

Atrevia® One Large

Ectoparásitico Oral de Acción Inmediata de Aplicación Mensual

Tabletas blandas masticables (Soft Chews) Altamente Palatables

Controla Pulgas, Garrapatas y Ácaros en Perros

Uso Veterinario



Composición

Perros large (20 a 40 kg)

Cada tableta masticable de 8,000 mg contiene:

Fluralaner..... 400 mg

Excipientes y saborizantes c.s.p..... 1 tableta

Forma Farmacéutica

Atrevia® One Large es una tableta blanda, masticable y de muy agradable sabor para los perros. Es de color marrón (de claro a oscuro) en forma de cono trunco. Puede presentar un aspecto marmoleado, moteado, o ambos.

Características

Atrevia® One Large es un novedoso tratamiento ectoparasitario sistémico contra pulgas, garrapatas y ácaros, en base a fluralaner, que protege a los perros por lo menos por 30 días. Puede utilizarse en animales infestados o como preventivo. Controla la infestación de pulgas en el medio ambiente y áreas donde el perro tratado tiene acceso. Empieza su acción en 90 minutos y mata a las pulgas en 8 horas y a las garrapatas en 12 horas. Existen 4 presentaciones comerciales de acuerdo al peso del perro.

Atrevia® One Large es altamente efectivo contra pulgas (*Ctenocephalides felis* y *Ctenocephalides canis*), garrapatas de diferentes especies en perros (*Rhipecephalus sanguineus*, *Ixodes hexagonus*, *Ixodes scapularis*, *Ixodes holocyclus*, *Dermacentor reticulatus*, *Dermacentor variabilis* y *Hippobates sanguineus* adultos y juveniles).

- Tratamiento de las infestaciones por ácaros de la piel: demodicosis (*Demodex canis*) y sarna sarcóptica (*Sarcopes scabiei var. canis*).

- Tratamiento de las infestaciones por ácaros de oido (*Otodectes cynotis*).

- Tratamiento de las infestaciones por chinches o chirimachas de la especie *Triatoma infestans*.

- Tratamiento y prevención de infestaciones por piojos (*Linognathus spp.*) por 7 semanas.

- Control de la dermatitis alérgica por picadura de pulgas (DAPP), como parte de una estrategia terapéutica.

- Prevención de la transmisión de *Babesia canis* (causante de la babesiosis canina), transmitida por garrapatas del género *Dermacentor reticulatus*.

ambiente y áreas donde el animal tiene acceso.

- Administración y prevención de las infestaciones por garrapatas (*Ixodes ricinus*, *Ixodes hexagonus*, *Ixodes scapularis*, *Ixodes holocyclus*, *Dermacentor reticulatus*, *Dermacentor variabilis* y *Hippobates sanguineus* adultos y juveniles).
- Tratamiento de las infestaciones por ácaros de la piel: demodicosis (*Demodex canis*) y sarna sarcóptica (*Sarcopes scabiei var. canis*).
- Tratamiento de las infestaciones por ácaros de oido (*Otodectes cynotis*).
- Tratamiento de las infestaciones por chinches o chirimachas de la especie *Triatoma infestans*.
- Tratamiento y prevención de infestaciones por piojos (*Linognathus spp.*) por 7 semanas.
- Control de la dermatitis alérgica por picadura de pulgas (DAPP), como parte de una estrategia terapéutica.
- Prevención de la transmisión de *Babesia canis* (causante de la babesiosis canina), transmitida por garrapatas del género *Dermacentor reticulatus*.

Consideraciones adicionales con respecto a las indicaciones de uso:

- La efectividad del producto está ligada a la fijación de pulgas y garrapatas al huésped y al inicio de su alimentación para así exponerse al fluralaner. Este efecto se da dentro de las 8 horas pos fijación en el caso de pulgas y 12 horas pos fijación en el caso de garrapatas.

- El efecto preventivo frente a las reinfecciones es el resultado de la actividad adulticida, de la reducción en la producción de huevos (las pulgas mueren antes de producir huevos viables), de la inviabilidad de los mismos (concentraciones muy bajas de fluralaner detienen la producción de huevos viables por las pulgas) y por su efecto contra el desarrollo de estadios inmaduros (garrapatas) y persiste hasta 4 semanas tras una única administración.

