SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Fiproclear Combo 50 mg / 60 mg spot-on solution for cats and ferrets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pipette of 0.5 ml contains:

Active substances:
Fipronil 50 mg
(S)-methoprene 60 mg

Excipients:
Butylhydroxyanisole (E320) 0.10 mg
Butylhydroxytoluene (E321) 0.05 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Spot-on solution
A clear, yellow solution

4. CLINICAL PARTICULARS

4.1 Target Species

Cats and ferrets.

4.2 Indications for use, specifying the target species

In cats:
To be used against infestations with fleas, alone or in association with ticks and/or biting lice.

- Elimination of fleas (*Ctenocephalides* spp.). Insecticidal efficacy against new infestations with adult fleas persists for 4 weeks. Prevention of the multiplication of fleas by inhibiting the development of eggs (ovicidal activity), larvae and pupae (larvicidal activity) originating from eggs laid by adult fleas for six weeks after application.
- Elimination of ticks (*Ixodes ricinus*, *Dermacentor variabilis*, *Rhipicephalus sanguineus*). The product has a persistent acaricidal efficacy for up to 2 weeks against ticks (based on experimental data).
- Elimination of biting lice (*Felicola subrostratus*).

In ferrets:
To be used against infestations with fleas, alone or in association with ticks.

- Elimination of fleas (*Ctenocephalides* spp.). Insecticidal efficacy against new infestations with adult fleas persists for 4 weeks. Prevention of the multiplication of fleas by inhibiting the development of eggs (ovicidal activity), larvae and pupae (larvicidal activity) originating from eggs laid by adult fleas.
- Elimination of ticks (*Ixodes ricinus*). The product has a persistent acaricidal efficacy for 4 weeks against ticks (based on experimental data).

4.3 Contraindications

In the absence of available data, the product should not be used on kittens less than 8 weeks old and/or weighing less than 1 kg. The product should not be used on ferrets less than 6 months old.
Do not use on sick (e.g. systemic diseases, fever) or convalescent animals.
Do not use in rabbits, as adverse drug reactions with even mortality could occur.
In absence of studies, the use of the product is not recommended in non-target species.
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

Avoid contact with the animal's eyes.

4.5 Special precautions for use

Special precautions for use in animals

It is important to make sure that the product is applied to an area where the animal cannot lick it off and to make sure that animals do not lick each other following treatment.

No data on the effect of bathing/shampooing on the efficacy of the product in cats and ferrets are available. However, based on information available for dogs shampooed as from 2 days after application of the product, it is not recommended to bath animals within 2 days after application of the product.

There may be an attachment of single ticks. For this reason a transmission of infectious diseases cannot be completely excluded if conditions are unfavourable.

Fleas from pets often infest the animal's basket, bedding and regular resting areas such as carpets and soft furnishings which should be treated, in case of massive infestation and at the beginning of the control measures, with a suitable insecticide and vacuumed regularly.

The potential toxicity of the product for kittens of less than 8 weeks of age in contact with a treated queen is not documented. Special care should be taken in this case.

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

This product can cause mucous membrane, skin and eye irritation. Therefore, contact of the product with mouth, skin and eyes should be avoided. Do not smoke, drink or eat during the application. In case of accidental eye contact, immediately and thoroughly rinse the eyes with clean water. If eye irritation persists seek medical advice and show the package leaflet or the label to the physician. If contact with the skin occurs, wash hands with soap and water.

People with a known hypersensitivity to insecticides or alcohol should avoid contact with the veterinary medicinal product.

Wash hands after use.

Ingestion of the product is harmful. Prevent children getting access to the pipettes and discard the used pipettes immediately after applying the product. In case of accidental ingestion of product, seek medical advice immediately.

Treated animals should not be handled until the application site is dry, and children should not be allowed to play with treated animals until the application site is dry. It is therefore recommended that animals are not treated during the day, but should be treated during the early evening, and that recently treated animals are not allowed to sleep with owners, especially children.

Other precautions
The alcohol carrier may have adverse effects on painted, varnished or other household surfaces or furnishings.

4.6 Adverse reactions (frequency and seriousness)

Cats:
Among the very rare suspected adverse reactions, transient skin reactions on the application site (scaling, local hair loss, itching, redness) and general itching or hair loss have been reported after use. Excessive salivation, reversible nervous signs (increased sensitivity to stimulation, depression, other nervous signs) or vomiting have also been observed after use.

The frequency of adverse reactions is defined using the following convention:
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

If licking occurs, a brief period of excessive salivation may be observed due mainly to the nature of the carrier.

4.7 Use during pregnancy, lactation or lay

Cats:
The product can be used during pregnancy.
For treatment during the lactating period, see section 4.5

Ferrets:
Laboratory studies in cats have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects. The safety of the veterinary medicinal product has not been established in ferrets during pregnancy and lactation. Use only according to the risk-benefit assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interactions

None known.

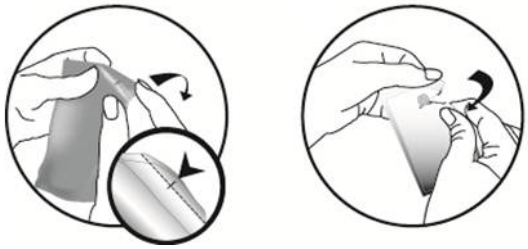
4.9 Amounts to be administered and administration route

Dosage:
One pipette of 0.5 ml per cat, corresponding to a minimum recommended dose of 5 mg/kg for fipronil and 6 mg/kg for (S)-methoprene.
In the absence of safety studies, the minimum treatment interval is 4 weeks.

One pipette of 0.5 ml per ferret corresponding to a dose of 50 mg for fipronil and 60 mg for (S)-methoprene per ferret.
The minimum treatment interval is 4 weeks.

