

SimparicaTRIO.

(sarolaner, moxidectin, and pyrantel
chewable tablets)

Simparica Trio is the first chew with

TRIPLE PROTECTION

HEARTWORM DISEASE

TICKS* & FLEAS

ROUNDWORMS & HOOKWORMS†



[SimparicaTrio.com](https://www.SimparicaTrio.com)

PETCARE
Rewards



Just one Simparica Trio chew does the job of 2 or 3 products for effective protection all month long

Ask your veterinarian about Simparica Trio for its winning protection.

	Simparica TRIO <i>(sarolaner, moxidectin, and pyrantel chewable tablets)</i>	NexGard® PLUS <i>(afoxolaner, moxidectin and pyrantel)¹</i>	Heartgard® Plus <i>(ivermectin/pyrantel)²</i>	NexGard® <i>(afoxolaner)³</i>	Bravecto® <i>(fluralaner)⁴</i>	Interceptor® Plus <i>(milbemycin oxime/praziquantel)⁵</i>
Kills 5 types of TICKS	✓*	Only 4 types [†]		✓ ^s	✓ ^{ll}	
Prevents HEARTWORM disease	✓	✓	✓			✓
Kills FLEAS before they can lay eggs ¹	✓	✓		✓	✓	
Treats ROUNDWORMS ¹	✓	✓	✓			✓
Treats HOOKWORMS ¹	✓	✓	✓			✓
Prevents LYME infections [#]	✓			✓		
Minimum age	8 weeks	8 weeks	6 weeks	8 weeks	6 months	6 weeks
Appropriate for dogs as small as 2.8 lb	✓		✓			✓
How is it given?	1 chew once a month	1 chew once a month	1 chew once a month	1 chew once a month	1 chew every 12 weeks ^{ll}	1 chew once a month

Sign up for worry-free reminders to keep up your dog's winning protection



TRIPLE PROTECTION made simple



Studies to support FDA approval showed that **1 dose provided 100% protection against heartworm disease**



Did you know just 1 bite from an infected mosquito can lead to heartworm disease?

- The American Heartworm Society recommends you give your pet heartworm preventative 12 months a year due to heartworm disease diagnosis in all 50 states⁶
- When your dog travels or moves with you to areas where heartworm disease is common, it raises their risk of getting infected⁷

Monthly Simparica Trio kills **5 types of ticks,*** including deer ticks that can spread Lyme disease

PREVENTS
LYME
INFECTIONS⁷



Ticks pass on diseases that can make your dog sick—including Lyme disease, Rocky Mountain spotted fever, anaplasmosis, and ehrlichiosis⁸

- Simparica Trio[®] (sarolaner, moxidectin, and pyrantel chewable tablets) is the first combination product proven to prevent infections that may cause Lyme disease by killing deer ticks
- Some ticks are active all year long⁸
- Infections that cause Lyme disease can be transmitted in as little as 24 hours⁸

Monthly Simparica Trio **starts killing fleas fast¹ before they can lay eggs**



Fleas travel by jumping from 1 person or animal to another

- It only takes 1 “pregnant” flea to infest your dog and your home—they multiply fast!⁹
- Home flea infestations need several months of consistent treatment and patience
- For some dogs, flea bites can cause skin problems and hair loss that can make them miserable⁹

Monthly Simparica Trio gives proven protection from intestinal worms



Roundworms & hookworms can harm more than just your dog

- Puppies can be infected at birth, and adult dogs can pick up worm eggs or larvae in the environment^{10**}
- Hookworms are blood suckers that can cause great harm to puppies¹⁰
- Roundworms can cause severe vomiting, weight issues, and other symptoms in puppies¹⁰
- Dogs and other pets can be at risk when these worms contaminate the environment¹⁰

For winning protection: Simparica Trio

Our Satisfaction Guarantee

We want you to be completely satisfied with Simparica Trio® (sarolaner, moxidectin, and pyrantel chewable tablets). We'll work with you to make sure you're satisfied with the product's performance. If for any reason you're still not completely happy, we'll give you your money back.

Simply give us a call at 1-888-ZOETIS1 or visit [SimparicaTrio.com](https://www.SimparicaTrio.com) to learn more

IMPORTANT SAFETY INFORMATION: See full Prescribing Information in pocket or visit [SimparicaTrioPI.com](https://www.SimparicaTrioPI.com). Use with caution in dogs with a history of seizures. Simparica Trio contains sarolaner, a member of the isoxazoline class, which has been associated with neurologic adverse reactions including tremors, ataxia, and seizures in dogs with or without a history of neurologic disorders. The safe use of Simparica Trio has not been evaluated in breeding, pregnant, or lactating dogs. The most frequently reported adverse reactions in clinical trials were vomiting and diarrhea.

