Name and Strength of Active Substance(s):

Each SIMPARICA CHEWABLE TABLETS FOR DOGS 5MG contains Sarolaner 5mg.

Each SIMPARICA CHEWABLE TABLETS FOR DOGS 10MG contains Sarolaner 10mg.

Each SIMPARICA CHEWABLE TABLETS FOR DOGS 20MG contains Sarolaner 20mg.

Each SIMPARICA CHEWABLE TABLETS FOR DOGS 40MG contains Sarolaner 40mg.

Each SIMPARICA CHEWABLE TABLETS FOR DOGS 80MG contains Sarolaner 80mg.

Each SIMPARICA CHEWABLE TABLETS FOR DOGS 120MG contains Sarolaner 120mg.

Product Description:

5mg: Mottled brown colored, square shaped tablet with rounded edges, tablet is debossed “5” on one face of the tablet

10 mg: Mottled brown colored, square shaped tablet with rounded edges, tablet is debossed “10” on one face of the tablet

20 mg: Mottled brown colored, square shaped tablet with rounded edges, tablet is debossed “20” on one face of the tablet

40 mg: Mottled brown colored, square shaped tablet with rounded edges, tablet is debossed “40” on one face of the tablet

80 mg: Mottled brown colored, square shaped tablet with rounded edges, tablet is debossed “80” on one face of the tablet

120 mg: Mottled brown colored, square shaped tablet with rounded edges, tablet is debossed “120” on one face of the tablet

Pharmacodynamics:

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 felis* and *Ctenocephalides canis*) as well as several tick species such as *Dermacentor reticulatus, Ixodes hexagonus, Ixodes ricinus, Rhipicephalus sanguineus* and the mites *Demodex canis, Otodectes cynotis* and *Sarcoptes scabiei*.

For fleas, the onset of efficacy is within 8 hours of attachment during the 28 day period after product administration. For ticks (*I. ricinus*), the onset of efficacy is within 12 hours of attachment during the 28 day period after product administration. Ticks on the animal prior to administration are killed within 24 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.

Pharmacokinetics:
The bioavailability of sarolaner following oral dosing was high at >85%. Sarolaner was dose proportional in Beagle dogs when dosed from the intended use dose of 2–4 mg/kg, to 20 mg/kg. The prandial state of the dog does not significantly affect the extent of its absorption.

Sarolaner was determined to have low clearance (0.12 ml/min/kg) and a moderate volume of distribution (2.81 l/kg). Half-life was comparable for the intravenous and oral routes at 12 and 11 days, respectively. Plasma protein binding was determined in vitro and calculated at ≥99.9%.

A distribution study determined that ^{14}C-sarolaner-related residues were widely distributed to the tissues. The depletion from tissues was consistent with the plasma half-life.
The primary route of elimination is biliary excretion of parent molecule, with elimination through the faeces.

Indications:
For the treatment of tick infestations (*Dermacentor reticulatus, Ixodes hexagonus, Ixodes ricinus* and *Rhipicephalus sanguineus*). The veterinary medicinal product has immediate and persistent tick killing activity for at least 5 weeks.

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 at least 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 *(Sarcoptes scabiei).*
For the treatment of ear mite infestations *(Otodectes cynotis).*
For the treatment of demodicosis *(Demodex canis).*
Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance.
For use in puppies from 8 weeks of age and weighing 1.3kg or more.

Target Species:

Dogs

Recommended Dose:

For oral use. Tablets can be administered with or without food.

The veterinary medicinal product should be administered at a dose of 2–4 mg/kg bodyweight in accordance with the following table:

Dosing Chart:

Dogs Weight (kg)	Tablet Strength (mg)	Number of tablets to be administered
1.3 - 2.5	5	One
> 2.5 - 5	10	One
> 5 - 10	20	One
> 10 – 20	40	One
> 20 – 40	80	One
> 40 – 60	120	One

> 60	Appropriate combination of tablets

Use appropriate combination of available strengths to achieve the recommended dose of 2–4 mg/kg.
Simparica tablets are chewable and palatable and readily consumed by 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:
For optimal control of tick and fleas infestations, the veterinary medicinal product should be administered at monthly intervals and continue throughout the flea and/or tick season based on local epidemiological situations.

For the treatment of ear mite infestations (*Otodectes cynotis*) a single dose should be administered. A further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment.

For the treatment of sarcoptic mange (caused by *Sarcoptes scabiei* var. *canis*) a single dose should be administered at monthly intervals for two consecutive months.

For the treatment of demodicosis (caused by *Demodex canis*) the administration of a single dose once monthly for three 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 multi-factorial disease, it is advisable to also treat any underlying disease appropriately.

Contraindications:

Do not use in case of hypersensitivity to the active substance or to any of the excipients.

Warnings & Precautions:

Special Warnings:
Parasites need to start feeding on the host to become exposed to sarolaner; therefore, the transmission of infectious parasite-borne diseases cannot be excluded.

Precautions:
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 1.3 kg bodyweight should be based on a benefit-risk assessment by the responsible veterinarian.

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 label to the physician.

For Animal Use Only.
Controlled Medicine / Ubat Terkawal
Keep out of reach of children / Jauhi dari kanak-kanak.

Interactions with Other Medicaments:
None known.

During clinical field trials, no interactions between Simparica chewable tablets for dogs and routinely used

veterinary medicinal products were observed.

In laboratory safety studies, no interactions were observed when sarolaner was co-administered with milbemycin oxime, moxidectin and pyrantel pamoate. (In these studies efficacy was not investigated).

Sarolaner is highly bound to plasma proteins and might compete with other highly bound drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) and the cumarin derivative warfarin.

Pregnancy and Lactation:

The safety of the veterinary medicinal product has not been established during pregnancy and lactation or in animals intended for breeding. Laboratory studies in rats and rabbits have not produced any evidence of any teratogenic effects. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

Side Effects:

Mild and transient gastrointestinal signs such as vomiting and diarrhoea, and systemic disorders such as lethargy, anorexia/inappetence may occur in very rare cases based on post marketing safety experience. These signs typically resolve without treatment. Neurological disorders such as tremor, ataxia or convulsion may occur in very rare cases 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).

Overdose:

In a margin of safety study, the veterinary medicinal product was administered orally to 8 week old Beagle puppies at doses of 0, 1, 3, and 5 times the maximum exposure dose of 4 mg/kg at 28 day intervals for 10 doses. No adverse effects were observed at the maximum exposure dose of 4 mg/kg. In the overdose groups, transient and self-limiting neurological signs were observed in some animals: mild tremors at 3 times the maximum exposure dose and convulsions at 5 times the maximum exposure dose. All dogs recovered without treatment.

Sarolaner is well tolerated in Collies with a deficient multidrug-resistance-protein 1 (MDR1 -/-) following single oral administration at 5 times the recommended dose. No treatment-related clinical signs were observed.

Storage Condition: Store below 30°C.

Shelf Life (as packaged for sale): 3 years.

Pack Size:

Alu-alu blister package (aluminium foil/foil blister package).

3 tablets in one blister card. Each carton contains one blister of 3 tablets.

Disposal: The material should be disposed in compliance with national and regional requirements.

Manufactured by:
Zoetis Inc
601 West Cornhusker Highway, Lincoln, Nebraska 68521, United States

Product Registration Holder:
Zoetis Malaysia Sdn bhd
Lot 3.1, Level 3, Tower 7, Avenue 3, Bangsar South,
No 8 Jalan Kerinchi, 59200 Kuala Lumpur, Malaysia

Date of Revision: 2 June 2021