



Simparica[®]

(sarolaner) Chewables

Monthly tick and flea protection for dogs that keeps going strong for 35 days.¹



Features/Functions:

Ticks: Simparica starts killing ticks in 8 hours,² reducing the likelihood of transmission of tick-borne pathogens.³ In a clinical study, Simparica was shown to block the transmission of Lyme Disease and Anaplasmosis from deer ticks to dogs.⁴

Fleas: Simparica starts killing fleas in 3 hours to provide rapid relief for pets with fleas— even dogs with flea allergic dermatitis (FAD). Simparica kills fleas before the reproductive breakpoint, meaning before they lay eggs. Simparica effectively protects pets and homes from infestations for 35 days.

Benefit:

Quick kill provides patient comfort and can protect against flea infestations and tick-borne diseases.

Features/Functions:

Simparica's monthly dosing makes it easy for clients to stick with a routine. Plus, if they dose a few days late, it's okay, Simparica continues to kill fleas and ticks for up to 35 days.¹ So you can rest assured you're not leaving your patients with risky gaps in protection.

Benefit:

Peak efficacy lasts for a full 35 days leaving no risky gaps.

Features/Functions:

Simparica will help practices compete against over-the-counter (OTC) brands and bring tick and flea protection back into the practice. Even if practices apply a 75% to 100% mark-up, clients may still pay less per dose for Simparica (after rewards program) than they do if they purchase Frontline[®] Plus online or at a low-cost retailer. Dispensing tick and flea protection to clients improves the economic health of practices and provides clients with a premium product at an affordable price.

Benefit:

Premium product without the premium price tag.

IMPORTANT SAFETY INFORMATION: Simparica is for use only in dogs, 6 months of age and older. Simparica may cause abnormal neurologic signs such as tremors, decreased conscious proprioception, ataxia, decreased or absent menace, and/or seizures. Simparica has not been evaluated in dogs that are pregnant, breeding or lactating. Simparica has been safely used in dogs treated with commonly prescribed vaccines, parasiticides and other medications. The most frequently reported adverse reactions were vomiting and diarrhea. See full Prescribing Information on page 87 and at ZoetisUS.com/Simparica.

1. Six RH, Everett WR, Young DR, et al. Efficacy of a novel oral formulation of sarolaner (Simparica[™]) against five common tick species infesting dogs in the United States. *Vet Parasitol.* 2016;222:28-32.
2. Six RH, Geurden T, et al. Evaluation of the speed of kill of sarolaner (Simparica[™]) against induced infestations of three species of ticks (*Amblyomma maculatum*, *Ixodes scapularis*, *Ixodes ricinus*) on dogs. *Veterinary Parasitology* 2016 May 30(222):37-42.
3. Little SE. Changing paradigms in understanding transmission of canine tick-borne disease: the role of interrupted feeding and intrastadial transmission. *Proceedings of the 2nd Canine Vector-Borne Disease (CVBD) Symposium.* April 25-28, 2007. Mazaro del Vallo, Sicily, Italy.
4. Honsberger NA, Six RH, Heinz TJ, Weber A, Mahabir SP, Berg TC. Efficacy of sarolaner in the prevention of *Borrelia burgdorferi* and *Anaplasma phagocytophilum* transmission from infected *Ixodes scapularis* to dogs. *Vet Parasitol.* 2016;222:67-72.

Sound Byte

ZoetisUS.com/Simparica

1-888-Zoetis1

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SATISFACTION GUARANTEE:

If you or your clients feel that Simparica (sarolaner) isn't providing sufficient tick and flea protection or if your client suspects that the dog may have Lyme disease, they can call our medical support team to discuss the Simparica Satisfaction Guarantee. Zoetis will work with them to ensure they are satisfied with the performance of Simparica, or refund the cost of the product.

- The Simparica Satisfaction Guarantee is available to any veterinarian or pet owner who has purchased Simparica from a veterinarian or via a veterinarian's prescription from a Zoetis-approved online distributor.



TICK COVERAGE



FLEA COVERAGE



LYME COVERAGE

*Zoetis will cover reasonable diagnostic and treatment cost for suspected cases of canine Lyme Disease, for qualified patients. For more details, contact Veterinary Medical Information and Product Support at 1-888-Zoetis1

A SIZE FOR EVERY DOG BREED

From pocket pet to mastiff, Simparica has a size for all patients, starting with dogs as small as 2.8 lbs.

**BODY
WEIGHT**

2.8-5.5 lb

>5.6-11.0 lb

>11.1-22.0 lb

>22.1-44.0 lb

>44.1-88.0 lb

>88.1-132.0 lb

DOSE:

1

TABLET
FOR EACH
BODY
WEIGHT
CATEGORY



Sound CHECK-OFF & ECHO NOTES Byte

Start an Effective Team to Pet Owner Conversation

If engaging in an initial discussion, start with:

Ms. Jones, Spot, like all dogs, should be on year-round tick and flea protection.

