

suralan®

Low Dose Oral Ectoparasitic of Immediate Action and for 5 Weeks
Controls Fleas, Ticks and Mites in Dogs

Soft Chews Highly Palatable
Veterinary Use



Composition

Suralan® X-Mini

Each 500 mg chewable tablet contains:	
Suralaner	5 mg
Excipients and flavoring.....q.s.ad.....	1 tablet

Suralan® Mini

Each 1000 mg chewable tablet contains:	
Suralaner	10 mg
Excipients and flavoring.....q.s.ad.....	1 tablet

Suralan® Small

Each 2000 mg chewable tablet contains:	
Suralaner	20 mg
Excipients and flavoring.....q.s.ad.....	1 tablet

Suralan® Medium

Each 1000 mg chewable tablet contains:	
Suralaner	40 mg
Excipients and flavoring.....q.s.ad.....	1 tablet

Suralan® Large

Each 2000 mg chewable tablet contains:	
Suralaner	80 mg
Excipients and flavoring.....q.s.ad.....	1 tablet

Suralan® X-Large

Each 3000 mg chewable tablet contains:	
Suralaner	120 mg
Excipients and flavoring.....q.s.ad.....	1 tablet

Pharmaceutical Form.

Suralan® is a soft, chewable and very pleasant tasting tablet for dogs. It is brown (light to dark) in the shape of a truncated cone. It may have a marbled or mottled appearance, or both.

Features

Suralan® is a novel systemic ectoparasitic treatment against fleas, ticks and mites, based on *sarolaner*¹, (**Suralan®** includes the S enantiomer of *sarolaner*). It protects dogs for at least 35 days.

Sarolaner is a new isoxazoline specifically designed for use in pets that reduces the amount of active ingredient needed to perform its activity, minimizing potential adverse effects.

The activity against fleas and ticks resides in the chirally pure S enantiomer, purified to mitigate possible side effects. In the case of isoxazolines, the racemic forms contain an inactive R enantiomer and an active S enantiomer. Synthesizing and administering an inactive enantiomer can affect the body's ability to utilize the active enantiomer, or have undesirable pharmacological effects. Thus, with the pure chiral form of *sarolaner*, not only is the amount of active ingredient needed to perform the antiparasitic activity reduced, but also the potential adverse effects resulting from the inactive enantiomer are minimized.

In addition to the pure S-enantiomer, *sarolaner* has unique characteristics that make it unique against fleas and ticks in dogs:

- The fluorine radical at the head of the molecule gives it superior potency against ticks.
- The spiroazetidinenbenzofuran group gives it rigidity, power and novelty.
- The methylsulfonylathanone group in the tail of the molecule increases its polar surface area and maximizes pharmacokinetic exposure to achieve rapid killing of fleas and ticks.

Sarolaner demonstrated superior in vitro potency compared to other isoxazolines - *afoxolaner* and *fluralaner* - against fleas (*C. felis*) and soft ticks (*O. turicata*). This further demonstrated that less active ingredient does not mean less efficacy.

Additionally, in a laboratory study, treatment with a single dose of *sarolaner* prevented transmission of *Borrelia burgdorferi* from infected wild *Ixodes scapularis* ticks to infested dogs 21 or 28 days after treatment. In the same study, prevention of *Anaplasma phagocytophilum* transmission was also demonstrated in all *sarolaner*-treated dogs.

Suralan® can be used on infested animals or as a preventative. It controls flea infestation in the environment and areas where the treated dog has access. It starts its action in 30 minutes and kills fleas in 8 hours and ticks in 12 hours. There are 6 commercial presentations according to the weight of the dog.

