SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Stronghold Plus 15 mg/2.5 mg spot-on solution for cats ≤2.5 kg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each unit dose (pipette) delivers:

Active substances:

Stronghold Plus spot-on solution	Pipette content (ml)	selamectin (mg)	sarolaner (mg)
Cats ≤2.5 kg	0.25	15	2.5

Excipients:
0.2 mg/ml butylhydroxytoluene.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Spot-on solution.
Clear, colourless to yellow 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 parasitic infestations by ticks and fleas, lice, mites, gastrointestinal nematodes or heartworm. The veterinary medicinal product is exclusively indicated when use against ticks and one or more of the other target parasites is indicated at the same time.

Ectoparasites:
- For the treatment and prevention of flea infestations (*Ctenocephalides* spp.). The veterinary medicinal product has immediate and persistent flea killing activity against new infestations for 5 weeks. The product kills adult fleas before they lay eggs for 5 weeks. Through its ovicidal and larvicidal action, the veterinary medicinal product may aid in the control of existing environmental flea infestations in areas to which the animal has access.

- The product can be used as part of a treatment strategy for flea allergy dermatitis (FAD).
- Treatment of tick infestations. The veterinary medicinal product has immediate and persistent acaricidal effect for 5 weeks against *Ixodes ricinus* and *Ixodes hexagonus*, and 4 weeks against *Dermacentor reticulatus* and *Rhipicephalus sanguineus*.
- Treatment of ear mites (*Otodectes cynotis*).
- Treatment of biting lice infestations *(Felicola subrostratus*).

Ticks must attach to the host and commence feeding in order to be exposed to sarolaner.

Nematodes:
- Treatment of adult roundworms (*Toxocara cati*) and adult intestinal hookworms (*Ancylostoma tubaeforme).*
- Prevention of heartworm disease caused by *Dirofilaria immitis* with monthly administration.

4.3 Contraindications

Do not use in cats that are suffering from concomitant disease, or are debilitated and underweight (for size and age).

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

It is recommended, in accordance with good veterinary practice, that all animals 6 months of age or more, living in countries where a vector exists should be tested for existing adult heartworm infections before beginning preventive use with the veterinary medicinal product.

This veterinary medicinal product is not effective against adult *D. immitis*. The administration to animals with adult heartworm infection did not pose safety concerns.

Whilst not routinely indicated, the potential benefits of performing periodic testing for heartworm infection in individual cases should be considered by the responsible veterinarian.

Ticks need to start feeding on the host to become exposed to sarolaner; therefore, the transmission of infectious tick-borne diseases cannot be excluded.

4.5 Special precautions for use

Special precautions for use in animals

Use of this veterinary medicinal product is indicated in cats aged at least 8 weeks old and weighing at least 1.25 kg bodyweight.

This veterinary medicinal product is to be applied to the skin surface only. Do not administer orally or parenterally.

Do not apply when the animal's hair coat is wet.

For ear mite treatment, do not apply directly to the ear canal.
It is important to apply the dose as indicated to prevent the animal from licking and ingesting the product. If significant ingestion occurs, transient gastrointestinal effects such as hypersalivation, emesis, soft faeces or reduced food consumption may be observed and should normally resolve without treatment.

Keep treated animals away from fires and other sources of ignition for at least 30 minutes or until the hair coat is dry.

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

The product is harmful after ingestion. Keep the product in the original packaging until use, in order to prevent children from getting direct access to the product. Used pipettes should be disposed of immediately. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

The product may cause eye irritation. Avoid eye contact including hand-to-eye-contact. Avoid direct contact with treated animals until the application area is dry. Wash hands after use and wash off any product in contact with the skin immediately with soap and water. If accidental eye exposure occurs, flush the eyes immediately with water and seek medical attention.

Children are not allowed to play with treated cats for 4 hours after treatment. It is recommended to treat animals in the evening. On the day of treatment, treated animals should not be permitted to sleep in the same bed as their owner, especially children.

People with sensitive skin or known allergy to veterinary medicinal products of this type should handle the veterinary medicinal product with caution.

The product is highly flammable. Keep away from heat, sparks, open flame or other sources of ignition.

