Simparica Trio and Simparica Satisfaction Guarantee

If you or your clients feel that Simparica Trio® (sarolaner, moxidectin, and pyrantel chewable tablets) or Simparica® (sarolaner) Chewables isn’t providing sufficient protection, please call our medical support team to discuss our Satisfaction Guarantee. We will work with you to ensure that you and your clients are satisfied with the performance of Simparica Trio or Simparica or we will refund the cost of your purchase.*

The Simparica Trio and Simparica Satisfaction Guarantee is available to any individual who has purchased Simparica Trio or Simparica from a veterinarian or via a veterinarian’s prescription from a Zoetis approved online distributor.**

HEARTWORM DISEASE GUIDELINES (SIMPARICA TRIO ONLY):

If any dog determined by a licensed veterinarian to be free of heartworm infection at the onset of treatment with Simparica Trio develops heartworm disease, we will provide reimbursement (up to $1,000 and provide Diroban® (melarsomine dihydrochloride) or provide reasonable acquisition costs of melarsomine dihydrochloride) associated with the diagnosis and treatment of heartworm disease and provide a year’s supply of Simparica Trio or ProHeart® 6 (moxidectin) or ProHeart® 12 (moxidectin).

Canine Heartworm Reimbursement Requirements:
• Simparica Trio was used, at all times, according to its label directions.
• Confirmation of heartworm-positive status by two separate blood samples using at least two different brands of antigen tests are required to document heartworm positive status.
  – The use of an antigen test will be the standard for determining heartworm status.
  – Knott’s or any filter test for the detection of microfilariae is not sufficient evidence for pretreatment heartworm negative status.
• Dogs previously treated for heartworm disease must have a negative antigen test prior to starting Simparica Trio.
• Dogs starting or changing heartworm preventatives are required to have two negative antigen tests at least 6 months apart after initiation of Simparica Trio treatment.†

HEARTWORM DISEASE GUIDELINES (SIMPARICA TRIO ONLY):

Simparica Trio and Simparica are indicated for the prevention of Borrelia burgdorferi infections, the causative agent of Lyme disease, as a direct result of killing Ixodes scapularis vector ticks. We will reimburse you up to $30.00 for an approved alternative tick treatment for dogs, or reimburse you the cost of one dose of Simparica Trio or Simparica. This Satisfaction Guarantee does not cover any other costs, including, but not limited to, those associated with the control of tick infestations in or around living quarters, or medical treatments or procedures.

Lyme Satisfaction Guarantee:
Zoetis will cover reasonable diagnostic and treatment costs for suspected cases of canine Lyme disease for qualifying patients. Coverage begins one month after a negative Lyme test* and administration of Simparica Trio or Simparica according to label directions. If diagnostic tests confirm exposure to Borrelia burgdorferi and the dog is showing clinical signs, this Satisfaction Guarantee will cover physical examination, ancillary diagnostic and therapeutic charges up to a maximum of $2,500.

Qualifying Patients:
1. The owner must show proof of the dog’s negative Lyme test within 1 month of starting treatment with Simparica Trio or Simparica and have a negative yearly test thereafter. Any qualitative antibody test for Lyme disease may be used as a screening tool to detect natural exposure to Borrelia burgdorferi. Examples include: Zoetis VetScan® Lyme Rapid Test, IDEXX SNAP® 3Dx® Test or SNAP® 4Dx® Test and ANTECH Diagnostics® AccuPlex™4 Test.
2. Client must be able to demonstrate that they purchased enough doses of Simparica Trio or Simparica to provide continuous protection to their dog from the date of the negative Lyme test through the date of the claim.
3. To qualify for additional benefits from the Zoetis Immunization Support Guarantee, the client must show that: (a) their dog is appropriately vaccinated for Lyme disease; (b) the most recent Lyme vaccine was administered in the preceding 12 months; and (c) the most recent Lyme vaccine was a Zoetis Lyme vaccine (Vanguard® crLyme or Lymevax®). If the dog is diagnosed with Lyme disease, Zoetis will reimburse diagnostic and treatment costs up to $7,500 if the patient has received continuous protection with Simparica Trio or Simparica, according to label directions, was vaccinated appropriately AND the last dose of Lyme vaccine administered was a Zoetis vaccine.
Simparica Trio and Simparica Satisfaction Guarantee

**FLEA GUIDELINES (SIMPARICA TRIO AND SIMPARICA):**

Simparica Trio and Simparica kills adult fleas, and treats and prevents flea infestations. The affected dog must have been on Simparica Trio or Simparica for a minimum of 30 days prior to the report. All other pets in the home must also be treated with a flea control product for a minimum of 30 days prior to the report. We will reimburse you up to $30.00 for an alternative approved flea treatment or reimburse you the cost of one dose of Simparica Trio or Simparica. The Satisfaction Guarantee does not cover any other costs, including, but not limited to, those associated with the control of flea infestations in and around living quarters, or medical treatments or procedures.