Suralan® is highly effective against fleas (*Ctenocephalides felis* and *Ctenocephalides canis*), ticks of different species in dogs (*Ixodes ricinus*, *Ixodes hexagonus*, *Ixodes scapularis*, *Ixodes holocyclus*, *Dermacentor reticulatus*, *Dermacentor variabilis*, *Amblyomma americanum*, *Amblyomma maculatum*, *Amblyomma cajennense*, *Haemaphysalis elliptica*, *Haemaphysalis longicornis* and *Rhipicephalus sanguineus*: nymphs and larvae) and skin and ear mites (*Demodex canis*, *Sarcoptes scabiei var. canis* and *Otodectes cynotis*). Effectiveness has also been observed against other ectoparasites such as lice and bedbugs.

Suralan® can be used from the age of 8 weeks and 1.25 kg of weight and can be administered without restrictions in young or adult dogs, reproducers, pregnant and lactating females, as well as in Collie breed dogs. Due to its systemic action, it does not require additional precautions for the treated pet to come into contact with other animals or humans.

Suralan® can be used in dogs of any age and is particularly suitable for dogs in the early stages of life as it can be dosed from 1.25 kg, starting with a monthly flea and tick protection regimen. Thus, owners can enjoy the early life experience of their puppies with a monthly

dosage. It is an ideal start for dogs in the early stages of life.

Mechanism of Action, Pharmacokinetics and Pharmacodynamics

Suralan® contains *sarolaner*, a new molecule belonging to the isoxazoline class. It is an acaricide and insecticide belonging to the isoxazoline family. It acts by functionally blocking the chloride channels activated by GABA and glutamate receptors in the nervous system of insects and mites. Disruption of these receptors prevents the uptake of chloride ions by GABA and glutamate ion channels, resulting in increased (uncontrolled activity) nerve stimulation and parasite death. *Sarolaner* exhibits increased functional potency to block insect/mite receptors compared to mammalian receptors. *Sarolaner* kills fleas before they lay eggs and thus helps to reduce contamination in the animal's environment.

Sarolaner acts systemically, i.e. after ingestion, it is absorbed into the blood, quickly through which it is distributed throughout the body of the treated animal. Thus, ectoparasites are affected and die when exposed to the dog's blood. It does not interact with insecticidal nicotinic receptors or with other insecticidal GABAergic receptors such as neonicotinoids, fiproles, milbemycins, avermectins and cyclodienes.

For fleas, onset of efficacy occurs 8 hours after attachment (during the 28-day period following *sarolaner* administration). For ticks (*I. ricinus*), onset of efficacy is 12 hours after attachment (during the 28-day period following *sarolaner* administration). Ticks on the animal prior to treatment are killed within 24 hours.

Sarolaner causes the death of fleas that have recently climbed on the dog before egg laying. Therefore, it interferes with oviposition (egg laying), larval development (thus indicating its larvicidal action) and reproduction of fleas (*Ctenocephalides felis*) in vitro. Thus, it contributes to the control of the environmental flea population in areas visited by treated dogs.

Sarolaner is very well and rapidly absorbed after oral administration. The time to maximum plasma concentration occurs during the first day after dosing. The bioavailability of *sarolaner* was estimated to be >85% (was dose proportional in Beagles treated with doses from 2-4 mg/kg to 20 mg/kg) and the compound is highly protein bound (>99.9%). The prandial state of the dog does not significantly affect the extent of its absorption.

The clearance of *sarolaner* is low (0.12 ml/min/kg) and its volume of distribution is moderate (2.81 l/kg). The half-life of *sarolaner* is 11-12 days (oral-intravenous). *Sarolaner* plasma concentrations indicated dose proportionality in the range 1.25-5 mg/kg, and these same doses provide robust efficacy (> 99%) for ≥35 days against fleas (*C. felis*) and multiple tick species (*Rhipicephalus sanguineus*, *Ixodes ricinus*, and *Dermacentor reticulatus*) following oral administration to dogs.

In vitro plasma protein binding was >99.9%. In a distribution study, it was determined that carbon-14-labeled *sarolaner*-derived residues were widely distributed throughout tissues. The depletion of the residues from tissues was consistent with the plasma half-life. The primary excretion route is biliary excretion of the parent molecule, and elimination is via the feces.