- Se ha demostrado que el efecto residual de Atrevia® One sobre el control de pulgas y garrapatas, luce de 3 aplicaciones cada 28 días, se mantiene hasta por un mínimo de 98 días.

- Atrevia® One Large contribuye al control de la población medio ambiental de pulgas en áreas visitadas por los perros tratados. En efecto, se ha demostrado que el efecto ambiental de Atrevia® One es capaz de reducir las infestaciones de pulgas en caninos no tratados que viven en el mismo ambiente que caninos tratados.

- En estudios de laboratorio, fluralaner ha mostrado también eficacia contra larvas de mosquitos (*Aedes aegypti*) y califardos (*Lucilia cuprina*), hembras adultas de *Rhipecephalus (Boophilus) microplus*, y ninfas de garrapatas blandas (*Ornithodoros moubata*).

Vía de Administración y Dosis, Consideraciones y Directivas para su Correcta Administración

Atrevia® One Large se administra por vía oral, de acuerdo con la siguiente tabla (las dosis corresponden a 10-22 mg de fluralaner/kg de peso vivo dentro de cada rango de peso):

| Atrevia® One Tabletas blandas masticables | | | | | |
|---|----------------------|---------------|-----------------------------------|------------------------------------|--|
| Producto | Tamaño de la mascota | Peso corporal | Tableta 1.000 mg Fluralaner 50 mg | Tableta 2.000 mg Fluralaner 100 mg | Tableta 4.000 mg Fluralaner 200 mg Fluralaner 400 mg |
| Atrevia® One Mini | Perros Mino | 2 - 4.5 Kg | △ | | |
| Atrevia® One Small | Perros Pequeños | 4.5 - 10 Kg | △ | | |
| Atrevia® One Medium | Perros Medianos | 10 - 20 Kg | | △ | |
| Atrevia® One Large | Perros Grandes | 20 - 40 Kg | | | △ |

* Para perros que pesen más de 40 kg, administrar una combinación apropiada de tabletas.

Frecuencia de dosis:

- Administrar una tableta de Atrevia® One Large cada 30 días. El producto se puede administrar durante todo el año. Atrevia® One Large debe administrarse con alimento o inmediatamente antes o después de haber comido. No dividir las tabletas.

- Para el tratamiento de sarna demódéctica, sarcóptica y/o otodéctica, administrar una dosis cada 30 días durante uno a tres meses consecutivos*. Atrevia® One ha demostrado 100% de efectividad para la resolución de casos de acarosis (demodicosis, escabiosis o sarna mixta) luego de 3 tratamientos consecutivos cada 4 semanas. Sin embargo, dado que la sarna demódéctica es multifactorial, es recomendable diagnosticar y tratar cualquier enfermedad subyacente. La necesidad y la frecuencia del refatrámiento deben seguir los consejos del médico veterinario.

- La ausencia de ácaros puede confirmarse mediante dos raspados consecutivos cada 15-30 días. Si se repite la infestación de ácaros, consulte con su veterinario. Para las infestaciones por ácaros del oído es necesario un control veterinario 28 días después del tratamiento. El veterinario decidirá si es necesario algún tratamiento adicional.

- La aplicación de Atrevia® One ayudó a reducir significativamente los signos clínicos relacionado a las acarosis, como son la presencia de placas, escamas y costras; comedones, pápulas y pústulas; alopecia y eritema.

Atrevia® One Large es una tableta altamente palatable, suave y masticable, lo que facilita su administración por su alta aceptación. Alternativamente, de ser el caso, puede administrarse con el alimento o abriendo la boca del animal y colocando la tableta en la parte posterior profunda de la lengua como cualquier otro medicamento.

El tratamiento con Atrevia® One Large puede iniciarse en cualquier época del año, preferentemente iniciando un mes antes de que las pulgas se vuelvan activas y luego, continuamente de acuerdo con el intervalo de tiempo mencionado previamente. En áreas donde las pulgas están presentes durante todo el año, el tratamiento deberá extenderse durante todo el año, sin interrupción. Para erradicar la posibilidad de reinfección de pulgas, se recomienda tratar a todos los animales de la casa al mismo tiempo.