**HOOKWORM, ROUNDWORM, WHIPWORM, TAPEWORM GUIDELINES (SIMPARICA TRIO ONLY):**

Simparica Trio treats and controls roundworm (immature and adult Toxocara canis and adult Toxascaris leonina) and adult hookworm (Ancylostoma caninum and Uncinaria stenocephala) infections. If you are dispensing Simparica Trio and the dog is found to be positive with roundworms or hookworms demonstrated in the fecal sample, we will provide reimbursement for the reasonable costs up to $100 for an approved treatment.

Simparica Trio has not demonstrated efficacy against whipworms or tapeworms in dogs or puppies. However, if you are dispensing Simparica Trio to a dog or puppy and such dog or puppy is found to be positive with tapeworms demonstrated in the fecal sample, we will provide you Cestex (epsiprantel) free of charge. If a dog is positive with whipworms, we will provide reimbursement for the reasonable costs up to $100 for an approved treatment.

**SIMPARICA TRIO IMPORTANT SAFETY INFORMATION:** 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. See full Prescribing Information, attached.

**SIMPARICA IMPORTANT SAFETY INFORMATION:** Simparica is for use only in dogs 6 months of age and older. Simparica may cause neurologic signs such as tremors, unsteadiness and/or seizures in dogs with or without a history of neurologic disorders. Simparica has not been evaluated in pregnant, breeding or lactating dogs. The most common adverse reactions in clinical trials were vomiting and diarrhea. See full Prescribing Information, attached.

Zoetis reserves the right to modify or discontinue this program at any time for any reason. Call Zoetis Veterinary Medical Information & Product Support with Satisfaction Guarantee questions at 1-888-ZOETIS1.

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* Subject to program requirements outlined in this document.

** Guarantee applies to current products purchased from a veterinarian or from a pharmacy through fulfillment of a valid veterinary prescription. Simparica Trio or Simparica obtained free of charge is not eligible. All claims via distribution must be accompanied by a valid proof of purchase.

† Dogs that have not previously received heartworm prevention, or those that have received inconsistent heartworm prevention, prior to starting Simparica Trio may test negative when therapy is initiated despite being infected. This may occur due to very low worm burdens, the inability of antigen heartworm tests to reliably detect infections less than five months post-infection, as well as the potential of macrocyclic lactones to delay the development of heartworms. As such, a single test—or two tests separated by six months after the initiation of a preventative regimen—will miss some infections. At this time, the American Heartworm Society recommends three consecutive “negative” antigen tests six months apart to potentially classify dogs as heartworm disease “negative.”
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/kg (24 mg/kg) moxidectin, and 2.27 mg/lb (5 mg/kg) pyrantel (as pamoate salt).

Sarolaner is a member of the isooxazoline 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-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 methylxime derivative of nemadectin which is a fermentation product of Stomoxys canescens subspecies nonagrigens. Moxidectin is a pentasaccharide 15-membered lactone macroclide. The chemical name for moxidectin is (IR,2E,3S,5)-8-D-Deoxy-2-deoxy-3β-[1E]-3-dimethyl-1-buten-1-β-L-2,6-dioxy (methylxime) methylbenzoate.

Pyrantel belongs to a family classified chemically as tetrahydropyrimidines and the chemical name is (E)-4,4′-Methylenebis[3-hydroxy-2-naphthoic]-1(11). It is a yellow, water-insoluble crystalline salt of the tetrahydropyrimidinyl 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 Toxocara cati, hookworm (L4, immature adult, and adult Ancylostoma caninum and adult Uncinaria stenocephala) infections. Simparica TRIO kills adult fleas (Chlorops rhinosus) 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 (lone star tick, and/or blacklegged 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/kg (24 mg/kg) moxidectin, and 2.27 mg/lb (5 mg/kg) pyrantel (as pamoate salt).