State the Solution

Simparica provides premium monthly tick and flea protection without the premium price tag that also gives wiggle room at the end of the month.

Make Your Recommendation

Ms. Jones, I believe Simparica will provide the tick and flea protection Spot needs but at a lower price than other brands offering this kind of protection. Do you want to give it a try?



FOR ORAL USE IN DOGS ONLY

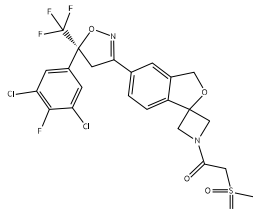
CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description:

SIMPARICA is a flavored, chewable tablet for administration to dogs over 6 months of age according to their weight. Each tablet is formulated to provide a minimum sarolaner dosage of 0.91 mg/lb (2 mg/kg) body weight.

Sarolaner is a member of the isoxazoline class of parasiticides and the chemical name is 1-(5'-((5S)-5-(3,5-Dichloro-4-fluorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-3'-H-spiro(azetidine-3,1'-(2)benzofuran)-1-yl)-2-(methylsulfonyl)ethanone. SIMPARICA contains the S-enantiomer of sarolaner.

The chemical structure of the S-enantiomer of sarolaner is:



Indications:

SIMPARICA kills adult fleas, and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*), and the treatment and control of tick infestations [*Amblyomma americanum* (lone star tick), *Amblyomma maculatum* (Gulf Coast tick), *Dermacentor variabilis* (American dog tick), *Ixodes scapularis* (black-legged tick), and *Rhipicephalus sanguineus* (brown dog tick)] for one month in dogs 6 months of age or older and weighing 2.8 pounds or greater.

Dosage and Administration:

SIMPARICA is given orally once a month at the recommended minimum dosage of 0.91 mg/lb (2 mg/kg).

Dosage Schedule:

Body Weight	SAROLANER per Tablet (mg)	Number of Tablets Administered
2.8 to 5.5 lbs	5	One
5.6 to 11.0 lbs	10	One
11.1 to 22.0 lbs	20	One
22.1 to 44.0 lbs	40	One
44.1 to 88.0 lbs	80	One
88.1 to 132.0 lbs	120	One
>132.1 lbs	Administer the appropriate combination of tablets	

SIMPARICA can be offered by hand, in the food, or administered like other tablet medications.

Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes to ensure that part of the dose is not lost or refused. If a dose is missed, administer SIMPARICA and resume a monthly dosing schedule.

SIMPARICA should be administered at monthly intervals.

Flea Treatment and Prevention:

Treatment with SIMPARICA may begin at any time of the year. In areas where fleas are common year-round, monthly treatment with SIMPARICA can continue the entire year without interruption.

To minimize the likelihood of flea re-infestation, it is important to treat all dogs and cats within a household with an approved flea control product.

Tick Treatment and Control:

Treatment with SIMPARICA can begin at any time of the year (see **Effectiveness**).

Contraindications:

There are no known contraindications for the use of SIMPARICA.

Warnings:

Not for use in humans. Keep this and all drugs out of reach of children and pets. For use in dogs only. Do not use SIMPARICA in cats.

SIMPARICA should not be used in dogs less than 6 months of age (see **Animal Safety**).

Precautions:

SIMPARICA may cause abnormal neurologic signs such as tremors, decreased conscious proprioception, ataxia, decreased or absent menace, and/or seizures (see **Animal Safety**).

The safe use of SIMPARICA has not been evaluated in breeding, pregnant, or lactating dogs.

Adverse Reactions:

SIMPARICA was administered in a well-controlled US field study, which included a total of 479 dogs (315 dogs treated with SIMPARICA and 164 dogs treated with active control once monthly for three treatments).

Over the 90-day study period, all observations of potential adverse reactions were recorded.

Table 1. Dogs with adverse reactions

Adverse reaction	sarolaner	sarolaner	active control	active control
	N	% (n = 315)	N	% (n = 164)
Vomiting	3	0.95%	9	5.50%
Diarrhea	2	0.63%	2	1.20%
Lethargy	1	0.32%	2	1.20%
Inappetence	0	0%	3	1.80%

Additionally, one female dog aged 8.6 years exhibited lethargy, ataxia while posturing to eliminate, elevated third eyelids, and inappetence one day after receiving SIMPARICA concurrently with a heartworm preventative (ivermectin/pyrantel pamoate). The signs resolved one day later. After the day 14 visit, the owner elected to withdraw the dog from the study.

For a copy of the Safety Data Sheet (SDS) or to report adverse reactions call Zoetis Inc. at 1-888-963-8471. Additional information can be found at www.SIMPARICA.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

Clinical Pharmacology:

Sarolaner is rapidly and well absorbed following oral administration of SIMPARICA. In a study of 12 Beagle dogs the mean maximum plasma concentration (C_{max}) was 1100 ng/mL and the mean time to maximum concentration (T_{max}) occurred at 3 hours following a single oral dose of 2 mg/kg to fasted animals. The mean oral bioavailability was 86% and 107% in fasted and fed dogs, respectively. The mean oral $T_{1/2}$ values for fasted and fed animals was 10 and 12 days respectively.

