

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Simparica 10 mg Veterinary chewable tablets
Simparica 20 mg Veterinary chewable tablets
Simparica 40 mg Veterinary chewable tablets
Simparica 80 mg Veterinary chewable tablets
Simparica 120 mg Veterinary chewable tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

Simparica chewable tablets	sarolaner (mg)
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: “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*).

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.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

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 2.5 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)

In very rare cases (less than 1 animal in 10,000 animals treated, including isolated reports) adverse reactions associated with mild and transient gastrointestinal effects such as vomiting and diarrhoea may occur. In very rare cases transient neurological disorders such as tremor, ataxia or convulsion may occur. These signs typically resolve without treatment.

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form (<http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.health.gov.il>).

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 coumarin 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
>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.

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: QP53BE03.

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 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.

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 $\geq 99.9\%$.

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

Wheat germ
Spray dried pork liver powder
Hydroxypropyl methyl cellulose acetate succinate
Corn Syrup (81.5% solids)
Sodium starch glycolate
Calcium phosphate dibasic anhydrous
Lactose monohydrate
Confectioner's sugar
Gelatin type A
Colloidal Silicon Dioxide
Magnesium stearate
Corn starch
Hydrolysed vegetable protein

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials. The expiry date refers to the last day of that month.

6.4. Special precautions for storage

Store below 30°C.

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 Israel Holding B.V. 5 Atir Yeda Street, Kfar Saba, Israel

8. MARKETING AUTHORISATION NUMBER

Simparica 10 mg Veterinary chewable tablets: 161-30-35031-00/01
 Simparica 20 mg Veterinary chewable tablets: 161-31-35032-00/01
 Simparica 40 mg Veterinary chewable tablets: 161-32-35033-00/01
 Simparica 80 mg Veterinary chewable tablets: 161-33-35034-00/01
 Simparica 120 mg Veterinary chewable tablets: 161-34-35035-00/01

9. MANUFACTURER

Zoetis LLC (Subsidiary of Zoetis Inc.), 601 West Cornhusker Highway, Lincoln, NE 68521, USA

10. DATE OF REVISION OF THE TEXT

Date: December 2018

הערות	אסמכתא לעדכון	פרקים שהתעדכנו	תאריך עדכון העלון
הכנת עלון לרופא במסגרת רישום תכשיר חדש	EMA SPC 08.12.2017	N/A	20.12.17

נבדק ע"י דניז
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