

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NexGard Combo spot-on solution for cats < 2.5 kg
NexGard Combo spot-on solution for cats 2.5-7.5 kg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances:

Each spot-on applicator delivers:

NexGard Combo	Volume of unit dose (ml)	Esafoxolaner (mg)	Eprinomectin (mg)	Praziquantel (mg)
Cats 0.8-<2.5 kg	0.3	3.60	1.20	24.90
Cats 2.5-<7.5 kg	0.9	10.80	3.60	74.70

Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Butylhydroxytoluene (E321)	1 mg/ml
Dimethyl isosorbide	-
Glycerol formal	-

Clear, colourless to light yellow to light brown solution.

3. CLINICAL INFORMATION

3.1 Target species

Cats

3.2 Indications for use for each target species

For cats with, or at risk from mixed infections by cestodes, nematodes and ectoparasites. The veterinary medicinal product is exclusively indicated when all three groups are targeted at the same time.

Ectoparasites

- Treatment of infestations by fleas (*Ctenocephalides felis*). One treatment provides immediate and persistent flea killing activity for one month.
- The product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).
- Treatment of infestations by ticks. One treatment provides immediate and persistent tick killing activity against *Ixodes scapularis* for one month and against *Ixodes ricinus* for five weeks.
- Persistent tick killing activity from 7 days to five weeks after treatment against *Rhipicephalus sanguineus*.
- Persistent tick killing activity from 7 days to four weeks after treatment against *Ixodes hexagonus*.
- Treatment of infestations by ear mites (*Otodectes cynotis*).
- Treatment of Notoedric mange (caused by *Notoedres cati*).

Gastro-intestinal cestodes

- Treatment of infections with tapeworms (*Dipylidium caninum*, *Taenia taeniaeformis*, *Echinococcus multilocularis*, *Joyeuxiella pasqualei* and *Joyeuxiella fuhrmanni*).

Nematodes

Gastro-intestinal nematodes

- Treatment of infections with gastrointestinal nematodes (L3, L4 larvae and adults of *Toxocara cati*, L4 larvae and adults of *Ancylostoma tubaeforme* and *Ancylostoma ceylanicum*, and adult forms of *Toxascaris leonina* and *Ancylostoma braziliense*).

Cardio-pulmonary nematodes

- Prevention of heartworm disease (*Dirofilaria immitis*) for one month.
- Treatment of infections with feline lungworms (L4 larvae and adults of *Troglostrongylus brevior*, L3, L4 larvae and adults of *Aelurostrongylus abstrusus*).
- Prevention of aelurostrongylosis (by reduction of the level of infection with L3, L4 larvae of *Aelurostrongylus abstrusus*).

Vesical nematodes

- Treatment of infections with vesical worms (*Capillaria plica*).

3.3 Contraindications

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

3.4 Special warnings

When applying the veterinary medicinal product, special attention should be paid to long hair breeds in order to ensure that the product is applied directly to the skin and not on the hair, as this could lead to a lower bioavailability of the active substance.

Ticks and fleas need to start feeding on the cat to become exposed to esafloxolaner; therefore, the risk of transmission of arthropod borne diseases cannot be excluded.

Cats in endemic areas for heartworm, or those which have travelled to endemic areas, may be infected with adult heartworms. Although the veterinary medicinal product may be safely administered to cats infected with adult heartworms, no therapeutic effect against adult *Dirofilaria immitis* has been established. It is, therefore, recommended that all cats 6 months of age or older, living in endemic areas for heartworm, should be tested for existing adult heartworm infection before being treated with the product for heartworm disease prevention.

Tapeworm infection may reoccur unless control of intermediate hosts such as fleas, mice etc. is undertaken. Some cats with patent *Joyeuxiella* spp. or *Dipylidium caninum* infection may nevertheless harbour a high proportion of juvenile worms, which may be less susceptible to the product; therefore, a post-treatment follow-up is recommended in case of such infections.

