ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NEXGARD SPECTRA 9 mg / 2 mg chewable tablets for dogs 1.35–3.5 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 1.35–3.5 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

Excipients:

Qualitative composition of excipients and other constituents
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)

Mottled red to reddish brown, circular shaped chewable tablets (for dogs 1.35–3.5 kg) or rectangular shaped chewable tablets (for dogs > 3.5–7.5 kg, for dogs > 7.5–15 kg, for dogs > 15–30 kg and for dogs > 30–60 kg).

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

For dogs with, or at risk from, mixed infestations by external and internal parasites. The veterinary medicinal product is only indicated when use against ticks, fleas, or mites and one or more of the other target parasites is indicated at the same time.

External parasites
Treatment of flea infestations (*Ctenocephalides felis* and *C. canis*). The veterinary medicinal product provides immediate and persistent killing activity for 5 weeks.

For reduction of the risk of infection with *Dipylidium caninum* via transmission by *Ctenocephalides felis* for 30 days. The effect is indirect due to the activity of the veterinary medicinal product against the vector.

The product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).

Treatment of tick infestations (*Dermacentor reticulatus*, *Ixodes ricinus*, *Ixodes hexagonus*, *Rhipicephalus sanguineus*, *Hyalomma marginatum*). The veterinary medicinal product provides immediate and persistent killing activity for 4 weeks.

For reduction of the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* for 28 days. The effect is indirect due to the activity of the veterinary medicinal product against the vector.

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance.

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*).

Gastrointestinal nematodes
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*).

Other nematodes
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.

3.3 Contraindications

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

3.4 Special warnings

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.

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features, for each individual animal.

In the absence of risk of co-infestation by external and internal parasites, a narrow spectrum product should be used.

The possibility that other animals in the same household can be a source of re-infestation with fleas, ticks, mites or gastrointestinal nematodes should be considered, and these should be treated as necessary with an appropriate product.

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.

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.

3.5 Special precautions for use

Special precautions for safe use in the target species:
In the absence of available data, treatment of puppies less than 8 weeks of age and dogs less than 1.35 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 the veterinary medicinal product. At the discretion of the veterinarian, infested dogs should be treated with an adulticide to remove adult heartworms. The veterinary medicinal product 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.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Uncommon (1 to 10 animals / 1 000 animals treated):	Vomiting[1], diarrhoea[1], Lethargy[1], anorexia[1], Pruritus[1]
Very rare (< 1 animal / 10 000 animals treated, including isolated reports):	Erythema Neurological signs (convulsion, ataxia and muscle tremor).

[1] Generally self-limiting and of short duration.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing

authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
Can be used in pregnant and lactating dogs.

Fertility:
Can be used in breeding females.
The safety of the veterinary medicinal product has not been established in breeding males.
In breeding males, use only according to the benefit-risk assessment by the responsible veterinarian.
Laboratory studies in rats and rabbits have not produced any evidence of teratogenic effects, or any adverse effect on the reproductive capacity in males.

3.8 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.

3.9 Administration routes and dosage

Oral use.

Dosage:
The veterinary medicinal product should be administered at a dose of 2.50 to 6.94 mg/kg of afoxolaner and 0.50 to 1.39 mg/kg of milbemycin oxime in accordance with the following table:

Bodyweight of dog (kg)	**Number and strength of chewable 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
1.35–3.5	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.
To ensure a correct dosage, body weight should be determined as accurately as possible.
The chewable tablets should not be divided. Underdosing could result in ineffective use and may favour resistance development.

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 need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

Treatment of flea and tick infestations and gastrointestinal nematodes:
The veterinary medicinal product 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.

Treatment of demodicosis (caused by *Demodex canis*):
Monthly administration of the veterinary medicinal product is efficacious and leads to a marked improvement of clinical signs. Treatment should be continued 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 veterinary medicinal product for two consecutive months. Further monthly administrations 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 may be recommended as some animals may require a second treatment.