En perros mayores de 8 semanas, se ha demostrado que el tratamiento mensual es bien tolerado. Los cachorros deben ser pesados regularmente. El tratamiento puede ser adaptado por el veterinario para adaptarse a los cambios de peso individuales.

Estudios realizados no evidenciaron diferencias estadísticas entre el tratamiento mensual de Atrevia® One y un producto de aplicación mensual en base a sarolaner.

Tolerancia y Seguridad

Estudios realizados demostraron que Atrevia® One es completamente seguro para su uso en el tratamiento y control de los principales ectoparásitos en caninos naturalmente infestados.

Fluralaner ha demostrado ser seguro en hembras reproductoras, gestantes o lactantes. En un estudio reproductivo, perros adultos Beagle se trataron hasta 3 veces la dosis recomendada, 3 tratamientos a intervalos de 8 semanas, iniciados 1.2 semanas (machos) y 4 semanas (hembras) antes de la copula prevista. El tratamiento continuó en los machos hasta el parto, y en las hembras hasta el desete de las crías. No se observaron efectos adversos ni en los adultos, ni en su rendimiento reproductivo, ni en el número de cachorros nacidos ni sobre vivientes.

Datos de seguridad recogidos sobre fluralaner durante estudios de campo en Europa y los EE.UU. mostraron que, por lo general, los animales tratados toleran bien el producto a la dosis recomendada. En los estudios europeos, diarrea, vértigo, falta de apetito y salivación excesiva de carácter leve y pasajero se observaron en 1.6% de los perros los primeros días tras el tratamiento. Estudios realizados demostraron que Atrevia® One es muy bien

tolerado, reportando efectos adversos en sólo el 0.85% de los casos.

Respecto a la seguridad del propietario, al ser fluralaner de administración oral y actuar sistemáticamente, no se encuentran residuos químicos sobre el pelaje de los perros tras el tratamiento. Por ello, a diferencia de los productos para administración tópica, no hay riesgo de contaminación ni toxicidad en otros animales, seres humanos (sobre todo niños) por contacto directo con los animales tratados.

Finalmente, teniendo en cuenta su mecanismo de acción, fluralaner es extremadamente selectivo para los receptores de artrópodos con respecto a los de los mamíferos, incluidos seres humanos, lo que extiende aún más su gran margen de seguridad.

Reacciones Adversas

- Estudios de tolerancia y de seguridad con Atrevia® One reportaron reacciones no deseadas en el 0.85% de los animales tratados, siendo diarrea (0.28%), letargo (0.28%) y polidipsia (0.28%) las únicas encontradas.

- A pesar de que existen reportes de reacciones neuroológicas por causas individuales luego de la aplicación de fluralaner, en estudios realizados con Atrevia® One no pudo evidenciarse algún caso. Sin embargo, de reportarse alguno, se debe realizar una visita inmediata al médico veterinario para la evaluación del animal.

- En general los perros toleran muy bien el fluralaner a la dosis terapéutica aparte de las posibles reacciones adversas mencionadas.

- Un error potencial al tratar perros que puede causar sobredosis y por ello debe evitarse la administración - a perros pequeños- de tabletas aprobadas solo para perros de mayor tamaño.

- Si observa o sospecha de alguna reacción grave u otras no mencionadas, contacte a su veterinario de inmediato.

Contraindicaciones

- No usar en caso de hipersensibilidad conocida a alguna de las sustancias activas o a algún excipiente.

- No hay contraindicaciones conocidas para el uso del producto.

- No usar en perros con hepatopatías graves o hipoproteinemia severa.

Precauciones

- No usar en perros menores a 8 semanas de edad ni de menos de 2 kg de peso.

- No partir o dividir las tabletas de Atrevia® One Large.

- No administrar Atrevia® One Large a animales de menor peso, aprobados para perros de mayor peso corporal.

- No administrar Atrevia® One Large a intervalos menores a 30 días.

