SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Simparica Trio chewable tablets for dogs 1.25–2.5 kg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:

Simparica Trio chewable tablets	sarolaner (mg)	moxidectin (mg)	pyrantel (as embonate) (mg)
for dogs 1.25–2.5 kg	3	0.06	12.5

Excipients:

Butylhydroxytoluene (E321, 0.018%). Colorants: Sunset Yellow FCF (E110), Allura Red (E129), Indigo Carmine (E132). For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablet.
A reddish-brown colored, pentagon shaped tablet with rounded edges. Tablet is debossed with the sarolaner strength on one face of the tablet.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

For dogs with, or at risk from, mixed external and internal parasitic infestations. The veterinary medicinal product is exclusively indicated when use against ticks, fleas or mites and gastrointestinal nematodes is indicated at the same time. The veterinary medicinal product also provides concurrent efficacy for the prevention of heartworm disease, angiostrongylosis and thelaziosis.

Ectoparasites

- For the treatment of tick infestations. The veterinary medicinal product has immediate and persistent tick killing activity for 5 weeks against *Ixodes hexagonus, Ixodes ricinus* and *Rhipicephalus sanguineus* and for 4 weeks against *Dermacentor reticulatus*;

- For the treatment of flea infestations (*Ctenocephalides felis* and *Ctenocephalides canis*). The veterinary medicinal product has immediate and persistent flea killing activity against new infestations for 5 weeks;
- The veterinary medicinal product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).
- For the treatment of sarcoptic mange (caused by *Sarcoptes scabiei* var. *canis*).
- For the treatment of demodicosis (caused by *Demodex canis*).

Gastrointestinal nematodes
For the treatment of gastrointestinal roundworm and hookworm infections:
- *Toxocara canis* immature adults (L5) and adults;
- *Ancylostoma caninum* L4 larvae, immature adults (L5) and adults;
- *Toxascaris leonina* adults;
- *Uncinaria stenocephala* adults.

Other nematodes
- For the prevention of heartworm disease (*Dirofilaria immitis*);
- For the prevention of angiostrongylosis by reducing the level of infection with immature adult (L5) stages of *Angiostrongylus vasorum.*
- For the prevention of establishment of thelaziosis (adult *Thelazia callipaeda* eyeworm infection).

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

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

This veterinary medicinal product is not effective against adult *D. immitis*. However, accidental administration to dogs infected with adult heartworms should not pose safety concerns. Dogs in areas endemic for heartworm (or those which have travelled to endemic areas) may be infected with adult heartworms. Maintenance of the efficacy of macrocyclic lactones is critical for *Dirofilaria immitis* control. To minimise the risk of resistance selection, it is recommended that dogs should be checked for both circulating antigens and blood microfilariae at the beginning of each season of preventative treatment. Only negative animals should be treated.

Parasite resistance to any particular class of parasiticides may develop following the frequent, repeated use of a product of that class. Therefore, the use of this product should be based on the assessment of each individual case and on local epidemiological information about the current susceptibility of the target species in order to limit the possibility of a future selection for resistance.

4.5 Special precautions for use

Special precautions for use in animals

In the absence of available data, treatment of puppies less than 8 weeks of age and/or dogs less than 1.25 kg bodyweight should be based on a benefit-risk assessment by the responsible veterinarian.

The product was well tolerated in dogs with a deficient multidrug-resistance-protein 1 (MDR1 -/-). However, in such sensitive breeds (which may include, but not necessarily limited to, Collies and related breeds), the recommended dose should be strictly observed.

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

Wash hands after handling the product.

The accidental ingestion of the product may potentially result in adverse effects, such as transient excitatory neurological signs. To prevent children from accessing the product, only one chewable tablet at a time should be removed from the blister pack and only when required. The blister pack should then be returned into the carton immediately after use and the carton should be stored out of the sight and reach of children. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

4.6 Adverse reactions (frequency and seriousness)

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Gastrointestinal signs (such as vomiting, diarrhoea)[1] Systemic disorders (such as lethargy, anorexia)[1] Neurological signs (such as tremor, ataxia, convulsions)[2]

[1]In most cases these signs are mild and transient.
[2]In most cases these signs are 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 also section “Contact details” of the package leaflet.

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 dogs intended for breeding.