4.6 Adverse reactions (frequency and seriousness)

Use of the veterinary medicinal product may result in mild and transient pruritus at the application site. Mild to moderate alopecia at the application site, erythema and drooling have been uncommonly observed.
Neurological signs (convulsions, ataxia) and gastrointestinal signs (emesis, diarrhoea) have been reported very rarely based on post-marketing safety experience. In most cases these signs are transient.

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

The safety of the veterinary medicinal product has not been established during pregnancy and lactation or in animals intended for breeding. However, selamectin is considered safe for use in breeding, pregnant and lactating cats. While the safety of sarolaner has not been evaluated in breeding, pregnant or lactating cats, laboratory studies with sarolaner in rats and rabbits have not produced any evidence of teratogenic effects. Use only according to the benefit-risk assessment by the prescribing veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

During clinical field testing, no interactions between this veterinary medicinal product and routinely used veterinary medicinal products were observed.

4.9 Amounts to be administered and administration route

Spot-on use.

Stronghold Plus should be administered as a single spot-on (topical) application in accordance with the following table (corresponding to a minimum of 6 mg/kg selamectin and 1 mg/kg sarolaner).

Bodyweight of cat (kg)	**Pipette content (ml)**	**Strength and number of pipettes to be administered**		
		Stronghold Plus 15 mg/2.5 mg (yellow cap)		
≤2.5	0.25	1		

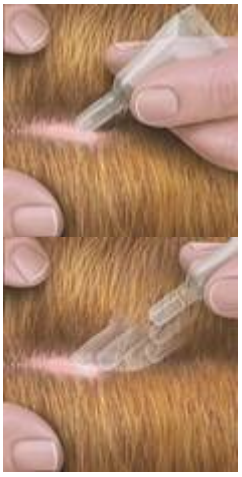
Method and route of administration

Apply topically to the skin at the base of the neck in front of the shoulder blades. The pipette should be removed from the protective package immediately prior to administration.

Holding the pipette upright, firmly depress the cap to puncture the applicator seal, then remove the cap.

Part the hair at the base of the cat's neck in front of the shoulder blades to expose a small area of skin. Apply the tip of the pipette directly to the skin, without massaging.

Squeeze the pipette firmly 3–4 times to empty the contents in one spot. Avoid contact between the product and your fingers.



Transient cosmetic effects may occur at the application site such as temporary clumping or spiking of the hair, greasiness or dry white deposits, which normally resolve within 24 hours after product application. These effects do not affect the safety or efficacy of the veterinary medicinal product.

Treatment schedule

Fleas and ticks
For optimal control of tick and flea infestations, the veterinary medicinal product should be administered at monthly intervals and continued throughout the flea and/or tick season based on local epidemiological situations.

Following administration of the product, the adult fleas on the animal are killed within 24 hours, no viable eggs are produced, and larvae (found only in the environment) are also killed. This stops flea reproduction, breaks the flea lifecycle and may aid in the control of existing environmental flea infestations in areas to which the animal has access.

Prevention of heartworm disease
The product may be administered year-round or at least within one month of the animal's first exposure to mosquitoes and monthly thereafter until the end of the mosquito season. The final dose must be given within one month after the last exposure to mosquitoes. If a dose is missed and a monthly interval between dosing is exceeded, then immediate administration of the product and resumption of monthly dosing will minimise the opportunity for the development of adult heartworms. When replacing another heartworm preventive product in a heartworm disease prevention programme, the first dose of the product must be given within a month of the last dose of the former veterinary medicinal product.

Treatment of roundworm and hookworm infections
A single dose of the product should be administered. The need for and frequency of re-treatment should be in accordance with the advice of the prescribing veterinarian.

Treatment of biting lice
A single dose of the product should be administered.

Treatment of ear mites
A single dose of the product should be administered. Seek further veterinary examination 30 days after treatment to determine whether a second administration is necessary.

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

No clinically significant adverse reactions were observed in kittens from 8 weeks of age treated with up to 5 times the maximum recommended dose of the product for up to 8 consecutive treatments at 28 day intervals, apart from a single cat administered 5 times the maximum dose that displayed transient hypersensitivity to touch, piloerection, mydriasis and mild tremor which resolved without treatment.

After accidental ingestion of a full product dose, transient gastrointestinal effects such as salivation, soft faeces, emesis, and reduced food consumption may occur, however, these should resolve without treatment.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiparasitic products, insecticides and repellents, macrocyclic lactones, combinations.
ATC vet code: QP54AA55.