Parasite resistance to any particular class of antiparasitics included in the fixed combination product may develop following repeated use of antiparasitics of those classes over an extended period of time. Therefore, epidemiological information about current susceptibility of the target species should be taken into account in order to limit the possibility of a future selection for resistance.

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-infection, a narrow spectrum product should be used.

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

Avoid shampooing the animal within the 2 days following application because the effectiveness of the product in this case has not been tested.

To reduce re-infestation from emergence of new fleas, it is recommended that all cats in a household are treated. Other animal species living in the same household should also be treated with a suitable product.

All stages of fleas can infest the cat's basket, bedding and regular resting areas such as carpets and soft furnishings. In case of massive flea infestation and at the beginning of the control measures, these areas should be treated with a suitable environmental product and then vacuumed regularly.

3.5 Special precautions for use

Special precautions for safe use in the target species :

Spot-on application only. Do not inject, do not administer orally or via any other route. Avoid contact with the cat's eyes. If accidental ocular contact occurs, flush the eyes immediately with clean water. If eye irritation persists, seek veterinary advice.

It is important to apply the veterinary medicinal product to a skin area where the cat cannot lick it off: on the midline of the neck, between the base of the skull and the shoulder blades. Ensure that animals do not lick each other until the treated area is no longer noticeable. Oral ingestion of the veterinary medicinal product has been observed to lead to hypersalivation.

The safety of the veterinary medicinal product has not been tested in kittens under 8 weeks of age. The product is for use in cats weighing at least 0.8 kg and from 8 weeks of age.

The veterinary medicinal product should exclusively be used in confirmed mixed infections or where cats are at significant risk of such mixed infection with ectoparasites and nematodes (including for heartworm disease prevention) and where concurrent treatment against cestodes is indicated. In the absence of risk of co-infestation, the use of a narrow spectrum parasiticide should be considered as a first line therapy.

The rationale for prescription and frequency of use should be tailored to the individual needs of the cat, based on clinical assessment, the animal's lifestyle and on the local epidemiological situation (including zoonotic risks, where relevant) in order to address exclusively situations of mixed infections/risk of infection.

The veterinary medicinal product should not be used in other cats without prior veterinary consultation.

Repeated treatments should be restricted to limited individual situations (see section 3.9 for treatment guidance) with a minimum treatment interval of 4 weeks. The safety was not evaluated beyond 6 months (see also sections 3.4, 3.10, and 4.2); therefore, no more than 6 consecutive treatments are recommended to be given within a 12-month period.

Echinococcosis represents a hazard for humans and is a notifiable disease to the World Organisation for Animal Health (WOAH). In case of echinococcosis, specific guidelines on the treatment and follow up and on the safeguard of persons have to be followed. Experts or institutes of parasitology should be consulted.

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

Do not smoke, drink or eat during application.

Wash hands immediately after use.

Used applicators should be disposed of immediately and not left within the sight or reach of children.

Avoid contact of the applicator content with the fingers. If this occurs, wash off with soap and water. This veterinary medicinal product can cause eye irritation, which might be in exceptional cases severe. In case of accidental eye exposure, flush the eyes immediately and thoroughly with water. Remove contact lenses, if present, after the first 5 minutes, and then continue rinsing. Seek medical advice and show the package leaflet or the label to the physician.

Ensure that the treated area is no longer noticeable before resuming contact with the site of application. Children should not be allowed to play with treated animals until the application site is no longer noticeable and it is recommended that recently treated animals do not sleep with owners, especially children. It is recommended to treat animals in the evening to reduce contact with people after treatment.

People with a known hypersensitivity to esafloxolaner, eprinomectin or praziquantel or to any of the excipients should avoid contact with the veterinary medicinal product.

Since foetotoxic and teratogenic effects are described in laboratory animals after significant daily exposure to glycerol formal, pregnant women should wear gloves during the administration to avoid direct contact with the product.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cats:

Uncommon (1 to 10 animals / 1 000 animals treated):	Hypersalivation ¹ , diarrhoea ¹ , emesis ¹ Application site alopecia ^{1,2} , application site pruritus ^{1,2} Lethargy ¹ , anorexia ¹
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¹ Mostly mild reactions, of short duration and self-limiting

² Transient

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 queens.