References: 1. NexGard® PLUS [package insert]. Duluth, GA: Boehringer Ingelheim Animal Health USA Inc; 2023. 2. Heartgard® Plus [package insert]. Duluth, GA: Boehringer Ingelheim Animal Health USA Inc; 2019. 3. NexGard® [package insert]. Duluth, GA: Boehringer Ingelheim Animal Health USA Inc; 2023. 4. Bravecto® [package insert]. Summit, NJ: Merck & Co; 2023. 5. Interceptor® Plus [package insert]. Greenfield, IN: Elanco; 2020. 6. American Heartworm Society. Current Canine Guidelines for the Prevention, Diagnosis, and Management of Heartworm (*Dirofilaria immitis*) Infection in Dogs. 2020. <https://www.heartwormsociety.org/veterinary-resources/american-heartworm-society-guidelines>. Accessed December 2, 2022. 7. Self SW, Pulaski CN, McMahan CS, Brown DA, Yabsley MJ, Gettings JR. Regional and local temporal trends in the prevalence of canine heartworm infection in the contiguous United States: 2012–2018. *Parasit Vectors*. 2019;12(1):380. 8. Companion Animal Parasite Council. Ticks. April 12, 2017. <https://capcvet.org/guidelines/ticks>. Accessed November 30, 2022. 9. Companion Animal Parasite Council. Fleas. September 19, 2017. <https://capcvet.org/guidelines/fleas>. Accessed November 30, 2022. 10. Companion Animal Parasite Council. Ascarid. September 12, 2022. <https://capcvet.org/guidelines/ascarid>. Accessed November 30, 2022.

*Lone Star tick (*Amblyomma americanum*), Gulf Coast tick (*Amblyomma maculatum*), American dog tick (*Dermacentor variabilis*), Black-legged tick (*Ixodes scapularis*), and Brown dog tick (*Rhipicephalus sanguineus*).
†For the treatment of roundworm (immature adult and adult *Toxocara canis* and adult *Toxascaris leonina*) and hookworm (L4, immature adult, and adult *Ancylostoma caninum* and adult *Uncinaria stenocephala*) infections.
‡Black-legged tick (*Ixodes scapularis*), American dog tick (*Dermacentor variabilis*), Lone Star tick (*Amblyomma americanum*), and Brown dog tick (*Rhipicephalus sanguineus*).
§Black-legged tick (*Ixodes scapularis*), American dog tick (*Dermacentor variabilis*), Lone Star tick (*Amblyomma americanum*), Brown dog tick (*Rhipicephalus sanguineus*), and Asian longhorned tick (*Haemaphysalis longicornis*).
||*Ixodes scapularis*, *Dermacentor variabilis*, *Rhipicephalus sanguineus*, and *Haemaphysalis longicornis* for 12 weeks. Bravecto is not effective against *Amblyomma americanum* beyond 8 weeks after dosing.
¶Simparica Trio starts killing deer ticks within 8 hours and starts killing fleas within 4 hours.
**As a direct result of killing deer ticks.
††In soil or animal feces.

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Simparica TRIO.

*(sarolaner, moxidectin, and pyrantel
chewable tablets)*

PETCARE
Rewards

**Earn Rewards with your
Simparica Trio® purchase**

How It Works



Purchase Simparica Trio, earn points



Redeem your points for Rewards



Spend your Rewards on vet care

Sign up at
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Zoetis Petcare Rewards program terms & conditions apply.

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Simparica TRIO[®]

(sarolaner, moxidectin, and pyrantel chewable tablets)

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 TRIO (sarolaner, moxidectin, and pyrantel chewable tablets) is a flavored, chewable tablet for administration to dogs 8 weeks of age and older. Each tablet is formulated to provide minimum dosages of 0.54 mg/lb (1.2 mg/kg) sarolaner, 0.011 mg/lb (24 µg/kg) moxidectin, and 2.27 mg/lb (5 mg/kg) pyrantel (as pamoate salt).

Sarolaner is a member of the isoxazoline class of parasitocides and the chemical name is 1-(5'-((S)-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 TRIO contains the S-enantiomer of sarolaner.