Target Species

Dogs.

Indications for Use

For the control of infestations of the main ectoparasites in dogs (ticks, fleas and mites) when protection is required for 5 weeks, either in young dogs (i.e. in early stages between 2 to 6 months) or adults. Immediate action systemic insecticide and acaricide.

- Treatment and prevention of flea infestations (*Ctenocephalides felis* and *Ctenocephalides canis*). Additionally it controls flea infestation in the environment and areas where the animal has access.
- Treatment and prevention of tick infestations (*Ixodes ricinus*, *Ixodes hexagonus*, *Ixodes scapularis*, *Ixodes holocyclus*, *Dermacentor reticulatus*, *Dermacentor variabilis*, *Amblyomma americanum*, *Amblyomma maculatum*, *Amblyomma cajennense*, *Haemaphysalis elliptica*, *Haemaphysalis longicornis* and *Rhipicephalus sanguineus* (adults and juveniles)).
- Treatment of skin mite infestations: demodicosis (*Demodex canis*) and sarcoptic mange (*Sarcoptes scabiei var. canis*).
- Treatment of ear mite (*Otodectes cynotis*) infestations.
- Control of flea bite allergic dermatitis (FAD) as part of a therapeutic strategy.
- Helps in the prevention of *Borrelia burgdorferi* and *Anaplasma phagocytophilum* transmission from infected ticks (*Ixodes scapularis*).

Additional considerations regarding indications for use:

- The effectiveness of the product is linked to the attachment of fleas and ticks to the host and the beginning of their feeding in order to be exposed to *sarolaner*. This effect occurs within 8 hours after attachment in the case of fleas and 12 hours after attachment in the case of ticks.
- The preventive effect against reinfestations is the result of the adulticidal activity, the reduction in egg production (fleas die before producing viable eggs), the non-viability of eggs (very low concentrations of *sarolaner* stop the production of viable eggs by fleas) and its effect against the development of immature stages (ticks) and persists for up to 4 weeks after a single administration.
- It has been demonstrated that the residual effect of **Suralan®** on flea and tick control, after 3 applications every 28 days, is maintained for a minimum of 98 days.
- **Suralan®** contributes to the control of the environmental flea population in areas visited by treated dogs, in fact, it has been demonstrated that the environmental effect of **Suralan®** is able to reduce flea infestations in untreated dogs living in the same environment as treated dogs.
- Fleas and ticks must be attached to the host and feeding to be exposed to the active substance.

Route of Administration and Dosage, Considerations and Guidelines for Proper Administration

Suralan® is administered orally, according to the following table (doses correspond to 2-4 mg *sarolaner*/kg live weight within each weight range).

Product	Dog Size	mg / tablet	Suralan® Soft Chewable Tablets		Dose (tablets)	Minimum dose (mg/kg)	Maximum dose (mg/kg)	Tablet Weight
			Body Weight Range (kg)					
			Min	Max				
Suralan® X-Mini	X-Miniature Dogs	5	1.25	2.5	☺	2	4	500
Suralan® Mini	Miniature Dogs	10	2.5	5	☺	2	4	1000
Suralan® Small	Small Dogs	20	5	10	☺	2	4	2000
Suralan® Medium	Medium Dogs	40	10	20	☺	2	4	1000
Suralan® Large	Large Dogs	80	20	40	☺	2	4	2000
Suralan® X-Large	X-Large Dogs	120	40	60	☺	2	4	3000

Dose frequency.

- For the treatment of tick and flea infestations, **Suralan®** should be administered once every 35 days during the flea and/or tick season.
- For the treatment of sarcoptic mange it is administered once a month for two consecutive

months.