- Para ayudar al control de la población de pulgas, se recomienda tratar a todos los animales de la casa con Atrevia® One Large al mismo tiempo.

- Con frecuencia, las pulgas infestan la cesta, cama y zonas habituales de descanso del animal, como alfombras y textiles, que deberían tratarse con un insecticida adecuado y aspirarse en caso de infestación masiva al comienzo del tratamiento.

- Fluralaner es miembro de la clase isoxazolina. Esta clase se ha asociado con reacciones adversas neurogénicas que incluyen temblores, ataxia y convulsiones. Se han reportado convulsiones en perros que reciben medicamentos de clase isoxazolina, incluso en perros sin antecedentes de convulsiones o trastornos neurológicos.

- Mantener el producto en el blister de aluminio hasta su uso.

- No comer, tomar bebidas o fumar mientras se manipula las tabletas.

- Lavarse las manos luego de la manipulación de las tabletas.

- Agrovet Market S.A. no se responsabiliza por las consecuencias derivadas por el uso (del producto) diferente al indicado en este inserto.

Interacciones con otros medicamentos y otras formas de interacción

- Ninguna conocida.

- Por su alta unión a las proteínas plasmáticas, fluralaner podría actuar competitivamente con otros medicamentos de similares características farmacológicas, entre ellas antiinflamatorios no esteroides (AINEs), warfarina, etc. La incubación de fluralaner en presencia de carprofeno o warfarina en el plasma del perro a concentraciones plasmáticas máximas esperadas no redujo la unión a las proteínas de fluralaner, carprofeno o warfarina.

- La seguridad de fluralaner asociado a otros principios activos como deltametrina, milbemicina oxima, moxidectina, pirantel, ivermectina o praziquantel ha sido documentada.

Almacenamiento

Conservar en un lugar fresco y seco, en su envase original, protegido de la luz entre 15°C y 30°C. Mantener alejado del alcance de los niños y de los animales domésticos.

Presentación Comercial

Atrevia® One Large se presenta en:

Caja x 1, 2 ó 4 tabletas blandas masticables (soft chews) en blister aluminizado sellado x 8.000 mg - Perros Large.

Reg. SENASA Perú: F.87.31.N.0462

Atrevia® es una marca registrada de Agrovet Market S.A.

Petmedica® es una división de Agrovet Market Animal Health.

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¹ El nombre químico de fluralaner es (-4-[5-(3,5-diclorofenil)-5-(trifluorometil)-4,5-dihidroxazol-3-il]-2-metil-N-[2-oxo-2-(2,2,2-trifluoroetilamino)etil]benzamida.

² Atrevia® One

Atrevia® One Large

Oral Ectoparasiticide of Immediate Action and Monthly Application

Highly Palatable Soft Chews

Controls Fleas, Ticks and Mites on Dogs

Veterinary Use



Composition

Large dogs (20 to 40 kg)

Each soft chew of 8,000 mg contains:
Fluralaner..... 400 mg
Excipients and flavorings q.s.ad..... 1 tablet

Pharmaceutical form

Atrevia® One Large is a soft, chewable tablet with a very pleasant taste for dogs. It is brown in color (light to dark) in the shape of a truncated cone. It can appear marbled, mottled, or both.

Features

Atrevia® One Large is a novel systemic ectoparasitic treatment against fleas, ticks and mites, based on *fluralaner*, which protects dogs up to 30 days. You can use it on infested animals or as a preventive. Control flea infestation in the environment and areas where the treated dog has access. It begins its action in 90 minutes and kills fleas in 8 hours and ticks in 12 hours. There are 4 commercial presentations according to the weight of the dog.

Atrevia® One Large is highly effective against fleas (*Ctenocephalides felis* and *Ctenocephalides canis*), ticks of different species in dogs (*Rhipicephalus sanguineus*, *Ixodes hexagonus*, *Ixodes scapularis*, *Ixodes ricinus*, *Ixodes holocyclus*, *Dermacentor reticulatus*, and *Dermacentor reticulatus* var. skin and ear (*Demodex canis*), *Sarcopes scabiei* var. *canis* and *Otodectes cynotis*). Effectiveness has also been observed against other ectoparasites such as lice (*Linognathus spp.*) and bed bugs (*Triatoma infestans*), a vector that transmits Chagas disease (American trypanosomiasis).