Route of administration: External use only, spot-on use.
Only remove pipette from sachet immediately prior to use.

Method of Administration:
Remove the pipette from the outer sachet using scissors or fold along diagonal line to expose nick; tear back at nick.



Hold the pipette upright. Tap the narrow part of the pipette to ensure the contents remain within the main body of the pipette. Twist or snap back the tip.

Part the coat on the back of the animal at the base of the neck in front of the shoulder blades until the skin is visible. Place the tip of the pipette on the skin and squeeze the

pipette several times to empty its contents completely and directly onto the skin in one spot.

Temporary changes to the coat (clumped/greasy hair) may be noted at the application site.

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

The risk of experiencing adverse effects may increase with overdosing (see section 4.6).

In cats:
No undesirable effects were observed in target animal safety studies in cats and kittens aged 8 weeks and older and weighing about 1 kg treated once a month at five times the recommended dose for six consecutive months.
Itching may occur following treatment.
Overdose application of the product will cause a sticky appearance of hairs at the treatment spot. However, should this occur, it will disappear within 24 hours post application.

In ferrets:
In ferrets aged 6 months and older and treated once every 2 weeks for four treatments, at five times the recommended dose, body weight loss was observed in some animals.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Ectoparasiticides for topical use, fipronil combinations.
ATCvet code: QP53AX65

5.1 Pharmacodynamic properties

Fipronil is an insecticide and acaricide belonging to the phenylpyrazole family. It acts by interacting with ligand-gated chloride channels, in particular those gated by the neurotransmitter gamma-aminobutyric acid (GABA), thereby blocking pre- and post-synaptic transfer of chloride ions across cell membranes. This results in uncontrolled activity of the central nervous system and death of insects or acarines. Fipronil kills fleas within 24 hours, ticks (*Dermacentor variabilis, Rhipicephalus sanguineus, Ixodes scapularis, Ixodes ricinus, Haemaphysalis longicornis,*

Haemaphysalis flava, Haemaphysalis campanulata) and lice within 48 hours post-exposure.

(S)-Methoprene is an insect growth regulator (IGR) of the class of compounds known as juvenile hormone analogues that inhibit the development of immature stages of insects. This compound mimics the action of juvenile hormone and causes impaired development and death of the developing stages of fleas. The on-animal ovicidal activity of (S)-methoprene results from either direct penetration of the eggshell of newly laid eggs or from absorption through the cuticle of the adult fleas. (S)-methoprene is also effective in preventing flea larvae and pupae from developing, which prevents contamination of the environment of treated animals with the immature stages of fleas.

5.2 Pharmacokinetic particulars

Studies of metabolism of fipronil have demonstrated that the major metabolite is the sulfone derivative of fipronil.

(S)-methoprene is extensively degraded into carbon dioxide and acetate that are subsequently incorporated into endogenous materials.

The pharmacokinetic profiles after topical application of fipronil and (S)-methoprene in combination were studied in cats in comparison to intravenous dosing of fipronil or (S)-methoprene alone. This established absorption and other pharmacokinetic parameters under conditions mimicking clinical practice. The topical application, with additional potential oral exposure from licking, resulted in overall systemic absorption of fipronil (18%) with a mean maximum concentration (C_{max}) of approximately 100 ng/ml fipronil and 13 ng/ml of fipronil sulfone in plasma. Peak fipronil plasma concentrations are rapidly attained (mean t_{max} approximately 6 h) and decline with a mean terminal half-life of approximately 25 h. Fipronil is slightly metabolised to fipronil sulfone in cats. Plasma concentrations of (S)-methoprene were generally below the limit of quantitation (20 ng/ml) in cats after topical application.

Both (S)-methoprene and fipronil, together with its major metabolite, are well-distributed in the haircoat of cats within one day after application. The concentrations of fipronil, fipronil sulfone and (S)-methoprene in the hair coat decrease with time and are detectable for at least 59 days after dosing. Parasites are killed through contact rather than by systemic exposure.

No pharmacological interaction between fipronil and (S)-methoprene was noted.

The pharmacokinetic profile of the product has not been investigated in ferrets.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxyanisole (E320)
Butylhydroxytoluene (E321)
Ethanol anhydrous
Polysorbate 80

Povidone K17
Diethylene glycol monoethyl ether

6.2 Major incompatibilities

None known.

6.3 Shelf life

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

6.4 Special precautions for storage

Store in the original package in order to protect from light and moisture.
This veterinary medicinal product does not require any special temperature storage conditions.

6.5 Nature and composition of immediate packaging

0.5 ml pipette, moulded from a film composed of 3 layers: a polypropylene/COC/polypropylene, solvent free lacquer laminate and a copolymer of polyethylene/EVOH/polyethylene. The pipettes are sealed within a child resistant 4-ply foil sachet composed of LDPE/nylon/aluminium foil/polyester film and presented in an outer box.

Boxes of 1, 2, 3, 4, 6, 8, 12 or 24 pipettes. Each pipette is individually sealed in a foil sachet.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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.

Fipronil and (S)-methoprene may adversely affect aquatic organisms. Do not contaminate ponds, waterways or ditches with the product or empty containers.

7. MARKETING AUTHORISATION HOLDER

Norbrook Laboratories Limited
Station Works
Camlough Road
Newry
Co. Down
BT35 6JP
United Kingdom

8. MARKETING AUTHORISATION NUMBER

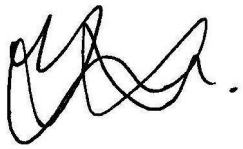
Vm 02000/4407

9. DATE OF FIRST AUTHORISATION

19 April 2017

10. DATE OF REVISION OF THE TEXT

April 2022



Approved: 13 April 2022