- For the treatment of demodectic mange, it is administered once a month for at least three consecutive months. However, since demodectic mange is multifactorial, it is advisable to diagnose and treat any underlying disease. The need and frequency of retreatment should follow the advice of the veterinarian.
- For the treatment of otodectic mange, administer a single dose.
- The absence of mites can be confirmed by two consecutive scrapings every 15-30 days. If mite infestation is repeated, consult your veterinarian. For ear mite infestations, a veterinary check-up is required 28 days after treatment. The veterinarian will decide if any additional treatment is necessary.
- The application of **Suralan®** helps to significantly reduce the clinical signs related to acarosis, such as the presence of plaques, scales and crusts; comedones, papules and pustules; alopecia and erythema.

Suralan® can be administered throughout the year. It can be administered without or with food (before or after eating). Do not split the tablets.

Suralan® is a highly palatable, soft and chewable tablet, which facilitates its administration due to its high acceptance. Alternatively, if necessary, it can be administered with the feed or by opening the animal's mouth and placing the tablet on the deep back of the tongue like any other medication.

Treatment with **Suralan®** can be initiated at any time of the year, preferably starting one month before fleas become active and then continuously according to the time interval mentioned above. In areas where fleas are present throughout the year, treatment should be extended throughout the year without interruption. To eradicate the possibility of flea reinfestation, it is recommended to treat all animals in the house at the same time.

In dogs older than 8 weeks, monthly treatment is well tolerated. Puppies should be weighed regularly. The treatment can be adapted by the veterinarian to suit individual weight changes.

Studies have shown no statistical differences between the monthly treatment with **Suralan®** and another monthly application product based on *sarolaner*.

Tolerance and Safety

Studies have shown that **Suralan®** is completely safe for use in the treatment and control of the main ectoparasites in naturally infested canines.

No serious adverse reactions were observed at the recommended dose of 2mg/kg. *Sarolaner* was tested at 5 times the recommended dose in 8-week-old canines for 9 months. Only 1% of the animals showed side effects.

Very rarely, adverse reactions associated with mild and transient gastrointestinal effects such as vomiting and diarrhea may occur. Very rarely, transient neurological disorders such as tremors, ataxia or convulsions may occur. These signs usually resolve without treatment.

The safety of *sarolaner* has not been demonstrated during pregnancy, lactation or in reproductive animals. Laboratory studies in rats and rabbits have not demonstrated teratogenic effects. Use only in accordance with the benefit/risk assessment performed by the responsible veterinarian.

Sarolaner has been 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 and 10 treatments. No adverse effects were observed at the maximum exposure dose of 4 mg/kg.

In the overdosed groups, transient, self-limiting neurological signs were observed in some animals: moderate tremors at a dose 3 times the maximum exposure dose and convulsions at a dose 5 times the maximum exposure dose. All dogs recovered without treatment.

Regarding the owner's safety, as *sarolaner* is orally administered and acts systemically, no chemical residues are found on the coat of the dogs after treatment. Therefore, unlike products for topical administration, there is no risk of contamination or toxicity in other animals, humans (especially children) by direct contact with treated animals.

A single treatment of *sarolaner* at 5 times the recommended dose is well tolerated by Collie breed dogs with multidrug-resistant protein 1-deficient (MDR1 -/-). No treatment-related clinical signs were observed.

Finally, considering its mechanism of action, *sarolaner* is extremely selective for arthropod receptors relative to those of mammals, including humans, which further extends its large margin of safety.

Adverse Reactions

- *Sarolaner* does not usually present adverse effects. However, the following adverse effects have been observed in studies in less than 1 in 10,000 dogs: Mild, short-lived vomiting and diarrhea as well as tremor (shaking), ataxia (inability to coordinate body movements) or convulsions. These effects usually resolve without treatment.
- In general, dogs tolerate *sarolaner* very well at the therapeutic dose apart from the possible adverse reactions mentioned above.
- A potential error when treating dogs that can cause overdose and therefore the administration -to small dogs- of tablets approved only for larger dogs should be avoided.
- If you observe or suspect any serious reactions or other reactions not mentioned, contact your veterinarian immediately.