Atrevia® One Large can be used from 8 weeks age and 2 kg of weight and can be administered without restrictions in young or adult dogs, breeders, 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.

Atrevia® One Large can be used on dogs of any age and is particularly suitable for dogs in the early stages of their life, starting with a monthly flea and tick protection regimen; thus, owners can enjoy their puppies' early life experience with monthly dosing and then easily switch to the longer lasting **Atrevia® XR Large** as the dog reaches six months of age, helping to ensure treatment and consistent compliance. It is an ideal start for dogs in the early stages of their life.

Mechanism of Action, Pharmacokinetics and Pharmacodynamics

Atrevia® One Large contains *fluralaner*, a new molecule belonging to the class of isoxazolines. It represents a new class of potent parasiticide for the control of fleas, ticks and mites in dogs. It is a powerful blocker that acts in a non-competitive antagonistic way on the chloride channels of ionotropic receptors (γ -aminobutyric acid (GABA) and L-glutamate receptors) of the arthropod nervous system. It is much more selective for receptors in arthropods than in mammals, including humans (hence its large margin of safety). This coupling to the chloride channels of nerve and muscle cells blocks the transmission of nerve impulses from the parasite. Fleas, ticks, mites and other affected ectoparasites are paralyzed and die quickly.

Fluralaner acts systematically, that is, 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.

The life cycle of the ectoparasite is interrupted because:

- An orally administered dose of *fluralaner* begins to eliminate fleas (*Ctenocephalides felis*) in the dog from 90 minutes after treatment.
- The oral administration of *fluralaner* through chewable tablets, at the doses present in **Atrevia® One Large**, has shown effectiveness in the control of flea and tick infestations in dogs, for a minimum of 98 days, after 3 applications every 28 days.
- It has been shown that *fluralaner* can interfere with oviposition (egg laying), larval development (thus indicating its larvical action) and flea (*Ctenocephalides felis*) reproduction *in vitro*.
- *Fluralaner* contributes to the control of the environmental population of fleas in areas visited by treated dogs.

Fluralaner has shown significantly higher efficacy than other currently available molecules. In the same way, "in vitro" studies showed that parasites with reduced sensitivity to other molecules did not have any resistance to the action of *fluralaner* (against amidines, organophosphates, cyclodienes, macrocyclic lactones, phenylpyrazoles, benzophenyl-ureas, pyrethrins or carbamates). To date, there are no reports of resistance to *fluralaner* by fleas or ticks of dogs. Isoxazolines do not appear to be cross-resistant with other antiparasitics that act on the same receptors.

Fluralaner is readily and rapidly absorbed after single-dose oral administration, having a very long residual period. Due to the reduced bioavailability of the drug in the fasted state, *fluralaner* should be administered with food. *Fluralaner* is distributed systemically and reaches the highest concentrations in fat tissue, followed by liver, kidney and muscle.

Target Species

Dogs.

Indications of use

For the control of infestations of the main ectoparasites in dogs (ticks, fleas and mites) when protection is required for a month, whether in young dogs (e.g. in early stages between 2 to 6 months) or adults. Insecticide and systemic acaricide of immediate action.

- Treatment and prevention of flea infestations (*Ctenocephalides felis* and *Ctenocephalides canis*). Additionally, it controls the infestation of fleas in the environment and areas where the animal has access.

- Treatment and prevention of infestations by ticks (*Ixodes ricinus*, *Ixodes hexagonus*, *Ixodes scapularis*, *Ixodes holocyclus*, *Dermacentor reticulatus*, *Dermacentor variabilis* and *Rhipicephalus sanguineus* (adults and juveniles)).

- Treatment of skin mite infestations: demodicosis (*Demodex canis*) and sarcoptic mange

¹The chemical name for fluralaner is (1)-4-[5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl]-2-methyl-N-[2-oxo-2-(2,2,2-trifluoroethylamino)ethyl]benzamide.

