FOR ANIMAL USE ONLY

SIMPARICA 5 mg/ 10 mg/ 20 mg/ 40 mg/ 80 mg/ 120 mg (chewable tablets for dogs)
5 mg: Reg. No. G4317 Act 36/1947
10 mg: Reg. No. G4322 Act 36/1947
20 mg: Reg. No. G4318 Act 36/1947
40 mg: Reg. No. G4319 Act 36/1947
80 mg: Reg. No. G4320 Act 36/1947
120 mg: Reg. No. G4321 Act 36/1947

INDICATIONS FOR USE:

For the treatment of tick infestations on dogs.

The product has immediate and persistent tick killing activity for at least 5 weeks.

For the treatment and prevention of flea infestations on dogs. The product has immediate and persistent flea killing activity against new infestations for 5 weeks. The product may be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD). **Consult your veterinarian.**

The product kills fleas before they can lay eggs.

Fleas and ticks must attach to the host and commence feeding to be exposed to the active substance. For fleas, the onset of effect is within 8 hours of attachment. For ticks, the onset of effect is within 12 hours of attachment.

COMPOSITION:

Active substance: Sarolaner 5 mg; 10 mg; 20 mg; 40 mg; 80 mg and 120 mg per chewable tablet.

Mottled brown coloured, square shaped chewable tablets with rounded edges.

The number embossed on one side refers to the different strengths (mg) of the tablets: "5", "10","20", "40", "80" or "120".

STORAGE:

Store at or below 30 °C in a cool, dry place.

WARNINGS:

Do not treat puppies less than 8 weeks of age and/or dogs weighing less than 1,3 kg.
Do not treat pregnant and lactating dogs.
IMPORTANT: Consult your veterinarian as the safety of this product has not been established during pregnancy and lactation. Use only as directed by your veterinarian according to a benefit/risk assessment by the responsible veterinarian.
Only one chewable tablet at a time should be removed from the blister to prevent children from accessing the product. The blister should be returned into the carton and kept out of reach of children, uninformed persons and animals.
Although this remedy has been extensively tested under a large variety of conditions, failure thereof may ensue because of a wide range of reasons. If this is suspected, seek veterinary advice and notify the registration holder.

PRECAUTIONS:

Wash hands after handling the product.
Dispose of any containers, disposable equipment and any other waste after use in accordance with National Environmental Management: Waste Act, 2008 (Act No. 59 of 2008).

Interaction with other medicinal products and other forms of interaction None known. Consult your veterinarian if you intend dosing SIMPARICA with other medications.

DIRECTIONS FOR USE:

Use only as directed
For oral use.

SIMPARICA is a chewable and palatable tablet 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.

Tablets can be administered with or without food.

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

Body weight (kg)	Tablet strength (mg sarolaner)	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
> 60.0	Appropriate combination of tablets	

If not all strengths are marketed, use appropriate combination of available strengths to achieve the recommended dose 2–4 mg/kg.

Treatment schedule:

For optimal control of tick and flea infestations, the product should be administered at monthly intervals. Treatment with SIMPARICA chewable tablets may begin at any time of the year and based on local epidemiological situations should continue without interruption in areas where fleas and ticks are common year-round.

NOTES FOR VETERINARIAN: PHARMACOLOGICAL PROPERTIES

Pharmacodynamic profile

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 and Glutamate). 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. The increased potency for insect/acarine receptors results in enhanced selectivity in targeting insects/acarines while increasing the margin of safety for people and animals. Sarolaner is structurally unique and does not interact with known insecticidal binding sites of nicotinic or other GABAnergic insecticides such as neonicotinoids, fiproles, milbemycins, avermectins, and cyclodienes. In addition to the"INDICATIONS FOR USE" an activity against *Haemaphysalis longicornis* has been demonstrated.

Sarolaner starts killing fleas 3 hours after administration; adequate treatment effect is achieved within 8 hours. Sarolaner starts killing ticks 8 hours after administration; adequate treatment effect is achieved within 12 hours (24 hours for ticks on the animal prior to administration). The product kills fleas before they can lay eggs and therefore it prevents environmental flea contamination in

areas to which the dog has access.

Pharmacokinetic particulars

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 11 and 12 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.

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.

SIMPARICA is well tolerated in dogs when co-administered with macrocyclic lactones.

List of excipients:

Lactose monohydrate

Sodium starch glycolate

Colloidal silicon dioxide

Magnesium stearate

Maize starch
Sucrose
Spray dried pork liver powder
Gelatin type A
Wheat germ
Calcium hydrogen phosphate anhydrous
Corn syrup

Shelf-life

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

For the treatment of tick infestations on dogs.

The product has immediate and persistent tick killing activity for 5 weeks. For the treatment and prevention of flea infestations on dogs.

The product has immediate and persistent flea killing activity against new infestations for 5 weeks.

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

Consult your veterinarian.

The product kills fleas before they can lay eggs.

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance. For fleas, the onset of effect is within 8 hours of attachment. For ticks the onset of effect is within 12 hours of attachment.

PACKAGING:
Mottled brown coloured, square shaped chewable tablets with rounded edges.

The number embossed on one side refers to the different strengths (mg) of the tablets: “5”, “10”,”20”, “40”, “80” or “120”.

Aluminium-aluminium cold form blister package. Blister card presentations of 1, 3 or 6 tablets, in a card board carton. Package insert included in carton.

Not all pack sizes may be marketed.

REGISTRATION HOLDER:
Zoetis South Africa (Pty) Ltd

Co. Reg. No. 2012/001825/07

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