Sarolaner is distributed widely; the mean volume of distribution (V_{dss}) was 2.81 L/kg bodyweight following a 2 mg/kg intravenous dose of sarolaner. Sarolaner is highly bound ($\geq 99.9\%$) to plasma proteins. The metabolism of sarolaner appears to be minimal in the dog. The primary route of sarolaner elimination from dogs is biliary excretion with elimination via the feces.

Following repeat administration of SIMPARICA once every 28 days for 10 doses to Beagle dogs at 1X, 3X, and 5X the maximum intended clinical dose of 4 mg/kg, steady-state plasma concentrations were reached after the 6th dose. Following treatment at 1X, 3X, and 5X the maximum intended clinical dose of 4 mg/kg, sarolaner systemic exposure was dose proportional over the range 1X to 5X.

Mode of Action:

The active substance of SIMPARICA, sarolaner, is an acaricide and insecticide belonging to the isoxazoline group. Sarolaner inhibits the function of the neurotransmitter gamma aminobutyric acid (GABA) receptor and glutamate receptor, and works at the neuromuscular junction in insects. This results in uncontrolled neuromuscular activity leading to death in insects or acarines.

Effectiveness:

In a well-controlled laboratory study, SIMPARICA began to kill fleas 3 hours after initial administration and reduced the number of live fleas by $\geq 96.2\%$ within 8 hours after flea infestation through Day 35.

In a separate well-controlled laboratory study, SIMPARICA demonstrated 100% effectiveness against adult fleas within 24 hours following treatment and maintained 100% effectiveness against weekly re-infestations for 35 days.

In a study to explore flea egg production and viability, SIMPARICA killed fleas before they could lay eggs for 35 days. In a study to simulate a flea-infested home environment, with flea infestations established prior to the start of treatment and re-infestations on Days 7, 37 and 67, SIMPARICA administered monthly for three months demonstrated $>95.6\%$ reduction in adult fleas within 14 days after treatment and reached 100% on Day 60.

In well-controlled laboratory studies, SIMPARICA demonstrated $\geq 99\%$ effectiveness against an initial infestation of *Amblyomma americanum*, *Amblyomma maculatum*, *Dermacentor variabilis*, *Ixodes scapularis*, and *Rhipicephalus sanguineus* 48 hours post-administration and maintained $>96\%$ effectiveness 48 hours post re-infestation for 30 days.

In a well-controlled 90-day US field study conducted in households with existing flea infestations of varying severity, the effectiveness of SIMPARICA against fleas on Day 30, 60 and 90 visits compared to baseline was 99.4%, 99.8%, and 100%, respectively. Dogs with signs of flea allergy dermatitis showed improvement in erythema, papules, scaling, alopecia, dermatitis/pyodermitis and pruritus as a direct result of eliminating fleas.

Animal Safety:

In a margin of safety study, SIMPARICA was administered orally to 8-week-old Beagle puppies at doses of 0, 1X, 3X, and 5X the maximum recommended dose (4 mg/kg) at 28-day intervals for 10 doses (8 dogs per group). The control group received placebo tablets. No neurologic signs were observed in the 1X group. In the 3X group, one male dog exhibited tremors and ataxia post-dose on Day 0; one female dog exhibited tremors on Days 1, 2, 3, and 5; and one female dog exhibited tremors on Day 1. In the 5X group, one female dog had a seizure on Day 61 (5 days after third dose); one female dog had tremors post-dose on Day 0 and abnormal head coordination after dosing on Day 140; and one female dog exhibited seizures associated with the second and fourth doses and tremors associated with the second and third doses. All dogs recovered without treatment. Except for the observation of abnormal head coordination in one dog in the 5X group two hours after dosing on Day 140 (dose 6). There were no treatment-related neurological signs observed once the dogs reached the age of 6 months.

In a separate exploratory pharmacokinetic study, one female dog dosed at 12 mg/kg (3X the maximum recommended dose) exhibited lethargy, anorexia, and multiple neurological signs including ataxia, tremors, disorientation, hypersalivation, diminished proprioception, and absent menace, approximately 2 days after a third monthly dose. The dog was not treated, and was ultimately euthanized. The first two doses resulted in plasma concentrations that were consistent with those of the other dogs in the treatment group. Starting at 7 hours after the third dose, there was a rapid 2.5 fold increase in plasma concentrations within 41 hours, resulting in a C_{max} more than 7-fold higher than the mean C_{max} at the maximum recommended use dose. No cause for the sudden increase in sarolaner plasma concentrations was identified.

Storage Information:

Store at or below 30°C (86°F) with excursions permitted up to 40°C (104°F).

How Supplied:

SIMPARICA (sarolaner) Chewables are available in six flavored tablet sizes: 5, 10, 20, 40, 80, and 120 mg. Each tablet size is available in color-coded packages of one, three, or six tablets.

NADA #141-452, Approved by FDA



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