# ANNEX I

# SUMMARY OF PRODUCT CHARACTERISTICS

# SIMPARICA™ (sarolaner) CHEWABLE TABLETS

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Simparica 5 mg chewable tablets for dogs 1.3–2.5 kg
Simparica 10 mg chewable tablets for dogs >2.5–5 kg
Simparica 20 mg chewable tablets for dogs >5–10 kg
Simparica 40 mg chewable tablets for dogs >10–20 kg
Simparica 80 mg chewable tablets for dogs >20–40 kg
Simparica 120 mg chewable tablets for dogs >40–60 kg

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

**Active substance:**

| Simparica chewable tablets | sarolaner (mg) |
|---|---|
| for dogs 1.3–2.5 kg | 5 |
| for dogs >2.5–5 kg | 10 |
| for dogs >5–10 kg | 20 |
| for dogs >10–20 kg | 40 |
| for dogs >20–40 kg | 80 |
| for dogs >40–60 kg | 120 |

**Excipients:**
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

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

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

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Dogs

### 4.2 Indications for use, specifying the target species

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*).

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance.

## 4.3 Contraindications

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

## 4.4 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.

## 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 1.3 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.

## 4.6 Adverse reactions (frequency and seriousness)

None known.

## 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. 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.

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

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.

## 4.9 Amounts to be administered and administration route

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:

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

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

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.

## 4.11 Withdrawal period(s)

Not applicable.

# 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Ectoparasiticides for systemic use.

ATC vet code: QP53BX06.

### 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. 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 mite *Sarcoptes scabiei*. In addition, in laboratory studies, sarolaner was shown to be active against other tick species such as *Dermacentor variabilis, Ixodes scapularis, Amblyomma americanum, Amblyomma maculatum* as well as the mite species *Demodex canis* and *Otodectes cynotis*.

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.

### 5.2 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 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.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Hypromellose acetate succinate, medium grade
Lactose monohydrate
Sodium starch glycolate
Silica, colloidal anhydrous
Magnesium stearate
Maize starch
Confectioner's sugar

Glucose, liquid (81.5% solids)
Spray dried pork liver powder
Hydrolysed vegetable protein
Gelatin type A
Wheat germ
Calcium hydrogen phosphate anhydrous

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

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

### 6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

### 6.5 Nature and composition of immediate packaging

Aluminium foil/foil blister package.
One carton contains one blister 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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

## 8. MARKETING AUTHORISATION NUMBER(S)

EU/2/15/191/001-018

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

## 10 DATE OF REVISION OF THE TEXT

{MM/YYYY}

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.emea.europa.eu/).

**PROHIBITION OF SALE, SUPPLY AND/OR USE**

Not applicable.