²Atrevia® One

(*Sarcopes scabiei* var. *canis*)

- Treatment of infestations by ear mites (*Otodectes cynotis*).
- Treatment of infestations by bed bugs of the *Triatoma infestans* species.
- Treatment and prevention of lice infestations (*Linognathus spp.*) for 7 weeks.
- Control of flea bite allergy dermatitis (DAPP), as part of a therapeutic strategy.
- Protection against infections by *Babesia canis* (transmitted by ticks of the genus *Dermacentor reticulatus*).

Additional considerations regarding indications for use:

- The effectiveness of the product is linked to the attachment of fleas and ticks to the host and at the beginning of their feeding in order to be exposed to fluralaner. This effect occurs within 8 hours post fixation in the case of fleas and 12 hours post fixation in the case of ticks.

- The preventive effect against reinfestations is the result of adulticidal activity, the reduction in egg production (fleas die before producing viable eggs), their non-viability (very low concentrations of fluralaner stop production of viable eggs by fleas) and for its effect against the development of immature stages (ticks) and persists up to 4 weeks after a single administration.

- It has been shown that the residual effect of **Atrevia® One** on the control of fleas and ticks, after 3 applications every 28 days, is maintained for up to a minimum of 98 days.

- **Atrevia® One Large** contributes to the control of the environmental population of fleas in areas visited by treated dogs. Indeed, it has been shown that the environmental effect of **Atrevia® One** is capable of reducing flea infestations in untreated canines that live in the same environment as treated canines.

- In laboratory studies, fluralaner has also shown efficacy against mosquito larvae (*Aedes aegypti*) and culicids (*Lucilia cuprina*), adult female *Rhipicephalus* (*Boophilus microplus*), and nymphs of soft ticks (*Ornithodoros moubata*).

Route of Administration and Dosage, Considerations and Guidelines for its Correct Administration

Atrevia® One Large is administered orally, according to the following table (the doses correspond to 10-22 mg of fluralaner/kg of body weight within each weight range):

| Atrevia® One Soft chewable tablets | | | | | | |
|------------------------------------|-------------|-------------|-------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|
| Product | Pet's size | Body weight | Tablet 1,000 mg Fluralaner 50 mg | Tablet 2,000 mg Fluralaner 100 mg | Tablet 4,000 mg Fluralaner 200 mg | Tablet 8,000 mg Fluralaner 400 mg |
| Atrevia® One Mini | Mini dogs | 2 - 4.5 Kg | △ | | | |
| Atrevia® One Small | Small dogs | 4.5 - 10 Kg | | △ | | |
| Atrevia® One Medium | Medium dogs | 10 - 20 Kg | | | △ | |
| Atrevia® One Large | Large dogs | 20 - 40 Kg | | | | △ |

* For dogs weighing more than 40 kg, administer an appropriate combination of tablets.

Dosage frequency:

- Administer one **Atrevia® One Large** tablet every 30 days. The product can be administered throughout the year. **Atrevia® One Large** should be administered with food or immediately before or after eating. Do not divide the tablets.

- For the treatment of demodicetic, sarcoptic and/or otodectic scabies, administer one dose every 30 days for one to three consecutive months³. **Atrevia® One** has shown 100% effectiveness for the resolution of cases of acarosis (demodicosis, scabies or mixed scabies) after 3 consecutive treatments every 4 weeks. However, since demodicetic 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.

- The absence of mites can be confirmed by two consecutive scrapings every 15-30 days. If the mite infestation recurs, consult your veterinarian. For ear mite infestations, a veterinary check is necessary 28 days after treatment. The vet will decide if any additional treatment is necessary.

- The application of **Atrevia® One** helped 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.

Atrevia® One Large is a highly palatable, soft and chewable tablet, which facilitates its administration. Alternatively, if applicable, it can be administered with food or by opening the animal's mouth and placing the tablet in the back of the tongue like any other medicine.

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

In dogs older than 8 weeks, monthly treatment has been shown to be well tolerated. Puppies should be weighed regularly. Treatment can be tailored by the veterinarian to suit individual weight changes.

Studies carried out did not show statistical differences between the monthly treatment of **Atrevia® One** and a monthly application based on sarolaner.