Fertility:

Can be used in breeding queens.

The safety of the veterinary medicinal product has not been established in breeding male cats.

Laboratory studies in rats and rabbits have not produced any evidence of adverse effects of the active substances on the reproductive capacity in males. In breeding males, use only according to the benefit-risk assessment by the prescribing veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Spot-on use.

Dosage:

The recommended minimum doses are 1.44 mg esafoxolaner, 0.48 mg eprinomectin and 10 mg praziquantel per kg bodyweight.

Select the appropriate applicator size for the weight of the cat. To ensure a correct dosage, body weight should be determined as accurately as possible. Underdosing could result in ineffective use and may favour resistance development.

Cat weight	Volume of unit dose (ml)	Esafoxolaner (mg)	Eprinomectin (mg)	Praziquantel (mg)
0.8-< 2.5 kg	0.3	3.60	1.20	24.90
2.5-<7.5 kg	0.9	10.80	3.60	74.70
≥7.5 kg	appropriate combination of applicators			

Method of administration:

1. Use scissors to cut the blister along the dotted line.
2. Then pull the lid away.
3. Remove the applicator from the package and hold it upright. Pull back the plunger slightly.
4. Twist and pull off the cap.
5. Part the hair on the midline of the neck, between the base of the skull and the shoulder blades until the skin is visible. Place the tip of the applicator on the skin and apply the entire content directly onto the skin in one spot. The product should be applied to dry skin on an area where the cat cannot lick it off. In long hair breeds, special attention should be paid to apply the product onto the skin, and not on the hair to ensure optimal efficacy.
6. Wash your hands after use.

Treatment schedule:

For the treatment of infestations with fleas and/or ticks and/or mites, and the concurrent treatment of gastrointestinal and/or pulmonary, and/or vesical nematodes, and cestodes, a single dose of the product should be applied. The need for and frequency of re-treatment(s) should be in accordance with the advice of the prescribing veterinarian and should take into account the local epidemiological situation and the animal's lifestyle (e.g. outdoors access). See also section 3.5.

Areas which are not-endemic areas for heartworm or feline lungworm:

Cats not exposed to a permanent risk of heartworm or feline lungworm infection should be treated according to a schedule prescribed by the veterinarian and adapted to each individual situation of re-infection/-infestation with parasites. Otherwise, a narrow spectrum product should be used to ensure sustainable treatment against relevant parasites.

Heartworm endemic areas:

Cats living in heartworm endemic areas and recognised as hunters might be treated at monthly intervals to ensure both appropriate heartworm disease prevention and treatment of potential re-infection with cestodes. Otherwise, a narrow spectrum product should be used for further treatment. Prevention of heartworm disease by killing *Dirofilaria immitis* larvae should start within 1 month after the first expected exposure to mosquitoes and should be continued until at least 1 month after the last exposure to mosquitoes.

Feline lungworm endemic area:

Cats at risk (hunting behaviour) living in endemic areas might be treated at monthly intervals to decrease the risk of establishment of adult lungworms responsible for clinical aelurostrongylosis and to treat potential re-infection with cestodes. Otherwise, a narrow spectrum product should be used for further treatment.

Lungworm treatment: No or little effect on the L1 larvae release of *A. abstrusus* in the faeces can be expected within approximately 2 weeks after treatment due to the transit period of L1 larvae from the

lungs through the digestive tract. Any faecal larval count to control effectiveness of treatment (and the decision if a second treatment with a narrow spectrum product is necessary) should, therefore, only be made two weeks after treatment at the earliest.

Ear mites:

For ear mites, seek further veterinary examination 4 weeks after treatment to determine whether an additional treatment with a narrow spectrum product is necessary.

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

Safety has been evaluated with up to 5 times the maximum recommended dose in healthy kittens aged 8 weeks and older treated up to 6 times at 4-week intervals. At 3 times the maximum recommended dose, no undesirable effects were observed. At 5 times the maximum recommended dose, a single severe adverse neurological reaction (ataxia, disorientation, apathy, tremors, hypothermia and pupil dilation) was observed after the third treatment and was reversible following washing of the application site, emergency measures and symptomatic treatment. In some animals, at 5 times the maximum recommended dose, dark red subcutaneous areas at the skin treatment sites were observed.

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: QP54AA54

4.2 Pharmacodynamics

Esafoxolaner is the (S)-enantiomer of afoxolaner and belongs to the isoxazoline class, which is active against arthropods. Esafoxolaner 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 GABA_ARs, thereby blocking pre- and post-synaptic transfer of chloride ions across cell membranes. Prolonged esafoxolaner-induced hyperexcitation results in uncontrolled activity of the central nervous system and death of arthropods. The selective toxicity of esafoxolaner between arthropods and mammals may be inferred by the differential sensitivity of the arthropods' GABA receptors versus mammalian GABA receptors.

Fleas and ticks are eliminated within 24 and 48 hours respectively after treatment, except for *R. sanguineus* and *I. hexagonus*.

Esafoxolaner kills fleas before egg production and therefore prevents the risk of household contamination. It has activity against mites (*N. cati*, *O. cynotis*) causing notoedric or ear mange.

Eprinomectin is a member of the macrocyclic lactone class of endectocides. Compounds of the class bind selectively and with high affinity to glutamate-gated chloride ion channels which occur in invertebrate nerve or muscle cells. This leads to an increase in the permeability of the cell membrane to chloride ions with hyperpolarisation of the nerve or muscle cell, resulting in paralysis and death of the parasite. The spectrum of efficacy of eprinomectin has been shown to cover gastrointestinal and extraintestinal nematodes, and is also considered to have activity against mites (*N. cati*, *O. cynotis*).

Praziquantel is a synthetic isoquinoline-pyrazine derivative with activity against tapeworms. Praziquantel is rapidly absorbed via the surface of the parasites and affects membrane permeability in cestodes, influencing divalent cation fluxes, particularly calcium ion homeostasis, which is thought to contribute to the rapid muscle contraction and vacuolisation. This results in severe damage to the parasite integument, contraction and paralysis, disruption of metabolism and finally leads to the death and expulsion of the parasite.

4.3 Pharmacokinetics

Esafoxolaner is systemically absorbed from the topical application site, reaching a maximum concentration in plasma between 4 and 14 days after application. Esafoxolaner is slowly eliminated from plasma ($t_{1/2}=21.7 \pm 2.8$ days following single administration) and excreted in faeces and urine.

Eprinomectin is systemically absorbed from the topical application site, reaching a maximum concentration in plasma between 1 and 2 day(s) after application. Eprinomectin is slowly eliminated from plasma ($t_{1/2}=5.4 \pm 2.7$ days following single administration) and excreted in faeces.

Praziquantel is systemically absorbed from the topical application site, reaching a maximum concentration in plasma between 4 and 8 hours after application. Praziquantel is slowly eliminated from plasma ($t_{1/2}=4.3 \pm 1.9$ days following single administration) and excreted in urine.

The pharmacokinetic profiles of praziquantel and eprinomectin are not affected by co-administration.

While no accumulation could be observed after repeated administration for praziquantel, accumulation was observed from the 2nd to the 5th monthly administration for esafoxolaner (ratios of 3.24 for C_{max} and of 3.09 for AUC) and for eprinomectin (ratios of 1.59 for C_{max} and of 1.87 for AUC). Please refer to section 3.5 for safe use after repeated treatment.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

5.3 Special precautions for storage

Keep the unused applicator in the blister package in order to protect from light.
Used applicators should be disposed of immediately.

5.4 Nature and composition of immediate packaging

Spot-on syringe-shaped applicator (barrel of clear siliconised cyclic olefin copolymer (COC), plunger of bromobutyl siliconized rubber and tip cap of bromobutyl rubber) containing 0.3 ml or 0.9 ml of product, and placed in individual plastic blisters.

Cardboard box containing 1, 3, 4 or 15 blister(s) of 1 applicator (0.3 ml each).
Cardboard box containing 1, 3, 4, 6 or 15 blister(s) of 1 applicator (0.9 ml each).

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.

The veterinary medicinal product or an empty applicator should not enter water courses as esafoxolaner may be dangerous for fish and other aquatic organisms.

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/2/20/267/001-009

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 06/01/2021

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

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, pack sizes of 1, 3, 4, 6 or 15 applicators

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NexGard Combo spot-on solution for cats < 2.5 kg
NexGard Combo spot-on solution for cats 2.5-7.5 kg

2. STATEMENT OF ACTIVE SUBSTANCES

Per dose:

esafoxolaner	3.60 mg
eprinomectin	1.20 mg
praziquantel	24.90 mg

esafoxolaner	10.80 mg
eprinomectin	3.60 mg
praziquantel	74.70 mg

3. PACKAGE SIZE

1 x 0.3 ml
3 x 0.3 ml
4 x 0.3 ml
15 x 0.3 ml

1 x 0.9 ml
3 x 0.9 ml
4 x 0.9 ml
6 x 0.9 ml
15 x 0.9 ml

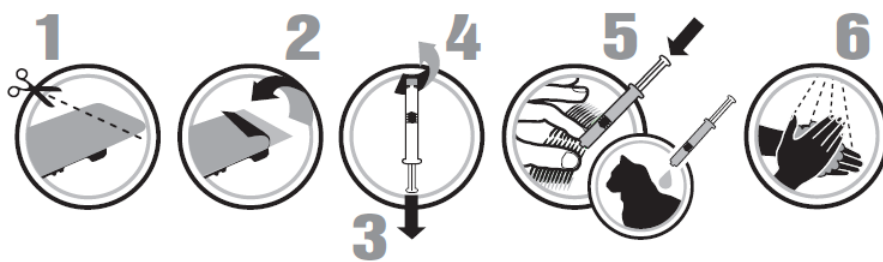
4. TARGET SPECIES

Cats

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Spot-on use.
External use only
Avoid contact of the product with your eyes.



7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Keep the unused applicator in the blister package.

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/2/20/267/001	1 x 0.3 ml
EU/2/20/267/002	3 x 0.3 ml
EU/2/20/267/003	4 x 0.3 ml
EU/2/20/267/004	15 x 0.3 ml

EU/2/20/267/005	1 x 0.9 ml
EU/2/20/267/006	3 x 0.9 ml
EU/2/20/267/007	4 x 0.9 ml
EU/2/20/267/008	6 x 0.9 ml

EU/2/20/267/009 15 x 0.9 ml

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**Blister****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

NexGard Combo < 2.5 kg

NexGard Combo 2.5 – 7.5 kg

**2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES**

0.3 ml

0.9 ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Applicator

1. NAME OF THE VETERINARY MEDICINAL PRODUCT
--

NexGard Combo

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

0.3 ml

0.9 ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

NexGard Combo spot-on solution for cats < 2.5 kg
NexGard Combo spot-on solution for cats 2.5-7.5 kg

2. Composition

Each spot-on applicator delivers:

Active substances:

NexGard Combo	Volume of unit dose (ml)	Esafoxolaner (mg)	Eprinomectin (mg)	Praziquantel (mg)
Cats 0.8-<2.5 kg	0.3	3.60	1.20	24.90
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Excipients:

Butylhydroxytoluene (E321) 1 mg/ml.

Clear, colourless to light yellow to light brown solution.

3. Target species

Cats

4. Indications for use

For cats with, or at risk from mixed infections by cestodes, nematodes and ectoparasites. The veterinary medicinal product is exclusively indicated when all three groups are targeted at the same time.

Ectoparasites

- Treatment of infestations by fleas (*Ctenocephalides felis*). One treatment provides immediate and persistent flea killing activity for one month.
- The product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).
- Treatment of infestations by ticks. One treatment provides immediate and persistent tick killing activity against *Ixodes scapularis* for one month and against *Ixodes ricinus* for five weeks.
- Persistent tick killing activity from 7 days to five weeks after treatment against *Rhipicephalus sanguineus*.
- Persistent tick killing activity from 7 days to four weeks after treatment against *Ixodes hexagonus*.
- Treatment of infestations by ear mites (*Otodectes cynotis*).
- Treatment of Notoedric mange (caused by *Notoedres cati*).

Cestodes

Treatment of infections with tapeworms (*Dipylidium caninum*, *Taenia taeniaeformis*, *Echinococcus multilocularis*, *Joyeuxiella pasqualei*, and *Joyeuxiella fuhrmanni*).

Nematodes

- Prevention of heartworm disease (*Dirofilaria immitis*) for one month.

- Treatment of infections with gastrointestinal nematodes (L3, L4 larvae and adults of *Toxocara cati*, L4 larvae and adults of *Ancylostoma tubaeforme* and *Ancylostoma ceylanicum*, and adult forms of *Toxascaris leonina* and *Ancylostoma braziliense*).
- Treatment of infections with feline lungworms (L4 larvae and adults of *Troglostrongylus brevior*, L3, L4 larvae and adults of *Aelurostrongylus abstrusus*).
- Prevention of aelurostrongylosis (by reduction of the level of infection with L3, L4 larvae of *Aelurostrongylus abstrusus*).
- Treatment of infections with vesical worms (*Capillaria plica*).

5. Contraindications

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

6. Special warnings

Special warnings:

When applying the veterinary medicinal product, special attention should be paid to long hair breeds in order to ensure that the product is applied directly to the skin and not on the hair, as this could lead to a lower bioavailability of the active substance.

Ticks and fleas need to start feeding on the cat to become exposed to esafloxolaner; therefore, the risk of transmission of arthropod borne diseases cannot be excluded.

Cats in areas endemic for heartworm, or those which have travelled to endemic areas, may be infected with adult heartworms. Although the veterinary medicinal product may be safely administered to cats infected with adult heartworms, no therapeutic effect against adult *Dirofilaria immitis* has been established. It is, therefore, recommended that all cats 6 months of age or more, living in areas endemic for heartworm, should be tested for existing adult heartworm infection before being treated with the product for heartworm disease prevention.

Tapeworm infection may reoccur unless control of intermediate hosts such as fleas, mice etc. is undertaken. Some cats with patent *Joyeuxiella* spp. or *Dipylidium caninum* infections may nevertheless harbour a high proportion of juvenile worms, which may be less susceptible to the product; therefore, a post-treatment follow-up is recommended in case of such infections.

Parasite resistance to any particular class of antiparasitics included in the fixed combination product may develop following repeated use of an antiparasitic of those classes over an extended period of time. Therefore, epidemiological information about current susceptibility of the target species should be taken into account in order to limit the possibility of a future selection for resistance.

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-infection, a narrow spectrum product should be used.

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

Avoid shampooing the animal within the 2 days following application because the effectiveness of the product in this case has not been tested.

To reduce re-infestation from emergence of new fleas, it is recommended that all cats in a household are treated. Other animal species living in the same household should also be treated with a suitable product.

All stages of fleas can infest the cat's basket, bedding and regular resting areas such as carpets and soft furnishings. In case of massive flea infestation and at the beginning of the control measures, these areas should be treated with a suitable environmental product and then vacuumed regularly.

Special precautions for safe use in the target species:

Spot-on application only. Do not inject, do not administer orally or via any other route. Avoid contact with the cat's eyes. If accidental ocular contact occurs, flush the eyes immediately with clean water. If eye irritation persists, seek veterinary advice.

It is important to apply the veterinary medicinal product to a skin area where the cat cannot lick it off: on the midline of the neck, in between the base of the skull and the shoulder blades. Ensure that animals do not lick each other until the treated area is no longer noticeable. Oral ingestion of the veterinary medicinal product has been observed to lead to hypersalivation.

