.5 kg	9.375	1.875
chewable tablets for dogs >3.5-7.5 kg	18.75	3.75
chewable tablets for dogs >7.5-15 kg	37.50	7.50
chewable tablets for dogs >15-30 kg	75.00	15.00
chewable tablets for dogs >30-60 kg	150.00	30.00

Mottled red to reddish brown, circular shaped (tablets for dogs 2–3.5 kg) or rectangular shaped (tablets for dogs >3.5–7.5 kg, tablets for dogs >7.5–15 kg, tablets for dogs >15–30 kg and tablets for dogs >30–60 kg).

PHARMACODYNAMICS
Afoxolaner is an insecticide and acaricide of the isoxazoline family. Afoxolaner acts as antagonist at ligand-gated chloride channels, in particular those gated by the neurotransmitter gamma-aminobutyric acid (GABA). Isoxazolines among the chloride channel modulators, binds to a distinct and unique target site within the insect GABACIs, 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, acarines and mammals may be inferred by the differential sensitivity of the insects and acarines's GABA receptors versus mammalian GABA receptors.
It is active against adult fleas as well as against several ticks species such as *Rhipicephalus sanguineus, Dermacentor reticulatus* and *D.variabilis, Ixodes ricinus* and *I.scapularis, Amblyomma americanum* and *Haemaphysalis longicornis*. Afoxolaner kills fleas before egg production and therefore prevents the risk of household contamination. It can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).
Milbemycin oxime is an antiparasitic endectocide belonging to the group of macrocyclic lactones. Milbemycin oxime contains two major factors, A3 and A4 (ratio of 20:80 for A3:A4). It is a fermentation product of *Streptomyces milbemycinicus*. Milbemycin oxime acts by disrupting the glutamate neuro-transmission in invertebrates. Milbemycin oxime increases glutamate binding with consequent enhanced chloride ion flow into the cell. This leads to hyperpolarisation of the neuromuscular membrane resulting in paralysis and death of the parasites.
Milbemycin oxime is active against several gastrointestinal worms (*Toxocara canis, Toxascaris leonine, Ancylostoma caninum, Ancylostoma braziliense, Ancylostoma ceylanicum, Trichuris vulpis*), the adults and immature adults (L5) of lungworm *Angiostrongylus vasorum* and heartworm (*Dirofilaria immitis* larvae).

PHARMACOKINETICS
Afoxolaner had high systemic absorption. The absolute bioavailability is 88%. The mean maximum concentration (Cmax) is 1822±165ng/ml in plasma found 2-4 hours (Tmax) after a 2.5mg/kg afoxolaner dose. Afoxolaner distributes into tissues with a volume of distribution of 2.6±0.61 l/kg and a systemic clearance value of 5.0±1.2ml/h/kg. The terminal plasma half life is approximately 2 weeks in dogs.
Milbemycin oxime plasma concentrations peak quickly within the first 1-2 hours (Tmax) indicating that absorption from the chewable is fast. The absolute bio-availability is 81% and 65% for the A3 and A4 forms, respectively. The terminal half-lives and maximum concentration (Cmax) following oral administration are 1.6±0.4 days and 42±11 ng/ml for the A3 form, 3.3±1.4 days and 246±71 ng/ml the A4 form.
Milbemycin oxime distributes into tissues with a volume of distribution of 2.7±0.4 and 2.6±0.6 l/kg for the A3 and A4 forms respectively. Both forms have low systemic clearance (75±22 ml/h/kg for the A3 form and 41±12 ml/h/kg for A4 form).

INDICATION
For the treatment of flea and tick infestations in dogs when the concurrent prevention of heartworm disease (*Dirofilaria immitis* larvae), angiostrongylosis (reduction in level of immature adults (L5) and adults of *Angiostrongylus vasorum*), thelaziosis (adult *Thelazia callipaeda*) and/or treatment of gastrointestinal nematode infestations is indicated. Treatment of flea infestations (*Ctenocephalides felis* and *C. canis*) in dogs for 5 weeks. Treatment of tick infestations (*Dermacentor reticulatus, Ixodes ricinus, Ixodes hexagonus, Riphicephalus sanguines)* in dogs for 4 weeks. Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance.
Treatment of infestations with adult gastrointestinal nematodes of the following species: roundworms (*Toxocara canis* and *Toxascaris leonine*), hookworms (*Ancylostoma caninum, Ancylostoma braziliense* and *Ancylostoma ceylanicum*) and whipworm (*Trichuris vulpis).*
Treatment of demodicosis (caused by *Demodex canis*).
Treatment of sarcoptic mange (caused by *Sarcoptes scabiei* var. *canis*).
Treatment of ear mite infestations (caused by *Otodectes cynotis).*
Prevention of heartworm disease (*Dirofilaria immitis* larvae) with monthly administration.
Prevention of angiostrongylosis (by reduction of the level of infection with immature adult (L5) and adult stages of *Angiostrongylus vasorum*) with monthly administration.
Prevention of establishment of thelaziosis (adult *Thelazia callipaeda* eyeworm infection) with monthly admistration.

