SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:

Active substances:

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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablets
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).

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

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, Rhipicephalus sanguineus*) 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 leonina*), 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*).

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 administration.

4.3 Contraindications

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

4.4 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 the transmission of vector-borne diseases 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 macrocyclic 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 preventative treatment. Only negative animals should be treated.

4.5 Special precautions for use

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 2 kg 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 adulticide to remove adult heartworms. NEXGARD SPECTRA is not indicated for microfilariae clearance.

The recommended dose should be strictly observed in collies or related breeds.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

- This product may cause gastrointestinal disturbances 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 the physician.
- Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Clinical studies
Vomiting, diarrhoea, lethargy, anorexia, and pruritus were uncommonly observed. These occurrences were generally self-limiting and of short duration.

Post-marketing safety experience
Erythema and neurological signs (convulsions, ataxia and muscle tremors) have been reported very rarely.

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).

4.7 Use during pregnancy, lactation or lay

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic effects, or any adverse effect on the reproductive capacity in males and females.

The safety of the veterinary medicinal product has not been established during pregnancy and lactation or in breeding dogs. Use only according to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

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.

4.9 Amounts to be administered and administration route

For oral

use.

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 should be 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 nematode 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 administrations of the product may be required based on clinical assessment and skin scrapings.

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 *Angiostrongylus vasorum* in the heart and lungs.

Prevention of thelaziosis:
Monthly administration of the product prevents establishment of infection with adult *Thelazia callipaeda* eyeworm.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

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

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group*:* antiparasitic products, endectocides*,* milbemycin combinations. ATC vet code: QP54AB51.

5.1 Pharmacodynamic properties

Afoxolaner:
Afoxolaner is an insecticide and acaricide of the isoxazoline family.

Afoxolaner acts as an antagonist at ligand-gated chloride channels, in particular those gated by the neurotransmitter gamma-aminobutyric acid (GABA). Isoxazolines, among the chloride channel modulators, bind 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' GABA receptors versus mammalian GABA receptors.

It is active against adult fleas as well as against several tick 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:
Milbemycin oxime is an antiparasitic endectocide belonging to the group of macrocyclic lactones. Milbemycin oxime contains two major components, 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 leonina*, *Ancylostoma caninum*, *Ancylostoma braziliense, Ancylostoma ceylanicum*, *Trichuris vulpis),* the adults and immature adults (L5) of lungworm *Angiostrongylus vasorum* and heartworm (*Dirofilaria immitis* larvae).

5.2 Pharmacokinetic particulars

The systemic absorption of afoxolaner is high. The absolute bioavailability is 88%. The mean maximum concentration (C_{max}) is 1822 ± 165 ng/ml in

plasma found 2–4 hours (T_{max}) after a
2.5 mg/kg afoxolaner dose.

Afoxolaner distributes into tissues with a volume of distribution of 2.6 ± 0.6 l/kg and a systemic clearance value of 5.0 ± 1.2 ml/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 (T_{max}) indicating that absorption from the chewable tablets is fast. The absolute bioavailability is 81% and 65% for the A3 and A4 forms, respectively. The terminal half-lives and maximum concentrations (C_{max}) 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 for the A4 form.

Milbemycin oxime distributes into tissues with a volume of distribution of 2.7 ± 0.4 l/kg 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 the A4 form).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Soy protein fines
Beef braised flavouring
Povidone (E1201)
Macrogol 400
Macrogol 4000
Macrogol 15 hydroxystearate
Glycerol (E422)
Triglycerides, medium-chain
Citric acid monohydrate (E330)
Butylhydroxytoluene (E321)

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.

6.4 Special precautions for storage

Keep the blister in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

The veterinary medicinal product is individually packaged in thermoformed laminated PVC blisters with paper-backed aluminium (Aclar/PVC/Alu).

One carton contains one blister of 1, 3 or 6 chewable tablets or 15 blisters of 1 chewable tablet or 2 blisters of 3 chewable tablets.
Not all pack sizes may be marketed.

6.6 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 materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Vetmedica
GmbH 55216 Ingelheim/Rhein
GERMANY

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/14/177/001-025

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:
15/01/2015 Date of last
renewal: 11/11/2019

10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.ema.europa.eu).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.