5.1 Pharmacodynamic properties

Selamectin is a semi-synthetic compound of the avermectin class. Selamectin paralyses and/or kills a wide range of invertebrate parasites through interference with their chloride channel conductance causing disruption of normal neurotransmission. This inhibits the electrical activity of nerve cells in nematodes and muscle cells in arthropods leading to their paralysis and/or death.

Selamectin has adulticidal, ovicidal and larvicidal activity against fleas. Therefore, it effectively breaks the flea life cycle by killing adults (on the animal), preventing the hatching of eggs (on the animal and in its environment) and by killing larvae (environment only). Debris from selamectin-treated pets kills flea eggs and larvae not previously exposed to selamectin and thus may aid in the control of existing environmental flea infestations in areas to which the animal has access. Selamectin is active against adult fleas (*Ctenocephalides* spp.) as well as mites (*Otodectes cynotis*), lice (*Felicola subrostratus*) and gastrointestinal nematodes (*Toxocara cati*, *Ancylostoma tubaeforme*). Activity has also been demonstrated against heartworm (*D. immitis)* larvae.

For fleas, the onset of efficacy is within 24 hours for 5 weeks after product application.

Sarolaner is an acaricide and insecticide belonging to the isoxazoline family. The primary target of action of sarolaner in insects and acarines is functional blockade of ligand-gated chloride channels (GABA-receptors and glutamate-receptors). Sarolaner blocks GABA- and glutamate-gated chloride channels in the central nervous system of insects and acarines. Disruption of these receptors by sarolaner prevents the uptake of chloride ions by GABA and glutamate gated ion channels, thus resulting in increased nerve stimulation and death of the target parasite. Sarolaner exhibits higher functional potency to block insect/acarine receptors compared to mammalian receptors. Sarolaner does not interact with known insecticidal binding sites of nicotinic or other GABAergic insecticides such as neonicotinoids, fiproles, milbemycins, avermectins, and cyclodienes. Sarolaner is active against adult fleas (*Ctenocephalides* spp.) as well as several tick species such as *Dermacentor reticulatus, Ixodes hexagonus, Ixodes ricinus*, and *Rhipicephalus sanguineus*.

For ticks (*I. ricinus*), the onset of efficacy is within 24 hours of attachment for one month after product application.

5.2 Pharmacokinetic particulars

Following topical administration of the Stronghold Plus both selamectin and sarolaner are well absorbed with bioavailability mean values of 40.5% and 57.9%, respectively and distribute systemically. In cats, selamectin and sarolaner are low clearance compounds with long half-life values, 12.5 days and 41.5 days respectively, following topical administration.

In cats the primary route of selamectin elimination is in faeces and the majority is parent compound. Identification of selamectin metabolites in faeces indicated that metabolic clearance also contributes to the elimination. The primary route of elimination for sarolaner is biliary elimination of parent sarolaner, with contributions by metabolic clearance.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene
Dipropyleneglycol monomethyl ether
Isopropyl alcohol

6.2 Major incompatibilities

None known.

6.3 Shelf life

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

6.4 Special precautions for storage

Store below 30 °C.

Do not remove the pipette from the blister until ready to use.

6.5 Nature and composition of immediate packaging

Translucent polypropylene unit dose pipettes individually packed in aluminium and aluminium/PVC blisters.

The pipette caps are colour-coded as follows:

Pipettes with yellow caps contain 0.25 ml of product and deliver 15 mg selamectin and 2.5 mg sarolaner.

The product is available in packs of three pipettes and six pipettes placed in cardboard boxes. 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 products should be disposed of in accordance with local requirements.

Stronghold Plus should not enter water courses as this may be dangerous to aquatic organisms. Containers and residual contents should be disposed of along with collected domestic refuse to avoid contamination of any water courses.

7. MARKETING AUTHORISATION HOLDER

Zoetis UK Limited
1st Floor, Birchwood Building
Springfield Drive
Leatherhead
Surrey
KT22 7LP

8. MARKETING AUTHORISATION NUMBER

Vm 42058/5068

9. DATE OF FIRST AUTHORISATION

9 February 2017

10. DATE OF REVISION OF THE TEXT

August 2022

Approved 22 August 2022