## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zeronil 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 | 50.00 mg |
| (S)-methoprene | 60.00 mg |

**Excipients:**

| **Qualitative composition of excipients and other constituents** | **Quantitative composition if that information is essential for proper administration of the veterinary medicinal product** |
|---|---|
| Butylhydroxyanisole (E320) | 0.10 mg |
| Butylhydroxytoluene (E321) | 0.05 mg |
| Ethanol, anhydrous | |
| Polysorbate 80 | |
| Povidone K17 | |
| Diethylene glycol monoethyl ether | |

Clear amber solution.

## 3. CLINICAL PARTICULARS

### 3.1 Target Species

Cats and ferrets.

### 3.2 Indications for use for each 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 veterinary medicinal product has a persistent acaricidal efficacy for up to 2 weeks against ticks (based on experimental data).
- Elimination of biting lice (*Felicola subrostratus*).

The veterinary medicinal product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD).

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 veterinary medicinal product has a persistent acaricidal efficacy for 4 weeks against ticks (based on experimental data).

## 3.3 Contraindications

In the absence of available data, the veterinary medicinal product should not be used on kittens less than 8 weeks old and/or weighing less than 1 kg. The veterinary medicinal 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 veterinary medicinal 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.

## 3.4 Special warnings

Avoid contact with the animal's eyes.

## 3.5 Special precautions for use

Special precautions for safe use in the target species:

It is important to make sure that the veterinary medicinal 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 veterinary medicinal product in cats and ferrets are available. However, based on information available for dogs shampooed as from 2 days after application of the veterinary medicinal product, it is not recommended to bath animals within 2 days after application of the veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal product can cause mucous membrane, skin and eye irritation. Therefore, contact of the veterinary medicinal product with mouth, skin and eyes should be avoided.
People with known hypersensitivity to insecticides or alcohol should avoid contact with the veterinary medicinal product.

Avoid contents coming into contact with the fingers. If this occurs, wash hands with soap and water.
After accidental ocular exposure the eye should be rinsed carefully with pure water.
Wash hands after use.

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.
Do not smoke, drink or eat during application.

Special precautions for the protection of the environment:

See section 5.5.

Other precautions:
Not applicable.

### 3.6 Adverse events

Cats and Ferrets

| | |
|---|---|
| Very rare<br>(<1 animal / 10,000 animals treated, including isolated reports): | Application site reactions (Skin scaling[1], Hair loss[1], Itching[1], Reddening of the skin[1]).<br><br>Generalised itching, Hair loss.<br><br>Hypersalivation[2], Vomiting.<br><br>Increased sensitivity to stimulation[3], Depression[3], Other nervous signs[3]. |

[1] Transient.
[2] If licking occurs, a brief period of excessive salivation may be observed due mainly to the nature of the carrier.
[3] Reversible.

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:

Cats:
Can be used during pregnancy. For treatment during the lactating period, see section 3.5.

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.

### 3.8 Interaction with other medicinal products and other forms of interaction

None known.

### 3.9 Administration routes and dosage

Spot-on use.
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, by topical application to the skin.
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, by topical application to the skin.
The minimum treatment interval is 4 weeks.

Method of administration:

1. Hold the pipette upright.
2. Tap the narrow part of the pipette to ensure the contents remain within the main body of the pipette.
3. Snap back the tip.
4. 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.
5. 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.

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

The risk of experiencing adverse effects may increase with overdosing (see section 3.6).

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.
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.

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

### 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 Period(s)

Not applicable.

## 4. PHARMACOLOGICAL PROPERTIES

### 4.1 ATCvet code:
QP53AX65

### 4.2 Pharmacodynamics

**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.

### 4.3 Pharmacokinetics

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 hours) and decline with a mean terminal half-life of approximately 25 hours.
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 veterinary medicinal product has not been investigated in ferrets.

## 5 PHARMACEUTICAL PARTICULARS

### 5.1 Major incompatibilities

None known.

### 5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 36 months.

### 5.3 Special precautions for storage

Store in the original package in order to protect from light.

### 5.4 Nature and composition of immediate packaging

A white pipette composed of a heat-formed shell of polypropylene/cyclic olefin copolymer/polypropylene layer and polyethylene/ethylene vinyl alcohol/polyethylene layer.

Box with 1, 2, 3, 4, 6, 8, 9, 10, 12, 15, 18, 20, 21, 24, 30, 60, 90, 150 or 160 pipettes in individual foil sachets.
Not all pack sizes may be marketed.

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

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

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

The veterinary medicinal product should not enter water courses as Fipronil and (S)-methoprene may be dangerous for fish and other aquatic organisms.

## 6. NAME OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd,

## 7. MARKETING AUTHORISATION NUMBER(S)

VPA10987/125/001

## 8. DATE OF FIRST AUTHORISATION

20/04/2018

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

28/02/2025

## 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)