DOSAGE AND ADMINISTRATION
For oral use. This product is to be administered monthly.
Dose: The veterinary medicinal product should be administered at a dose of 2.50 -5.36 mg/kg of afoxolaner and 0.50-1.07 mg/kg of milbemycin oxime in accordance with the following table :

Bodyweight (kg) of dog	Number and strength of tablet to be administered				
	NEXGARD SPECTRA 9 mg/ 2 mg	NEXGARD SPECTRA 19 mg/ 4 mg	NEXGARD SPECTRA 38 mg/ 8 mg	NEXGARD SPECTRA 75 mg/ 15 mg	NEXGARD SPECTRA 150 mg/ 30 mg
2–3.5	1				
>3.5–7.5		1			
>7.5–15			1		
>15–30				1	
>30–60					1

For dogs above 60 kg appropriate combinations of chewable tablets are used.
Method of administration: The tablets are chewable and palatable to most dogs. If the dog does not accept the tablets directly they may be administered with food.
Treatment schedule : The treatment schedule should be based on veterinary diagnosis and on the local epidemiological situation.
Treatment of flea and tick infestations and gastrointestinal nematodes :
NEXGARD SPECTRA can be used as part of the seasonal treatment of fleas and ticks (replacing treatment with a monovalent flea and tick product) in dogs with diagnosed concurrent gastrointestinal nematodes infestations. A single treatment is effective for the treatment of gastrointestinal nematodes.
After treatment of the nematode infestations, further flea and tick treatment should be continued with a monovalent product.
Treatment of demodicosis (caused by Demodex canis) :
Monthly administration of the product until two negative skin scrapings are obtained one month apart. Severe cases may require prolonged monthly treatments. As demodicosis is a multi-factorial disease, where possible, it is advisable to also treat any underlying disease appropriately
Treatment of sarcoptic mange (caused by Sarcoptes scabiei var. canis) :
Monthly administration of the product for two consecutive months. Further monthly administration of the product may be required based on clinical assessment and skin scrapings.
Treatment of ear mite infestations (caused by Otodectes cynotis) :
A single dose of the veterinary medicinal product should be administered. A further veterinary examination one month after the initial treatment is recommended as some animals may require a second treatment.
Prevention of heartworm disease :
NEXGARD SPECTRA kills *Dirofilaria immitis* larvae up to one month after their transmission by mosquitoes therefore the product should be administered at regular monthly intervals during the time of the year when vectors are present, starting in the month after the first expected exposure to mosquitoes. Treatment should continue until 1 month after the last exposure to mosquitoes. To establish a treatment routine, it is recommended that the same day or date be used each month.
When replacing another heartworm preventative product in a heartworm prevention programme, the first treatment with NEXGARD SPECTRA should start on the date when the former medication was due to have been administered. Dogs living in heartworm endemic areas, or those which have travelled to endemic areas, may be infested with adult heartworms. No therapeutic effect against adult *Dirofilaria immitis* has been established. It is therefore recommended that all dogs 8 months of age or more, living in heartworm endemic areas, should be tested for existing adult heartworm infestation before being treated with the product for heartworm prevention.
Prevention of angiostrongylosis :
In endemic areas, monthly administration of the product will reduce the level of infection with immature adults (L5) and adults of *Angiostroylus vasorum* in the heart and lungs.
Prevention of thelaziosis :
Monthly administration of the product prevents establishment of infection with adult *Thelazia callipaeda* eyeworm.

CONTRAINDICATION Do not use in case of hypersensitivity to the active substances or to any of the excipients.