Moxidectin is a semi-synthetic methoxime derivative of nemadectin which is a fermentation product of *Streptomyces cyanogriseus* subspecies *nancyanogenus*. Moxidectin is a pentacyclic 16-membered lactone macrolide. The chemical name for moxidectin is (6R,23E,25S)-5-O-Demethyl-28-deoxy-25-[1E]-1,3-dimethyl-1-buten-1-yl]-6,28-epoxy-23-(methoxyimino)milbemycin B.

Pyrantel belongs to a family classified chemically as tetrahydropyrimidines and the chemical name is (E)-1,4,5,6-Tetrahydro-1-methyl-2-[2-(2-thienyl) vinyl] pyrimidine 4,4' methylenebis [3-hydroxy-2-naphthoate](1:1). It is a yellow, water-insoluble crystalline salt of the tetrahydropyrimidine base and pamoic acid containing 34.7% base activity.

INDICATIONS

SIMPARICA TRIO is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis* and for the treatment and control of roundworm (immature adult and adult *Toxocara canis* and adult *Toxascaris leonina*) and hookworm (L4, immature adult, and adult *Ancylostoma caninum* and adult *Uncinaria stenocephala*) infections. SIMPARICA TRIO kills adult fleas (*Ctenocephalides felis*) and is indicated for the treatment and prevention of flea infestations, and the treatment and control of tick infestations with *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 and puppies 8 weeks of age and older, and weighing 2.8 pounds or greater. SIMPARICA TRIO is indicated for the prevention of *Borrelia burgdorferi* infections as a direct result of killing *Ixodes scapularis* vector ticks.

DOSEAGE AND ADMINISTRATION

SIMPARICA TRIO is given orally once a month, at the recommended minimum dose of 0.54 mg/lb (1.2 mg/kg) sarolaner, 0.011 mg/lb (24 µg/kg) moxidectin, and 2.27 mg/lb (5 mg/kg) pyrantel (as pamoate salt).

Dosage Schedule

Body Weight (lbs)	Sarolaner per Tablet (mg)	Moxidectin per Tablet (mg)	Pyrantel per Tablet (mg)	Number of Tablets Administered
2.8 to 5.5	3	0.06	12.5	One
5.6 to 11.0	6	0.12	25	One
11.1 to 22.0	12	0.24	50	One
22.1 to 44.0	24	0.48	100	One
44.1 to 88.0	48	0.96	200	One
88.1 to 132.0	72	1.44	300	One
>132.0	Administer the appropriate combination of tablets			

SIMPARICA TRIO can be offered to the dog with or without food.

Care should be taken to ensure that the dog consumes the complete dose and that part of the dose is not lost or refused. If a dose is missed, give SIMPARICA TRIO immediately and resume monthly dosing.

Heartworm Prevention:

SIMPARICA TRIO should be administered at monthly intervals year-round or at least within one month of the animal's first seasonal exposure to mosquitoes and continuing until at least 1 month after the dog's last seasonal exposure. If a dose is missed, give SIMPARICA TRIO immediately and resume monthly dosing. When replacing a monthly heartworm preventive product, SIMPARICA TRIO should be given within one month of the last dose of the former medication.

Flea Treatment and Prevention:

Treatment with SIMPARICA TRIO may begin at any time of the year. SIMPARICA TRIO should be administered year-round at monthly intervals or started at least one month before fleas become active.

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

Tick Treatment and Control:

Treatment with SIMPARICA TRIO can begin at any time of the year. SIMPARICA TRIO should be administered year-round at monthly intervals or started at least one month before ticks become active.

Intestinal Nematode Treatment and Control:

For the treatment of roundworm (immature adult and adult *Toxocara canis* and adult *Toxascaris leonina*) and hookworm (L4, immature adult, and adult *Ancylostoma caninum* and adult *Uncinaria stenocephala*) infections, SIMPARICA TRIO should be administered once as a single dose. Monthly use of SIMPARICA TRIO will control any subsequent infections.

CONTRAINDICATIONS

There are no known contraindications for the use of SIMPARICA TRIO.

WARNINGS

Not for use in humans. Keep this and all drugs out of reach of children.

Keep SIMPARICA TRIO in a secure location out of reach of dogs, cats and other animals to prevent accidental ingestion or overdose.

PRECAUTIONS

Sarolaner, one of the ingredients in SIMPARICA TRIO, is a member of the isoxazoline class. This class has been associated with neurologic adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in dogs receiving isoxazoline class drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders.

Prior to administration of SIMPARICA TRIO, dogs should be tested for existing heartworm infections. Infected dogs should be treated with an antidiuretic to remove adult heartworms. SIMPARICA TRIO is not effective against adult *D. immitis*.

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

ADVERSE REACTIONS

In a field safety and effectiveness study, SIMPARICA TRIO was administered to dogs for the prevention of heartworm disease. The study included a total of 410 dogs treated once monthly for 11 treatments (272 treated with SIMPARICA TRIO and 138 treated with an active control). Over the 330-day study period, all observations of potential adverse reactions were recorded. The most frequent reactions reported in the SIMPARICA TRIO group are presented in the following table.

Table 1. Dogs with Adverse Reactions

Clinical Sign	SIMPARICA TRIO n = 272	Active Control n = 138
Vomiting	14.3%	10.9%
Diarrhea	13.2%	8.0%
Lethargy	8.5%	6.5%
Anorexia	5.1%	5.8%
Polyuria	3.7%	3.6%
Hyperactivity	2.2%	0.7%
Polydipsia	2.2%	2.9%

In a second field safety and effectiveness study, SIMPARICA TRIO was administered to 278 dogs with fleas. Adverse reactions in dogs treated with SIMPARICA TRIO included diarrhea.

In a third field safety and effectiveness study, SIMPARICA TRIO was administered to 120 dogs with roundworms. Adverse reactions in dogs treated with SIMPARICA TRIO included diarrhea and vomiting.

CONTACT INFORMATION

For a copy of the Safety Data Sheet or to report adverse reactions, call Zoetis Inc. at 1-888-963-8471. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae.

CLINICAL PHARMACOLOGY

Following oral administration of SIMPARICA TRIO in Beagle dogs (13 to 15 months of age at the time of initial dosing), sarolaner and moxidectin were rapidly and well-absorbed. Following a single oral dose of SIMPARICA TRIO (sarolaner dose of 1.2 mg/kg), the sarolaner mean maximum plasma concentration (C_{max}) was 523 ng/mL with a mean time to maximum concentration (T_{max}) of 3.5 hours and an absolute bioavailability of 88%. At a moxidectin dose of 0.024 mg/kg, the moxidectin mean C_{max} was 13.1 ng/mL with a mean T_{max} of 2.4 hours and an absolute bioavailability of 67%.

Following intravenous (IV) dosing of a combination solution of sarolaner and moxidectin, the sarolaner volume of distribution (V_d) was 2.4 L/kg and systemic clearance (CL) was 6.0 mL/kg/hr. For moxidectin the V_d was 7.65 L/kg and CL was 26.6 mL/kg/hr. The terminal half-lives were similar after oral and IV dosing for both sarolaner (12 days) and moxidectin (11 days). The primary route of elimination of both sarolaner and moxidectin is biliary excretion with minimal metabolism.

Following an oral dose of SIMPARICA TRIO containing 5 mg/kg pyrantel (as pamoate salt), pyrantel has measurable plasma concentrations, but they are low and highly variable. Pyrantel pamoate is intended to remain in the gastrointestinal tract allowing for delivery of effective concentrations to gastrointestinal nematodes.

MODE OF ACTION

SIMPARICA TRIO contains three active pharmaceutical ingredients, sarolaner, moxidectin, and pyrantel pamoate.

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.

Moxidectin is an endectocide in the macrocyclic lactone class. Moxidectin acts by interfering with the chloride channel-mediated neurotransmission in the parasite. This results in paralysis and death of the parasite.

Pyrantel pamoate is a nematocide belonging to the tetrahydropyrimidine class. Pyrantel acts as a depolarizing, neuromuscular-blocking agent in susceptible parasites, which causes paralysis and death or expulsion of the organism.

EFFECTIVENESS

Heartworm Prevention

In two well-controlled laboratory studies, a single oral dose of SIMPARICA TRIO was 100% effective in preventing the development of adult *D. immitis* in dogs inoculated with infective larvae 30 days before treatment.

In a well-controlled US field study consisting of 246 dogs administered SIMPARICA TRIO and 119 administered an active control, no dogs treated with SIMPARICA TRIO tested positive for heartworm disease. All dogs treated with SIMPARICA TRIO were negative for *D. immitis* antigen and blood microfilariae at study completion on day 330.

Flea Treatment and Prevention

In a well-controlled laboratory study, SIMPARICA TRIO began to kill fleas at 4 hours and demonstrated 100% effectiveness at 8 hours after initial administration. After weekly re-infestations, SIMPARICA TRIO reduced the number of live fleas by ≥97.8% within 12 hours of infestation for 28 days.

In a separate well-controlled laboratory study, SIMPARICA TRIO demonstrated 100% effectiveness against adult fleas within 24 hours following treatment and maintained ≥99.7% effectiveness against weekly re-infestations for 35 days.

In a study to explore flea egg production and viability, SIMPARICA TRIO killed fleas before they could lay eggs for 35 days.

In a well-controlled 60-day US field study conducted in dogs with existing flea infestations of varying severity, the effectiveness of SIMPARICA TRIO against fleas on Day 30 and 60 visits was 99.0% and 99.7%, respectively, compared to baseline. 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.

Tick Treatment and Control

In a well-controlled laboratory study, SIMPARICA TRIO began to kill existing *I. scapularis* within 8 hours, SIMPARICA TRIO reduced the number of live ticks by ≥94.2% within 24 hours of infestation for 28 days.

In well-controlled laboratory studies, SIMPARICA TRIO demonstrated ≥98.9% effectiveness against an existing infestation of *Amblyomma maculatum*, *Ixodes scapularis*, *Rhipicephalus sanguineus*, and *Dermacentor variabilis* 48 hours post-administration and maintained ≥90.4% effectiveness 48 hours after re-infestation for at least 28 days. Against *Amblyomma americanum*, SIMPARICA TRIO demonstrated ≥99.4% effectiveness 72 hours after treatment of existing infestations, and maintained ≥98.4% effectiveness 72 hours after re-infestation for at least 28 days. In two separate, well-controlled laboratory studies, SIMPARICA TRIO was effective at preventing *Borrelia burgdorferi* infections after dogs were infested with *Ixodes scapularis* vector ticks 28 days post-treatment.

Intestinal Nematode Treatment and Control

Elimination of roundworms (immature adult and adult *Toxocara canis* and adult *Toxascaris leonina*) and hookworm (L4, immature adult, and adult *Ancylostoma caninum* and adult *Uncinaria stenocephala*) was demonstrated in well-controlled laboratory studies.

In a 10-day multi-center field study, SIMPARICA TRIO was effective against *Toxocara canis* and reduced fecal egg counts 99.2%.

ANIMAL SAFETY

Margin of Safety: SIMPARICA TRIO was administered orally to 8-week-old Beagle puppies at doses of 1, 3, and 5X the maximum labeled dose (2.4 mg/kg sarolaner, 48 µg/kg moxidectin, and 10 mg/kg pyrantel) at 28 day intervals for 7 treatments. Dogs in the control group received placebo. There were no clinically-relevant, treatment related effects on clinical observations, body weights, food consumption, clinical pathology (hematology, coagulation, serum chemistry, and urinalysis), gross pathology, histopathology, or organ weights. During the end-of-study ophthalmic examination, the following change was found: one 1X dog had retinal dysplasia (OS folds).

Ivermectin-sensitive Collie Safety:

SIMPARICA TRIO was administered orally once at 1, 3 and 5X the maximum labeled dose to Collies that had been pre-screened for ivermectin sensitivity. Dogs in the control group received placebo. Clinical signs (ataxia, muscle fasciculations, mydriasis) associated with ivermectin sensitivity were observed in the 5X group. All dogs were completely recovered by the third day of the study.

Heartworm-Positive Safety:

SIMPARICA TRIO was administered orally at 1 and 3X the maximum labeled dose at 28 day intervals for 3 treatments to Beagle dogs with patent adult heartworm infections and circulating microfilariae. Dogs in the control group received placebo. Diarrhea occurred more commonly in the treated dogs and also more often in the 3X group compared with the 1X group. Two dogs (1 each in 1X and 3X) developed a fever less than 24 hours after the first dose. The fever may have been a transient reaction to a rapid microfilaria reduction. Both dogs recovered without treatment.

Field Safety: In three well-controlled field studies, SIMPARICA TRIO was used concurrently with other medications such as vaccines, antimicrobials, anthelmintics, antiprotozoals, steroidal and non-steroidal anti-inflammatory agents, anesthetic agents and analgesics. No adverse reactions were associated with the concurrent use of SIMPARICA TRIO and other medications.

STORAGE CONDITIONS

Store at or below 30°C (86°F).

HOW SUPPLIED

SIMPARICA TRIO (sarolaner, moxidectin, and pyrantel chewable tablets) is available in six flavored tablet sizes (see **DOSEAGE AND ADMINISTRATION**). Each tablet size is available in packages of one, three, or six tablets.

Approved by FDA under NADA # 141-521

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