Dosage Schedule

<table>
<thead>
<tr>
<th>Body Weight (lbs)</th>
<th>Sarolaner per Tablet (mg)</th>
<th>Moxidectin per Tablet (mg)</th>
<th>Pyrantel per Tablet (mg)</th>
<th>Number of Tablets Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.8 to 5.5</td>
<td>3</td>
<td>0.06</td>
<td>12.5</td>
<td>One</td>
</tr>
<tr>
<td>5.6 to 11.0</td>
<td>6</td>
<td>0.12</td>
<td>25.0</td>
<td>Six</td>
</tr>
<tr>
<td>11.1 to 22.0</td>
<td>12</td>
<td>0.24</td>
<td>50.0</td>
<td>Fifty</td>
</tr>
<tr>
<td>22.1 to 44.0</td>
<td>24</td>
<td>0.48</td>
<td>100.0</td>
<td>One hundred</td>
</tr>
<tr>
<td>44.1 to 88.0</td>
<td>48</td>
<td>0.96</td>
<td>200.0</td>
<td>Two hundred</td>
</tr>
<tr>
<td>88.1 to 132.0</td>
<td>72</td>
<td>1.44</td>
<td>300.0</td>
<td>Three hundred</td>
</tr>
<tr>
<td>&gt;132.0</td>
<td>Administer the appropriate combination of tablets</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 once within one month of the animal’s first exposure to mosquitoes and continuing until at least 1 month after the last dog’s seasonal exposure. If a dose is missed, give Simparica TRIO immediately and resume monthly dosing. When re-starting 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 with 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.

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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. To minimize the likelihood of flea re-infestation, it is important to treat all dogs and cats with a household with a flea control product.
**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-(5,5-Dichloro-4-fluorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-3'-H-spiro(azetidine-3,1'-(2-benzoxazolyl)-2'-methylsulfonfuryl)ethane. SIMPARICA contains the 5-endo-tetranor of sarolaner.

**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. SIMPARICA is indicated for the prevention of *Borrelia burgdorferi* infections as a direct result of killing *Ixodes scapularis* vector ticks.

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

### Body Weight SAROLANER per Tablet (mg) Number of Tablets Administered

<table>
<thead>
<tr>
<th>Weight Range (lbs)</th>
<th>SAROLANER mg</th>
<th>Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.8 to 5.5</td>
<td>5</td>
<td>One</td>
</tr>
<tr>
<td>5.6 to 11.0</td>
<td>10</td>
<td>One</td>
</tr>
<tr>
<td>11.1 to 22.0</td>
<td>20</td>
<td>One</td>
</tr>
<tr>
<td>22.1 to 44.0</td>
<td>40</td>
<td>One</td>
</tr>
<tr>
<td>44.1 to 88.0</td>
<td>80</td>
<td>One</td>
</tr>
<tr>
<td>88.1 to 130.2</td>
<td>120</td>
<td>One</td>
</tr>
<tr>
<td>&gt;132.1</td>
<td>Administer the appropriate combination of tablets</td>
<td></td>
</tr>
</tbody>
</table>

**Dosage Schedule:** 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 the dose is not lost or refused. If a dose is missed, administer SIMPARICA and resume a monthly dosing schedule.

**Precautions:** 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-infection, 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. For use in dogs only. Do not use SIMPARICA in cats.

**Animal Safety:** Sarolaner 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.

**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

<table>
<thead>
<tr>
<th>Adverse reaction</th>
<th>sarolaner</th>
<th>N (n = 315)</th>
<th>sarolaner</th>
<th>N (n = 164)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>1</td>
<td>0.95%</td>
<td>2</td>
<td>5.50%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>0.63%</td>
<td>2</td>
<td>1.20%</td>
</tr>
<tr>
<td>Lethargy</td>
<td>0</td>
<td>0%</td>
<td>3</td>
<td>1.80%</td>
</tr>
</tbody>
</table>

**Additional information:** In a study of 12 Beagle dogs, the maximum plasma concentration (Cmax) was 110 ng/ml, and the mean time to maximum concentration (Tmax) 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 T1/2 values for fasted and fed animals was 10 and 12 days respectively.

**Clinical Pharmacology:** Sarolaner is rapidly and well absorbed following oral administration of SIMPARICA. In a study of 12 Beagle dogs, the maximum plasma concentration (Cmax) was 110 ng/ml, and the mean time to maximum concentration (Tmax) 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 T1/2 values for fasted and fed animals was 10 and 12 days respectively.

**Revised: November 2020 50070903A&P**