WARNING AND PRECAUTIONS
Special warnings for each target species
Fleas and ticks need to start feeding on the host to become exposed to afoxolaner, therefore the risk of transmission of vector-borne disease cannot be excluded.
Ancylostoma ceylanicum is reported as being endemic only in South-East Asia, China, India, Japan, some Pacific islands, Australia, the Arab Peninsula, South Africa and South America.
Parasite resistance to any particular class of parasiticides may develop following the frequent, repeated use of a product of that class. Therefore, the use of this product should be based on the assessment of each individual case and on local epidemiological information about the current susceptibility of the target species in order to limit the possibility of a future selection for resistance. Maintenance of the efficacy of macrocylic lactones is critical for Dirofilaria immitis control. To minimise the risk of resistance selection, it is recommended that dogs should be checked for both circulating antigens and blood microfilariae at the beginning of each season of preventive treatment. Only negative animals should be treated.
Special precautions for use in animals
In the absence of available data, treatment of puppies less than 8 weeks of age and dogs less than 2kg bodyweight should be based on a benefit-risk assessment by the responsible veterinarian. In heartworm endemic areas, dogs should be tested for existing heartworm infestation prior to administration of Nexgard Spectra
At the discretion of the veterinarian, infested dogs should be treated with an adultice to remove adult heartworm. Nexgard Spectra is not indicated for microfilariae clearance. The recommended dose should be strictly observed in collies or related breeds.
Special precaution to be taken by the person administering the medicinal product to animals
This product may cause gastrointestinal disturbance if ingested. Keep tablets in the blister packs until required, and keep the blisters in the outer carton. In case of accidental ingestion, particularly in the case of children, seek medical advice immediately and show the package leaflet or the label to physician.
Wash hands after use.
Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products
Any unused veterinary medicinal product or waste material derived from such veterinary medicinal products should be disposed of in accordance with local requirement.

INTERACTION WITH OTHER MEDICAMENTS
Milbemycin oxime is a substrate for P-glycoprotein (P-gp) and therefore could interact with other P-gp substrates (for example digoxin, doxorubicin) or other macrocyclic lactones. Therefore, concomitant treatment with other P-gp substrates could lead to enhanced toxicity.

STATEMENT ON USAGE DURING PREGNANCY AND LACTATION
Can be used in breeding, pregnant and lactating dogs. The safety of the veterinary medicinal product has not been established in breeding males. Laboratoty studies in rats and rabbits have not produced any evidence of teratogenic effects, or any adverse effect on the reproductive capacity in males.
In breeding males, use only according to the benefit-risk assessment by the responsible veterinarian.

ADVERSE EFFECT
In clinical studies, no serious adverse reactions were attributed to the combination of afoxolaner and milbemycin oxime. Adverse reactions such as vomiting, diarrhea, lethargy, anorexia and pruritus were uncommonly observed. These occurences were generally self-limiting and of short duration.
The frequency of adverse reactions is defined using the following convention:
-very common (more than 1 in 10 animals treated displaying adverse reaction (s))
-common (more than 1 but less than 10 animals in 100 animals treated)
-uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
-rare (more than 1 but less than 10 animals in 10,000 animals treated)
-very rare (less than 1 animal in 10,000 animals treated, including isolated reports)

OVERDOSE AND TREATMENT No adverse reactions were observed in eight-week old healthy puppies after 6 treatments at up to 5 times the maximum dose.

STORAGE CONDITION Store below 30°C. Keep in dry place. Keep the blister in the outer carton in order to protect from light.

PACKING
Carton with 1 blister of 3 chewable tablets.
Carton with 1 blister of 6 chewable tablets.

FOR VETERINARY USE ONLY

Boehringer Ingelheim

Date of revision : 5LNESXS3-003 09/XXX

LABEL CODE	VERSION	COLORS
5LNESXS3-003		Noir/Black
Product : NEXGARD SPECTRA CHEWABLE TABLETS FOR DOGS **Pack Size :** 3 TABLETS, 6 TABLETS **Country :** MY **Dimensions à plat (mm):** 170 x 550 **Dimensions plié(e)s:** 170 x 51	**VERSION : 09** **MMM/YY :**	! Please use the official PANTONE® (P) matching system for an accurate color representation.

Marketing approval:	**Regulatory** approval:	**GMP** approval:
COMPLETE NAME: DATE + SIGNATURE:	COMPLETE NAME: DATE + SIGNATURE:	COMPLETE NAME: DATE + SIGNATURE: