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:
Butylhydroxytoluene (E321) 1 mg/ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Spot-on solution.
Clear, colourless to light yellow to light brown solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cats.

4.2 Indications for use, specifying the 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.
- 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*).

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

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 esafoxolaner; 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.

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.

4.5 Special precautions for use

Special precautions for use in animals
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 4.9 for treatment guidance) with a minimum treatment interval of 4 weeks. The safety was not evaluated beyond 6 months (see also sections 4.4, 4.10, and 5.2); 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 (OIE). 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 esafoxolaner, 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.

4.6 Adverse reactions (frequency and seriousness)

Hypersalivation, diarrhoea, transient skin reactions at the application site (alopecia, pruritus), anorexia, lethargy and emesis were uncommonly observed in clinical trials shortly after administration. They are mostly mild reactions, of short duration and self-limiting.

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

Can be used in breeding, pregnant and lactating 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.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

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.

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 4.5.

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.

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

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.

4.11 Withdrawal period

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antiparasitic products, insecticides and repellents, avermectins, eprinomectin, combinations.
ATCvet code: QP54AA54.

5.1 Pharmacodynamic properties

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 GABACls, 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.
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.

5.2 Pharmacokinetic particulars

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 ± 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 +/- 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 +/- 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 4.5 for safe use after repeated treatment.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol formal
Dimethyl isosorbide
Butylhydroxytoluene (E321)

6.2 Major incompatibilities

None known.

6.3 Shelf life

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

6.4 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.

6.5 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.

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.
NexGard Combo or an empty applicator should not enter water courses as this may be dangerous for fish and other aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim/Rhein
Germany

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/20/267/001-009

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06/01/2021

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.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release
Boehringer Ingelheim Animal Health France SCS
4 Chemin du Calquet,
31000 Toulouse
FRANCE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable.

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. PHARMACEUTICAL FORM

Spot-on solution

4. 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

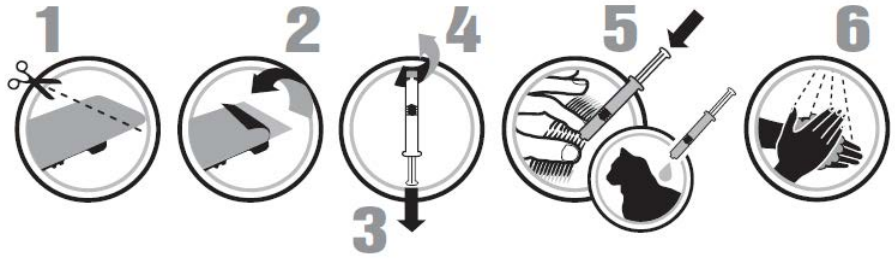
5. TARGET SPECIES

Cats

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Spot-on use.
External use only
Read the package leaflet before use.



8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Avoid contact of the product with your eyes.
Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Keep the unused applicator in the blister package.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim/Rhein
Germany

16. MARKETING AUTHORISATION NUMBER(S)

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

17. MANUFACTURER'S BATCH NUMBER

Lot

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NexGard Combo < 2.5 kg
NexGard Combo 2.5-7.5 kg
esafoxolaner, eprinomectin, praziquantel

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Applicator

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NexGard Combo

2. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

0.3 ml
0.9 ml

3. ROUTE(S) OF ADMINISTRATION

4. WITHDRAWAL PERIOD(S)

5. BATCH NUMBER

Lot

6. EXPIRY DATE

EXP

B. PACKAGE LEAFLET

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

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim/Rhein
Germany

Manufacturer responsible for batch release:
Boehringer Ingelheim Animal Health France SCS
4 Chemin du Calquet
31000 Toulouse
France

2. 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
esafoxolaner, eprinomectin, praziquantel

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENTS

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
Cats 2.5-<7.5 kg	0.9	10.80	3.60	74.70

Excipients:
Butylhydroxytoluene (E321) 1 mg/ml.

Spot-on solution.
Clear, colourless to light yellow to light brown solution.

4. INDICATION(S)

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.
- 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. ADVERSE REACTIONS

Hypersalivation, diarrhoea, transient skin reactions at the application site (alopecia, pruritus), anorexia, lethargy and emesis were uncommonly observed in clinical trials shortly after administration. They are mostly mild reactions, of short duration and self-limiting.

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).

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 inform your veterinary surgeon.

7. TARGET SPECIES

Cats.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

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

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

9. ADVICE ON CORRECT ADMINISTRATION

Use the applicator size adapted to the weight of the cat (0.3 or 0.9 ml, see section "statement of the active substance(s) and other ingredient(s)").

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 warning(s)".

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 PERIOD(S)

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 after EXP.

12. SPECIAL WARNING(S)

Special warnings for each target species:
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.

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

Ticks and fleas need to start feeding on the cat to become exposed to esafoxolaner; 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.

To reduce re-infestation from emergence of new fleas, it is recommended that all cats in a household are treated. Other animals 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 use in animals:
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 for each target species" 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 (OIE). 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 esafoxolaner, 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 breeding, pregnant and lactating 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 (symptoms, emergency procedures, 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.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment. The product or an empty applicator should not enter water courses as this may be dangerous for fish and other aquatic organisms.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

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

15. OTHER INFORMATION

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

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.