The safety of the veterinary medicinal product has not been tested in kittens under 8 weeks of age. The product is for use in cats weighing at least 0.8 kg and from 8 weeks of age.

The veterinary medicinal product should exclusively be used in confirmed mixed infections or where cats are at significant risk of such mixed infection with ectoparasites and nematodes (including for heartworm disease prevention) and where concurrent treatment against cestodes is indicated. In the absence of risk of co-infestation, the use of a narrow spectrum parasiticide should be considered as a first line therapy.

The rationale for prescription and frequency of use should be tailored to the individual needs of the cat, based on clinical assessment, the cat's lifestyle and on the local epidemiological situation (including zoonotic risks, where relevant) in order to address exclusively situations of mixed infections/risk of infection.

The veterinary medicinal product should not be used in other cats without prior veterinary consultation.

Repeated treatments should be restricted to limited individual situations (see section "advice on correct administration" for treatment guidance) with a minimum treatment interval of 4 weeks. The safety was not evaluated beyond 6 months (see also sections "Special warnings" and "Overdose"); therefore, no more than 6 consecutive treatments are recommended to be given within a 12-month period.

Echinococcosis represents a hazard for humans, and is a notifiable disease to the World Organisation for Animal Health (WOAH). In case of echinococcosis, specific guidelines on the treatment and follow up and on the safeguard of persons have to be followed. Experts or institutes of parasitology should be consulted.

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

Do not smoke, drink or eat during application.

Wash hands immediately after use.

Used applicators should be disposed of immediately and not left within the sight or reach of children.

Avoid contact of the applicator content with the fingers. If this occurs, wash off with soap and water. This veterinary medicinal product can cause eye irritation, which might be in exceptional cases severe. In case of accidental eye exposure, flush the eyes immediately and thoroughly with water. Remove contact lenses, if present, after the first 5 minutes, and then continue rinsing. Seek medical advice and show the package leaflet or the label to the physician.

Ensure that the treated area is no longer noticeable before resuming contact with the site of application. Children should not be allowed to play with treated animals until the application site is no longer noticeable and it is recommended that recently treated animals do not sleep with owners,

especially children. It is recommended to treat animals in the evening to reduce contact with people after treatment.

People with a known hypersensitivity to esafloxolaner, eprinomectin or praziquantel or to any of the excipients should avoid contact with the veterinary medicinal product.

Since foetotoxic and teratogenic effects are described in laboratory animals after significant daily exposure to glycerol formal, pregnant women should wear gloves during the administration to avoid direct contact with the product.

Pregnancy and lactation:

Can be used in pregnant and lactating queens.

Fertility:

Can be used in breeding queens.

The safety of the veterinary medicinal product has not been established in breeding male cats.

Laboratory studies in rats and rabbits have not produced any evidence of adverse effects of the active substances on the reproductive capacity in males. In breeding males, use only according to the benefit-risk assessment by the prescribing veterinarian.

Overdose:

Safety has been evaluated with up to 5 times the maximum recommended dose in healthy kittens aged 8 weeks and older treated up to 6 times at 4-week intervals. At 3 times the maximum recommended dose, no undesirable effects were observed. At 5 times the maximum recommended dose, a single severe adverse neurological reaction (ataxia, disorientation, apathy, tremors, hypothermia and pupil dilation) was observed after the third treatment and was reversible following washing of the application site, emergency measures and symptomatic treatment. In some animals, at 5 times the maximum recommended dose, dark red subcutaneous areas at the skin treatment sites were observed.

7. Adverse events

Cats:

Uncommon (1 to 10 animals / 1 000 animals treated):

Hypersalivation¹ (increased salivation), diarrhoea¹, emesis¹ (vomiting), application site alopecia^{1,2} (hair loss), application site pruritus^{1,2} (itching), lethargy¹ (decreased activity) and anorexia¹ (appetite loss).

¹ Mostly mild reactions, of short duration and self-limiting.