Pregnancy and lactation:
The use in these animals is not recommended.

Fertility:
The use in breeding animals is not recommended.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

Macrocyclic lactones including moxidectin have been shown to be substrates for p-glycoprotein. Therefore, during treatment with the veterinary medicinal product, other products that can inhibit p-glycoprotein (e.g. cyclosporine, ketoconazole, spinosad, verapamil) should only be used concomitantly according to the benefit-risk assessment of the responsible veterinarian.

4.9 Amount(s) to be administered and administration route

Oral use.

Dose
The veterinary medicinal product should be administered at a dose of 1.2–2.4 mg/kg of sarolaner, 0.024–0.048 mg/kg of moxidectin and 5–10 mg/kg of pyrantel in accordance with the following table:

Bodyweight (kg)	Tablet strength 3 mg/0.06 mg/12.5 mg
1.25–2.5 kg	1

To ensure a correct dosage, bodyweight should be determined as accurately as possible.

Method of administration
Tablets can be administered with or without food.

Simparica Trio tablets are palatable and readily consumed by the majority of dogs when offered by the owner. If the tablet is not taken up voluntarily by the dog it can also be given with food or directly into the mouth. The tablets should not be divided.

Treatment schedule:
The treatment schedule should be based on veterinary diagnosis, the local epidemiological situation and/or the epidemiological situation of other areas the dog has visited or is going to visit. If based on veterinarian opinion re-administration(s) of the product is required, any subsequent administration(s) must follow the minimum 1-month interval schedule.

The product should only be used in dogs when treatment of ticks / fleas / mites and gastrointestinal nematodes is indicated at the same time. In the absence of the risk of mixed co-infestation, a narrower spectrum parasiticide should be used.

Treatment of flea and tick infestations and gastrointestinal nematodes:
The veterinary medicinal product can be used as part of the seasonal treatment of fleas and ticks (replacing treatment with a mono-active flea and tick product) in dogs with diagnosed concurrent gastrointestinal nematode infections. A single treatment is efficacious for the treatment of gastrointestinal nematodes. After treatment of the nematode infections, further flea and tick treatment should be continued with a mono-active product.

Prevention of heartworm disease and angiostrongylosis:
A single administration also prevents lungworm disease (by reducing the immature adults (L5) of *A. vasorum*) and heartworm disease (*D. immitis*) for one month. When the product replaces another lungworm or heartworm preventive product, the first dose of the product should be given within a month of the last dose of the former veterinary medicinal product. In endemic areas, dogs should receive lungworm and/or heartworm preventive treatments at monthly intervals. It is recommended that heartworm prevention treatment should be continued until at least 1 month after the last exposure to mosquitoes.

Prevention of establishment of thelaziosis (adult Thelazia callipaeda eyeworm infection):
Monthly administration of the product prevents establishment of infection with adult *Thelazia callipaeda* eyeworm.

Treatment of demodicosis (caused by Demodex canis):
Administration of a single dose once monthly for two consecutive months is efficacious and leads to a marked improvement of clinical signs. Treatment should be continued until skin scrapings are negative on at least two consecutive occasions one month apart. As demodicosis is a multifactorial disease, it is advisable to also treat any contributing, underlying conditions appropriately.

Treatment of sarcoptic mange (caused by Sarcoptes scabiei var. canis):
Administration of a single dose at monthly intervals for two consecutive months. Further monthly administrations of the product may be required based on clinical assessment and skin scrapings.

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

No adverse reactions were observed in 8-weeks old healthy puppies administered with up to 5 times the maximum recommended dose for 7 consecutive monthly administrations.

In a laboratory study, the product was well tolerated in dogs with a deficient multidrug-resistance-protein 1 (MDR1 -/-) following single oral administration at 3 times the recommended dose. After a single administration of 5 times the maximum recommended dose to this sensitive dog breed, transient ataxia and/or muscle fasciculation were observed.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antiparasitic products, moxidectin combinations.

ATC Vet Code: QP54AB52.

5.1 Pharmacodynamic properties

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. Sarolaner binding to these receptors 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 felis* and *Ctenocephalides canis*), several tick species such as *Dermacentor reticulatus, Ixodes hexagonus, Ixodes ricinus* and *Rhipicephalus sanguineus*, as well as the mites *Demodex canis* and *Sarcoptes scabei* var. *canis*.