Prevention of heartworm disease:
The veterinary medicinal product kills *Dirofilaria immitis* larvae up to one month after their transmission by mosquitoes, therefore the veterinary medicinal 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 the veterinary medicinal product 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 veterinary medicinal product for heartworm prevention.

Prevention of angiostrongylosis:
In endemic areas, monthly administration of the veterinary medicinal 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 veterinary medicinal product prevents establishment of infection with adult *Thelazia callipaeda* eyeworm.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QP54AB51.

4.2 Pharmacodynamics

Afoxolaner:
Afoxolaner is an insecticide and acaricide belonging to 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 GABACls, 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, Ixodes hexagonus* and *I. scapularis, Amblyomma americanum, Haemaphysalis longicornis,* and *Hyalomma marginatum.*

Afoxolaner kills fleas before egg production and therefore prevents the risk of household contamination.

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).

4.3 Pharmacokinetics

The systemic absorption of afoxolaner is high. The absolute bioavailability is 88 %. The mean maximum concentration (C_{max}) is 1,822 ± 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).

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months.

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

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

Cardboard box with 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.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Vetmedica GmbH

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/14/177/001-025

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 15/01/2015

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

DD/MM/YYYY

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

ANNEX II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NEXGARD SPECTRA 9 mg / 2 mg chewable tablets for dogs 1.35–3.5 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. STATEMENT OF ACTIVE SUBSTANCES

Each chewable tablet contains:
9.375 mg afoxolaner and 1.875 mg milbemycin oxime
18.75 mg afoxolaner and 3.75 mg milbemycin oxime
37.5 mg afoxolaner and 7.5 mg milbemycin oxime
75 mg afoxolaner and 15 mg milbemycin oxime
150 mg afoxolaner and 30 mg milbemycin oxime

3. PACKAGE SIZE

1 chewable tablet
3 chewable tablets
6 chewable tablets (1 blister of 6 tablets)
6 chewable tablets (2 blisters of 3 tablets)
15 chewable tablets

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

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

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Vetmedica GmbH

14. MARKETING AUTHORISATION NUMBERS

EU/2/14/177/001 – 9 mg / 2 mg, 1 chewable tablet
EU/2/14/177/002 – 9 mg / 2 mg, 3 chewable tablets
EU/2/14/177/003 – 9 mg / 2 mg, 6 chewable tablets
EU/2/14/177/016 – 9 mg / 2 mg, 15 chewable tablets
EU/2/14/177/021 – 9 mg / 2 mg, 6 chewable tablets
EU/2/14/177/004 – 19 mg / 4 mg, 1 chewable tablet
EU/2/14/177/005 – 19 mg / 4 mg, 3 chewable tablets
EU/2/14/177/006 – 19 mg / 4 mg, 6 chewable tablets
EU/2/14/177/017 – 19 mg / 4 mg, 15 chewable tablets
EU/2/14/177/022 – 19 mg / 4 mg, 6 chewable tablets
EU/2/14/177/007 – 38 mg / 8 mg, 1 chewable tablet
EU/2/14/177/008 – 38 mg / 8 mg, 3 chewable tablets
EU/2/14/177/009 – 38 mg / 8 mg, 6 chewable tablets
EU/2/14/177/018 – 38 mg / 8 mg, 15 chewable tablets
EU/2/14/177/023 – 38 mg / 8 mg, 6 chewable tablets
EU/2/14/177/010 – 75 mg / 15 mg, 1 chewable tablet
EU/2/14/177/011 – 75 mg / 15 mg, 3 chewable tablets
EU/2/14/177/012 – 75 mg / 15 mg, 6 chewable tablets
EU/2/14/177/019 – 75 mg / 15 mg, 15 chewable tablets
EU/2/14/177/024 – 75 mg / 15 mg, 6 chewable tablets
EU/2/14/177/013 –150 mg / 30 mg, 1 chewable tablet
EU/2/14/177/014 –150 mg / 30 mg, 3 chewable tablets
EU/2/14/177/015 –150 mg / 30 mg, 6 chewable tablets
EU/2/14/177/020 –150 mg / 30 mg, 15 chewable tablets
EU/2/14/177/025 –150 mg / 30 mg, 6 chewable tablets