² Transient

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 the local representative of the marketing authorisation holder 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

For topical application onto the skin (spot-on use).



Dosage:

The recommended minimum doses are 1.44 mg esafloxolaner, 0.48 mg eprinomectin and 10 mg praziquantel per kg bodyweight.

9. Advice on correct administration

Select the appropriate applicator size for the weight of the cat (0.3 or 0.9 ml, see section “Composition”). To ensure a correct dosage, body weight should be determined as accurately as possible. Underdosing could result in ineffective use and may favour resistance development.

Method of administration:

1. Use scissors to cut the blister along the dotted line.
2. Then pull the lid away.
3. Remove the applicator from the package and hold it upright. Pull back the plunger slightly.
4. Twist and pull off the cap.
5. Part the hair on the midline of the neck, between the base of the skull and the shoulder blades until the skin is visible. Place the tip of the applicator on the skin and apply the entire content directly onto the skin in one spot. The product should be applied to dry skin on an area where the cat cannot lick it off. In long hair breeds, special attention should be paid to apply the product onto the skin, and not on the hair to ensure optimal efficacy.
6. Wash your hands after use.

Treatment schedule:

For the treatment of infestations with fleas and/or ticks and/or mites, and the concurrent treatment of gastrointestinal and/or pulmonary, and/or vesical nematodes, and cestodes, a single dose of the product should be applied. The need for and frequency of re-treatment(s) should be in accordance with the advice of the prescribing veterinarian and should take into account the local epidemiological situation and the animal's lifestyle (e.g. outdoors access). See also section “special warnings”.

Areas which are not-endemic for heartworm or feline lungworm:

Cats not exposed to a permanent risk of heartworm or feline lungworm infection should be treated according to a schedule prescribed by the veterinarian and adapted to each individual situation of re-infection/-infestation with parasites. Otherwise, a narrow spectrum product should be used to ensure sustainable treatment against relevant parasites.

Heartworm endemic areas:

Cats living in heartworm endemic areas and recognised as hunters might be treated at monthly intervals to ensure both appropriate heartworm disease prevention and treatment of potential re-infection with cestodes. Otherwise, a narrow spectrum product should be used for further treatment. Prevention of heartworm disease by killing *Dirofilaria immitis* larvae should start within 1 month after the first expected exposure to mosquitoes and should be continued until at least 1 month after the last exposure to mosquitoes.

Feline lungworm endemic area:

Cats at risk (hunting behaviour) living in endemic areas might be treated at monthly intervals to decrease the risk of establishment of adult lungworms responsible for clinical aelurostrongylosis and to treat potential re-infection with cestodes. Otherwise, a narrow spectrum product should be used for further treatment.

Lungworm treatment: No or little effect on the L1 larvae release of *A. abstrusus* in the faeces can be expected within approximately 2 weeks after treatment due to the transit period of L1 larvae from the lungs through the digestive tract. Any faecal larval count to control effectiveness of treatment (and the decision if a second treatment with a narrow spectrum product is necessary) should, therefore, only be made two weeks after treatment at the earliest.

Ear mites

For ear mites, seek further veterinary examination 4 weeks after treatment to determine whether an additional treatment with a narrow spectrum product is necessary.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Keep the unused applicator in the blister package in order to protect from light.

Used applicators should be disposed of immediately.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton, blister and applicator after Exp.

12. Special precautions for disposal

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

This veterinary medicinal product or an empty applicator should not enter water courses as esafoxolaner may be dangerous for fish and other aquatic organisms.

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 to the veterinary medicinal product concerned. 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/2/20/267/001-009

Cardboard box containing 1, 3, 4 or 15 blister(s) of 1 applicator (0.3 ml each).

Cardboard box containing 1, 3, 4, 6 or 15 blister(s) of 1 applicator (0.9 ml each).

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:

Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim/Rhein
Germany

Manufacturer responsible for batch release:

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Local representatives and contact details to report suspected adverse events:

België/Belgique/Belgien

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17. Other information

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