

Fipronex® Duo Drop On

Topical Dermal Solution

Ectoparasiticide with environmental effect

agrovetmarket s.a.

FORMULATION

Each 100 mL contains:

Fipronil.....	10 g
Pyriproxyfen.....	10 g
Excipients.....	q.s.ad..... 100 mL

BACKGROUND

It is a fact that in the new approach for flea's control, the insecticides against adult stages are combined with Insect Growth Regulators (IGR), to achieve a more effective control and prevent the emergence of the next generation of fleas. In the other hand, the use of products with different action mechanisms will delay the onset of drug resistance in the flea's population.

INDICATIONS

Fipronex® Duo Drop On combines the effectiveness of fipronil (**Fipronex®**) with pyriproxyfen, an Insect Growth Regulator (IGR), offering the most effective drug association for the integral control of fleas (*Ctenocephalides canis*, *Ctenocephalides felis felis*) and ticks (*Rhipicephalus sanguineus*) in dogs and puppies since the eight week of age. It has additional action against louse and sarcoptic mange (var. *canis*).

The addition of pyriproxyfen gives to the product a residual effectiveness against eggs and larvae, which confers an environmental control of adult fleas (reduction in environmental burden). This is due to its action at different levels of the flea's life cycle, preventing the insects to re infest the pet and its environment.

Fipronex® Duo Drop On can be considered an important auxiliary method for cestode infestations (*Dipylidium caninum*) affecting dogs, since fleas are intermediary hosts of these parasites. On the other side, babesiosis and ehrlichiosis, caused by *Babesia canis* and *Ehrlichia canis* respectively, are transmitted to dogs through the bite of infected ticks (*Rhipicephalus sanguineus*). It is therefore essential to fight ticks in order to control pathologies.

CHARACTERISTICS

Fipronex® Duo Drop On is an insecticide with rapid and prolonged action. It combines an insecticide against adult stages with a Insect Growth Regulator, controlling fleas in all their life stages with only one application, killing adult fleas before they put their eggs. It prevents the reinfestation and eliminates the stress on pets, caused by the pain due to the fleas and ticks, by the loss of blood, itch and allergic reaction from the flea bite.

Fipronil is a widely known drug that eliminates fleas and ticks in the adult stage; while the IGR pyriproxyfen inhibits the eggs eclosion and inhibits the flea's larvae development. **Fipronex® Duo Drop On** is efficient against adult fleas up to 90 days (from 60 to 90 days, depending on the environmental burden) and inhibits the egg and fertile larvae development (from adult fleas) for up to 120 days. It also guarantees the total protection against all kind of ticks during one month with one single dose.

Pyriproxyfen is a very well known third generation IGR, that had demonstrated a high effectiveness in the control of immature stages of fleas including eggs and larvae for up to 11 months in the environment (applied to rugs and carpets) and in dogs for more than 150 days; it is not affected by sun light, temperature changes or microbial activity (in contrast with other IGR such as methoprene). It also has certain retarded effectiveness in adult fleas.

In the other hand, it posses a high safety for animals and human beings (previous studies demonstrated that there is no lethal dose for humans or animals), this substance is also known as a biosmart insecticide, because is non toxic for humans or animals, and does not contaminates the environment.

These characteristics make this product the perfect complement of fipronil for the integral control of fleas in animals and the environment.

Fipronex® Duo Drop On offers an immediate long term action, bath proof, in very young, very old and even pregnant animals. It kills fleas, larvae and eggs and stops the development of pupae, controlling the environmental parasites burden.

The residual effect of **Fipronex® Duo Drop On** prevents the re infestation killing fleas (and its intermediate stages) and ticks for at least 60 days. Previous studies have demonstrated that **Fipronex® Duo Drop On** may protect adult dogs against adult fleas for more than 90 days and inhibit the development of eggs and fertile larvae (from adult fleas) for more than 120 days.

MECHANISM OF ACTION

Fipronil, the active ingredient of **Fipronex® Duo Drop On** acts destabilizing the normal nervous functions of fleas and ticks. It blocks the chloride channels of the GABA barrier (gamma amino butyric acid) of neurons in the central nervous system. The GABA receptive system is responsible for inhibiting the normal neuronal activity (e.g. prevents the excessive stimulation of nerves). When the system's regular functions are blocked by fipronil, it causes neuronal excitation and the insect's death. Fipronil kills the insect by contact or ingestion. The main activity course depends on the target insect. It is highly specific against adults and larvae stages. It's been demonstrated that fipronil has no affinity for the chloride channels on vertebrates, which explains its high safety on host (dogs) and men.

Fipronil spreads rapidly through the epidermis and pilo-sebaceous units and then it is gradually released through follicular conducts. In spite of its formulation, such characteristic guarantees its efficacy, even if animals get wet or are bathed. When the hair of treated animals sheds, they exert an important control. When it exerts its altudicide effect with contact action, fipronil kills fleas immediately, even before the first ingestion of blood takes place. It is also indicated for animals suffering from flea allergy dermatitis (FAD).

Pyriproxyfen is a synthetic juvenile hormone (IGR), a powerful analogous component that mimics the action of the juvenile hormone (growth regulator) that the fleas produce during their development. It is a powerful embryogenesis, metamorphosis and adult stages formation inhibitor in fleas. It acts interfering in the normal maturation or developing process of the different stages in the flea's life cycle. In a normal cycle the insect goes from egg to larvae, pupae and eventually adult. Its effect artificially prevents the blastoderm formation in the flea egg, while it does not let the larvae to mature into the pupae stage by inhibiting ecdysis. In summary, when the egg and larvae are exposed to this hormone, the first will not reach eclosion and the later will not progress into pupae, preventing reproduction when absorbed by the female flea and concentrates in its ovaries (obviously the eggs laid by the female will not reach eclosion).