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NEXGARD SPECTRA

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE

1.35–3.5 kg
> 3.5–7.5 kg
> 7.5–15 kg
> 15–30 kg
> 30–60 kg

9 mg / 2 mg afoxolaner / milbemycin oxime
19 mg/ 4 mg afoxolaner / milbemycin oxime
38 mg / 8 mg afoxolaner / milbemycin oxime
75 mg / 15 mg afoxolaner / milbemycin oxime
150 mg / 30 mg afoxolaner / milbemycin oxime

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

NEXGARD SPECTRA 9 mg / 2 mg chewable tablets for dogs 1.35–3.5 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. Composition

Each chewable tablet contains:

Active substances:

NEXGARD SPECTRA	Afoxolaner (mg)	Milbemycin oxime (mg)
chewable tablets for dogs 1.35–3.5 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 chewable tablets (for dogs 1.35–3.5 kg) or rectangular shaped chewable tablets (for dogs > 3.5–7.5 kg, for dogs > 7.5–15 kg, for dogs > 15–30 kg and for dogs > 30–60 kg).

3. Target species

Dogs. 

4. Indications for use

For dogs with, or at risk from, mixed infestations by external and internal parasites. The veterinary medicinal product is only indicated for use when use against ticks, fleas or mites and one or more of the other target parasites is indicated at the same time.

External parasites:
Treatment of flea (*Ctenocephalides felis* and *C. canis*) and tick (*Dermacentor reticulatus, Ixodes ricinus, Ixodes hexagonus, Rhipicephalus sanguineus, Hyalomma marginatum*) infestations in dogs. Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance.

For reduction of the risk of infection with *Dipylidium caninum* via transmission by *Ctenocephalides felis* for 30 days. The effect is indirect due to the activity of the veterinary medicinal product against the vector.

The veterinary medicinal product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).

For reduction of the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* for 28 days. The effect is indirect due to the activity of the veterinary medicinal product against the vector.

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*).

Gastrointestinal nematodes
Treatment of 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*).

Other nematodes
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.

5. Contraindications

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

6. Special warnings

Special warnings:
Fleas and ticks need to start feeding on the host to become exposed to the substance afoxolaner; therefore, the risk of the transmission of diseases by fleas and ticks cannot be excluded.

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features, for each individual animal.

In the absence of risk of co-infestation by external and internal parasites, a narrow spectrum product should be used.

The possibility that other animals in the same household can be a source of re-infestation with fleas, ticks, mites or gastrointestinal nematodes should be considered, and these should be treated as necessary with an appropriate product.

Ancylostoma ceylanicum is reported as being endemic only in Southeast Asia, China, India, Japan, some Pacific islands, Australia, the Arab Peninsula, South Africa and South America.

Heartworm disease prevention is critical. 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.

Special precautions for safe use in the target species:
In the absence of available data, treatment of puppies less than 8 weeks of age and dogs less than 1.35 kg bodyweight should be based on a benefit-risk assessment by the responsible veterinarian.

In regions where heartworm disease is present, dogs should be tested for existing heartworm infestation prior to administration of the veterinary medicinal product. At the discretion of the veterinarian, infested dogs should be treated with an adulticide to remove adult heartworms. the veterinary medicinal product is not indicated for removal of microfilariae from positive dogs.

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.

Pregnancy and lactation:
Can be used in pregnant and lactating dogs.

Fertility:
Can be used in breeding females.
The safety of the veterinary medicinal product has not been established in breeding males.
In breeding males, use only according to the benefit-risk assessment by the responsible veterinarian.
Laboratory studies in rats and rabbits have not produced any evidence of birth defects, or any adverse effect on the reproductive capacity in males.