Contraindications

- Do not use in case of known hypersensitivity to *sarolaner* or to any of the excipients.
- There are no known contraindications for the use of the product.
- In dogs with severe hepatopathies or severe hypoproteinemia, the veterinarian should evaluate the risk/benefit ratio prior to treatment.

Precautions

- Do not use in dogs less than 8 weeks of age or less than 1.25 kg body weight. Treatment of puppies under 8 weeks of age or dogs under 1.25 kg live weight should be performed based on the benefit-risk assessment performed by the responsible veterinarian.
- Do not split or divide **Suralan®** tablets.
- Do not administer **Suralan®** to animals of lower weight, approved for dogs of more body weight.
- Do not administer **Suralan®** at intervals of less than 30 days.
- Upon initiation of treatment, the risk of ectoparasite-mediated disease transmission is greatly reduced due to the rapid onset of action of **Suralan®**. However, as parasites must initiate feeding in the pet to be exposed to *sarolaner*, the risk of transmission of such diseases cannot be excluded.
- To help control the flea population, it is recommended to treat all animals in the household with **Suralan®** at the same time.
- Fleas often infest the animal's basket, bedding and usual resting areas, such as carpets and textiles, which should be treated with an appropriate insecticide and vacuumed in case of massive infestation at the beginning of treatment.

- *Sarolaner* is a member of the isoxazoline class. This class has been associated with neurological adverse reactions including tremors, ataxia and seizures. Seizures have been reported in dogs receiving isoxazoline class drugs, even in dogs with no history of seizures. Use with caution in dogs with a history of seizures or neurological disorders.
- Keep the product in the aluminum blister until use.
- Do not eat, drink or smoke while handling the tablets.
- Wash hands after handling the tablets.
- In case of accidental ingestion by a person, seek medical advice immediately.
- Agrovet Market S.A. is not responsible for the consequences derived from the use (of the product) different from the one indicated in this leaflet.

Interactions with other drugs and other forms of interaction

Although *sarolaner* has a high binding to plasma proteins and could compete with other substances of similar action such as non-steroidal anti-inflammatory drugs (NSAIDs) or coumarin derivatives such as warfarin, no adverse reactions have been reported in the concomitant use of *sarolaner* with other drugs.

Storage

Store in a cool and dry place, in its original container, protected from light, between 15°C and 30°C. Keep out of reach of children and domestic animals.

Commercial Presentation

Suralan® is presented in 6 concentrations of the active ingredient, containing: 5, 10, 20, 40, 80 and 120 mg of *sarolaner* per soft tablet, and are presented in:

Suralan® X-Mini (5 mg):

Box x 1 or 4 soft chewable tablets in sealed aluminized blister x 500 mg.

Suralan® Mini (10 mg):

Box x 1 or 4 soft chewable tablets in sealed aluminized blister x 1000 mg.

Suralan® Small (20 mg):

Box x 1 or 4 soft chewable tablets in sealed aluminized blister x 2000 mg.

Suralan® Medium (40 mg):

Box x 1 or 4 soft chewable tablets in sealed aluminized blister x 1000 mg.

Suralan® Large (80 mg):

Box x 1 or 4 soft chewable tablets in sealed aluminized blister x 2000 mg.

Suralan® X-Large (120 mg):

Box x 1 or 4 soft chewable tablets in sealed aluminized blister x 3000 mg.

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Petmedica® is a division of Agrovet Market Animal Health

Manufactured in Peru by Pharmadix Corp. S.A.C.
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MARKET

¹ The chemical name of *sarolaner* is 1'(5'-((5S)-5-(3,5-dichloro-4-fluorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-3'-Hespiro[azetidine-3,1'-(2)benzofuran]-1-yl)-2-(methylsulfonyl)ethanone.