All this prevents the massive reproduction of the parasite, controlling the environmental burden of the parasite. Pyriproxyfen also accumulates and stays in the skin and hair of the animal, protecting it from baths and giving an extremely long residual effect. The effect is so powerful that the only contact of the dog with its bed is enough to transfer minimum but effective amounts of the drug.

DIRECTIONS OF USE

To kill all the stages of fleas and ticks, apply in dogs and puppies, from the wight week of age, following the indications:

For external use, direct application to the skin.

Cut off the pipette tip, and apply the content directly to the animal's dry skin at the back of the neck or at the withers region to avoid the animal to lick itself. It is important to separate the animal's hair to facilitate the skin application of the product. Do not pour the content into the animal's hair.

The dose is based on the animal's weight:

From 1 to 10 kilogram body weight.....	One 0,67 mL pipette
From 11 to 20 kilogram body weight.....	One 1,34 mL pipette
From 21 a 40 kilogram body weight.....	One 2,68 mL pipette
From 41 a 60 kilogram body weight.....	One 4,02 mL pipette

To prevent the increase or re infestation with fleas, use **Fipronex® Duo Drop On** before the start of summer season and from then every two months or according to the recommendation of your veterinarian. It is not recommended for applications within an interval of less than 60 days.

It is not recommended to bath or wet the animal 2 days before or after the treatment because during this period **Fipronex® Duo Drop On** action time is affected by the exposure to rain or baths with shampoo.

To prevent any damage to you or to your pet, it is recommended to read the whole label, box and insert before its use. Follow completely the indications and directions. Use it only in dogs.

INTERVAL OF APPLICATIONS

It must be applied with a 2-month interval for the treatment and prevention of flea infestation and with a 30-month interval for the treatment and prevention of tick infestation.

Fipronex® Duo Drop On may be reapplied at shorter intervals in case the animal is located in highly infested areas or if it suffers from flea allergy dermatitis, always prior opinion of the veterinarian.

GENERAL PRECAUTIONS

Humans: **Fipronex® Duo Drop On** is very safe when used according to the instructions given. Though, it can be harmful if swallowed or absorbed through skin. It may cause severe irritation in the eyes. Avoid contact with skin, face, eyes or clothing. After application, wash hands and exposed skin with plenty of soap and water. Do not touch the animal until the product is completely absorbed.

Animals: For external use only. Previous studies performed with **Fipronex® Duo Drop On** demonstrated that it is very safe when used according to the instructions given. Individual sensitivities may occur after using any insecticide for pets, although they are rare. If the signs persist or increase, seek for veterinary attention immediately.

Fipronil

The GABA receptor of vertebrates significantly differs from the one from invertebrates, what explains the great security margin of fipronil in vertebrates.

Its LD50 (Lethal Dose) has been classified by the EPA as toxicity class III (low toxicity). It does not have any incompatibilities.

Two consecutive treatments with a 28 days interval, at the double of the recommended dose, did not show any clinical drawback in puppies of between 2 and 45 days of age. Pregnant females or lactating females may be treated with no risk.

Pyriproxyfen

Its action is specific against insects, for what it is innocuous for man and pets. Its safety is based in the fact that mammal hosts does not have juvenile hormones or their receptors and are not susceptible to any biological effect of the drug. In fact, pyriproxyfen toxicity for mammals is extremely low.

As these hormones are specific for insects, the product that have them among their ingredients are innocuous to man and pets (in studies previously performed, extremely high oral doses of 10 mg/kg/day during 1 year demonstrated to be completely innocuous to the dogs under study).

Physic and Chemical properties: Flammable. Keep away from heat and fire.

First aid:

When ingested: seek medical attention immediately. Drink 1 or 2 glasses of water and induce vomiting by touching the back side of the throat with one finger. If the patient is unconscious, do not give any drinks or induce vomiting.

If aspirated: take the victim to open air. If the victim is not breathing give artificial respiration, mouth to mouth. Seek medical attention immediately.

Eyes contact: wash the eyes with plenty of water. Seek medical attention if irritation persists.

Skin contact: wash immediately with plenty soap and water. Seek medical attention if irritation persists.

The intoxication signs are not specific but it can occur neurologic signs such as excitation, tremors or excessive sedation.

There is no specific antidote. Apply a symptomatic treatment.

ADDITIONAL INFORMATION

Fipronex® Duo Drop On can be applied to lactating and pregnant females.

Fipronex® Duo Drop On can be applied to puppies older than two months and when they have more than one kg.

Do not bath the animals before or after 48 hours of the application of the product.

Ticks are killed during the first 24 hours, avoiding to suck the animal blood and therefore transmit diseases like canine Ehrlichiosis and canine Babesiosis.

Once killed, ticks may come away and fall down; or they may be pulled out carefully.

STORAGE AND CONTAINERS DISPOSAL

When is well stored it does not contaminate food or water.

Store new products in its original container only, keep out of reach of children and animals.

Keep in a dry cool place, protected from light exposure. Do not expose to extreme temperatures.

Do not reuse the container. Do not incinerate. Wrap the empty pipette in enough paper and discard it in the trash.

WARNINGS

Keep away from reach of children. The responsible distributor and the salesman does not offer any express or implicit guarantee if the product is used in a different way than the one indicated in the label, box or insert. The buyer assumes all risk of using and handling the product when its use is different to what is indicated in the instructions.

COMMERCIAL PRESENTATION

Individual box containing one pipette of: 0.67 mL, 1.34 mL, 2.68 mL and 4.02 mL for dogs.

Reg. SENASA Perú: F.07.08.N.0298; Reg. Albania: NR-0805;
Costa Rica: Reg. MAG PE2-43-06-3265; Reg. Ecuador: 3B2-9285-SESA-U;
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