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.

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

7. Adverse events

Dogs:

Uncommon (1 to 10 animals / 1 000 animals treated):
Vomiting[1], diarrhoea[1],
Lethargy[1], anorexia[1],
Pruritus (itching)[1]

Very rare (< 1 animal / 10 000 animals treated, including isolated reports):
Erythema (redness)
Neurological signs (convulsion, ataxia (incoordination) and muscle tremor).

[1] Generally self-limiting and of short duration.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or its local representative using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

Oral use.

Dosage:
The veterinary medicinal product should be administered at a dose of 2.50 to 6.94 mg/kg of afoxolaner and 0.50 to 1.39 mg/kg of milbemycin oxime in accordance with the following table:

Bodyweight of dog (kg)	**Number and strength of chewable 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
1.35–3.5	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.
To ensure a correct dosage, body weight should be determined as accurately as possible.

The chewable tablets should not be divided. Underdosing could result in ineffective use and may favour resistance development.

The tablets are chewable and palatable to most dogs. If the dog does not accept the tablets directly, they may be administered with food.

9. Advice on correct administration

Treatment schedule:
The need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

Treatment of flea and tick infestations and gastrointestinal worms:
The veterinary medicinal product can be used as part of the seasonal treatment of fleas and ticks (replacing a product authorised for the treatment of fleas/ticks only) in dogs with diagnosed concurrent gastrointestinal worm infestations. A single treatment is effective for gastrointestinal worms.

Efficacy of the treatment against flea and tick infestations lasts for one month. Further treatments may be indicated throughout the flea and/or tick season. Ask your veterinarian how to continue flea and tick treatment.

Treatment of demodicosis (caused by *Demodex canis*):
Monthly administration of the veterinary medicinal product is efficacious and leads to a marked improvement of clinical signs. Treatment should be continued 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 veterinary medicinal product for two consecutive months. Further monthly administrations 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 may be recommended as some animals may require a second treatment.

Prevention of heartworm disease:
The veterinary medicinal product kills *Dirofilaria immitis* larvae (heartworm) up to one month after their transmission by mosquitoes. Therefore, the veterinary medicinal product should be administered at regular monthly intervals during the time of the year when mosquitoes are present, starting in the month after the first expected exposure to them.

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 the veterinary medicinal product should start on the date when the former medication was due to have been administered.

Dogs living in heartworm endemic areas (where heartworm disease is present), 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 veterinary medicinal product for heartworm prevention.

Prevention of angiostrongylosis:
In endemic areas, monthly administration of the veterinary medicinal 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 veterinary medicinal product prevents establishment of infection with adult *Thelazia callipaeda* eyeworm.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Keep the blister in the outer carton in order to protect from light.
Do not use this veterinary medicinal product after the expiry date which is stated on the packaging after Exp. The expiry date refers to the last day of that month.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

EU/2/14/177/001-025
For each strength, the chewable tablets are available in the following pack sizes:
Cardboard box with 1 blister containing 1, 3 or 6 chewable tablets or 15 blisters of 1 chewable tablet or 2 blisters containing 3 chewable tablets.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

16. Contact details

Marketing authorisation holder:
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55216 Ingelheim/Rhein
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Manufacturer responsible for batch release:
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Local representatives and contact details to report suspected adverse events:

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17. Other information

Afoxolaner is an insecticide and acaricide belonging to the isoxazoline family. It is active against adult fleas as well as against several tick species such as *Rhipicephalus sanguineus*, *Dermacentor reticulatus* and *D. variabilis, Ixodes ricinus, Ixodes hexagonus* and *I. scapularis, Amblyomma americanum*, *Haemaphysalis longicornis*, and *Hyalomma marginatum.*

Afoxolaner kills fleas before egg production and therefore prevents the risk of household contamination.

Milbemycin oxime is an antiparasitic endectocide belonging to the group of macrocyclic lactones. It 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 larvae of the heartworm *Dirofilaria immitis*.