Ticks on the animal prior to administration or from new infestations after product administration are killed within 48 hours. For the species *I. ricinus*, this onset of efficacy is within 24 hours, during the 35-day period after product administration.

For fleas, the onset of efficacy is within 12 to 24 hours of attachment for five weeks after product administration. Fleas on the animal prior to administration are killed within 8 hours. The veterinary medicinal product kills newly emerged fleas on the dog before they can lay eggs and therefore it prevents environmental flea contamination in areas to which the dog has access.

Moxidectin is a second-generation macrocyclic lactone of the milbemycin family. Its principal mode of action is interfering with neuromuscular transmission at the level of the glutamate-gated chloride channels and, to a lesser extent, of GABA (gamma amino butyric acid)-gated channels. This interference leads to the opening of the chloride channels on the postsynaptic junction to allow the inflow of chloride ions. This results in flaccid paralysis and eventual death of parasites exposed to the drug. Moxidectin is active against adults of *Toxocara canis*, L4 larvae and immature stages (L5) of *Ancylostoma caninum*, L4 of *Dirofilaria immitis*, immature stages (L5) of *Angiostrongylus vasorum* and *Thelazia callipaeda.*

Pyrantel is a nicotinic acetylcholine (ACh) channel receptor (nAChR) agonist. Pyrantel mimics the agonist effects of ACh through high affinity binding to

subtype specific ionophoric nAChRs in nematodes, while not binding at muscarinic mAChRs. Following receptor binding, the channel opens to allow the influx of cations resulting in a depolarization and excitatory effects on nematode muscle, ultimately leading to spastic paralysis of the worm and death. Pyrantel is active against immature stages (L5) and adults of *Toxocara canis*, adults of *Ancylostoma caninum*, *Toxascaris leonina* and *Uncinaria stenocephala*.

In this fixed combination, moxidectin and pyrantel provide complementary anthelmintic efficacy through distinct mechanisms of action. In particular, both active substances contribute to the overall efficacy against the gastrointestinal nematodes *Ancylostoma caninum* and *Toxocara canis.*

5.2 Pharmacokinetic particulars

Sarolaner is readily and rapidly absorbed systemically following oral dosing, reaching maximum concentrations in plasma within 3.5 hours (t_{max}) after administration with a high bioavailability of 86.7%. Sarolaner is slowly eliminated from plasma (half-life of approximately 12 days) via biliary excretion and elimination through the faeces with minor contributions of metabolic clearance.

Moxidectin is readily and rapidly absorbed systemically following oral dosing, reaching maximum concentrations in plasma within 2.4 hours (t_{max}) after administration and with 66.9% bioavailability. Moxidectin is slowly eliminated from plasma (half-life of approximately 11 days) via biliary excretion and elimination through the faeces with minor contributions of metabolic clearance.

Pyrantel embonate is poorly absorbed and the absorbed portion has a t_{max} of 1.5 hours and half-life of 7.7 hours. Pyrantel is eliminated through faeces and the small absorbed portion is eliminated mainly via urine.

The prandial state of the dogs does not affect the extent of absorption of sarolaner and moxidectin.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hypromellose
Lactose monohydrate
Sodium starch glycolate type A
Meglumine
Butylhydroxytoluene (E321)
Pigment blend 018 (E110, E129, E132)
Hydroxypropylcellulose
Silica, colloidal anhydrous
Magnesium stearate
Maize starch
Confectioner’s sugar
Glucose, liquid
Pork liver powder
Hydrolysed vegetable protein
Gelatin

Wheat germ
Calcium hydrogen phosphate anhydrous

6.2 Major Incompatibilities

Not applicable.

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.

6.5 Nature and composition of immediate packaging

The tablets are packaged in aluminium foil/foil blisters packaged into an outer carton box.
Each tablet strength is available in pack sizes of 1, 3 or 6 tablets.

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

Medicines should not be disposed of via wastewater.
Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER

Vm 42058/5059

9. DATE OF FIRST AUTHORISATION

17 September 2019

10. DATE OF REVISION OF THE TEXT

June 2023

PROHIBITION OF SALE, SUPPLY AND/OR USE

11. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Approved 01 February 2024