Toxicology and Safety

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

Fluralaner has been shown to be safe in: Breeding, pregnant or lactating females. In a reproductive study, adult Beagle dogs were treated up to 3 times the recommended dose, 3 treatments at 8 week intervals, starting 12 weeks (males) and 4 weeks (females) prior to anticipated copulation. Treatment continued in males until the females were delivered, and in females until the offspring were weaning. No adverse effects were observed either in the adults, nor in their reproductive performance, nor in the number of puppies born or survivors.

Safety data collected on fluralaner during field studies in Europe and the USA showed that treated animals generally tolerate the product well at the recommended dose. In European studies, mild and transient diarrhea, vomiting, poor appetite and excessive salivation were observed in 1.6% of dogs in the first few days after treatment. Studies have shown that **Atrevia® One** is very well tolerated, reporting adverse effects in only 0.85% of cases.

Regarding the safety of the owner, as fluralaner is administered orally and acts systemically, no chemical residues are found on the dog's coat after treatment. For this reason, 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.

Finally, taking into account its action mechanism, fluralaner is extremely selective for arthropod receptors over those of mammals, including humans, further extending its large margin of safety.

Adverse reactions

- Tolerance and safety studies with **Atrevia® One** reported unwanted reactions in 0.85% of the treated animals, being diarrhea (0.28%), lethargy (0.28%) and polydipsia (0.28%) the only ones found.
- Despite the fact that there are reports of neurological reactions due to individual causes after the application of fluralaner, in studies carried out with **Atrevia® One** no case could be evidenced. However, if any are reported, an immediate visit to the veterinarian should be made to evaluate the animal.
- In general, dogs tolerate fluralaner very well at the therapeutic dose apart from the possible adverse reactions mentioned.
- A potential mistake when treating dogs that can cause overdose and therefore should be avoided is the administration to small dogs of tablets approved only for larger dogs.
- If you observe or suspect any serious reaction or others not mentioned, contact your veterinarian immediately.

Contraindications

- Do not use in case of known hypersensitivity to any of the active substances or to any excipient.
- There are no known contraindications to the use of the product.
- Do not use in dogs with severe liver disease or severe hypoproteinemia.

Precautions

- Do not use in dogs less than 8 weeks old or less than 2 kg in weight.
- Do not split or divide the **Atrevia® One Large** tablets.
- Do not administer **Atrevia® One Large** to animals of less weight, approved for dogs of greater body weight.
- Do not administer **Atrevia® One Large** at intervals of less than 30 days.
- When starting treatment, the risk of transmission of diseases mediated by ectoparasites is greatly reduced due to the rapid onset of action of **Atrevia® One Large**. However, as the parasites must initiate feeding in the pet to be exposed to fluralaner, the risk of the transmission of these diseases cannot be excluded.
- To help control the flea population, it is recommended to treat all the animals in the house with **Atrevia® One Large** at the same time.
- Fleas frequently infest the animal's basket, bedding, and usual resting areas, such as carpets and textiles, which should be treated with a suitable insecticide and vacuumed in case of massive infestation at the beginning of treatment.
- Fluralaner is a member of the isoxazole class. This class has been associated with neurological adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in dogs receiving isoxazole class medications, even in dogs without a history of seizures. Use cautiously 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 your hands after handling the tablets.
- Agrovet Market S.A. is not responsible for the consequences derived from the use (of the product) different from that indicated in this insert.

Interactions with other drugs and other forms of interaction

- None known.
- Due to its high binding to plasma proteins, fluralaner could act competitively with other drugs with similar pharmacological characteristics, including non-steroidal anti-inflammatory drugs (NSAIDs), warfarin, etc. Incubation of fluralaner in the presence of carprofen or warfarin in dog plasma at expected maximum plasma concentrations did not reduce the binding of fluralaner, carprofen, or warfarin proteins.
- The safety of fluralaner in combination with other active substances such as deltamethrin, milbemycin oxime, moxidectin, pyrantel, ivermectin or praziquantel has been documented.

Storage

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

Commercial presentation

Atrevia® One Large is presented in:
Box x 1, 2 or 4 soft chews in sealed aluminum blister x 8,000 mg - Large Dogs.

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