

Advocate Spot-on Solution

Species:Cats, Dogs, Ferrets

Therapeutic indication:Pharmaceuticals: Endoparasiticides: Anthelmintics for dogs, Anthelmintics for cats, For dogs, For cats, For companion animals

Active ingredient:Imidacloprid, Moxidectin

Product:Advocate® 40 mg + 4 mg spot-on solution for small cats and ferrets

Advocate® 80 mg + 8 mg spot-on solution for large cats

Advocate® 40 mg + 10 mg spot-on solution for small dogs

Advocate® 100 mg + 25 mg spot-on solution for medium dogs

Advocate® 250 mg + 62.5 mg spot-on solution for large dogs

Advocate® 400 mg + 100 mg spot-on solution for extra-large dogs

Product index:Advocate Spot-on Solution

Incorporating:Advocate 40 mg + 4 mg spot-on solution for small cats and ferrets

Advocate 80 mg + 8 mg spot-on solution for large cats

Advocate 40 mg + 10 mg spot-on solution for small dogs

Advocate 100 mg + 25 mg spot-on solution for medium dogs

Advocate 250 mg + 62.5 mg spot-on solution for large dogs

Advocate 400 mg + 100 mg spot-on solution for extra-large dogs

Presentation

Advocate spot-on solution for cats and ferrets is a clear yellow to brownish solution containing 100 mg/ml imidacloprid and 10 mg/ml moxidectin with benzyl alcohol and Butylhydroxytoluene 1 mg/ml (E 321 as an antioxidant). Each pipette of the small cat and ferret presentation contains 0.4 ml (40 mg imidacloprid, 4 mg moxidectin), the large cat presentation contains 0.8 ml (80 mg imidacloprid, 8 mg moxidectin).

Advocate spot-on solution for dogs is a clear yellow to brownish solution containing 100 mg/ml imidacloprid and 25 mg/ml moxidectin with benzyl alcohol and Butylhydroxytoluene 1 mg/ml (E321 as an antioxidant). Each pipette of the dog presentations contains either 0.4 ml (40 mg imidacloprid, 10 mg moxidectin), 1.0 ml (100 mg imidacloprid, 25 mg moxidectin), 2.5 ml (250 mg imidacloprid, 62.5 mg moxidectin) or 4.0 ml (400 mg imidacloprid, 100 mg moxidectin).

Uses

For use in cats, ferrets and dogs suffering from, or at risk from, mixed parasitic infections:

For cats:

- For the treatment and prevention of flea infestation (*Ctenocephalides felis*),
- the treatment of ear mite infestation (*Otodectes cynotis*),
- the treatment of notoedric mange (*Notoedres cati*),
- the treatment of the lungworm *Eucoleus aerophilus* (syn. *Capillaria aerophila*) (adults),
- the prevention of lungworm disease (L3/L4 larvae of *Aelurostrongylus abstrusus*),
- the treatment of the lungworm *Aelurostrongylus abstrusus* (adults),
- the treatment of the eye worm *Thelazia callipaeda* (adults),
- the prevention of heartworm disease (L3 and L4 larvae of *Dirofilaria immitis*),
- the treatment of infections with gastrointestinal nematodes (L4 larvae, immature adults and adults of *Toxocara cati* and *Ancylostoma tubaeforme*). The product can be used as part of a treatment strategy for flea allergy dermatitis (FAD).

For ferrets: For the treatment and prevention of flea infestation (*Ctenocephalides felis*) and the prevention of heartworm disease (L3 and L4 larvae of *Dirofilaria immitis*).

For dogs:

- For the treatment and prevention of flea infestation (*Ctenocephalides felis*),
- the treatment of biting lice (*Trichodectes canis*),
- the treatment of ear mite infestation (*Otodectes cynotis*)
- the treatment of sarcoptic mange (caused by *Sarcoptes scabiei* var. *canis*)
- the treatment of demodicosis (caused by *Demodex canis*),
- the prevention of heartworm disease (L3 and L4 larvae of *Dirofilaria immitis*),
- the treatment of circulating microfilariae (*Dirofilaria immitis*),
- the treatment of cutaneous dirofilariosis (adult stages of *Dirofilaria repens*),
- the prevention of cutaneous dirofilariosis (L3 larvae of *Dirofilaria repens*),
- the reduction of circulating microfilariae (*Dirofilaria repens*),
- the prevention of angiostrongylosis (L4 larvae and immature adults of *Angiostrongylus vasorum*),
- the treatment of *Angiostrongylus vasorum* and *Crenosoma vulpis*,
- the prevention of spirocercosis (*Spirocerca lupi*),
- the treatment of *Eucoleus* (syn. *Capillaria*) *boehmi* (adults),
- the treatment of the eye worm *Thelazia callipaeda* (adults),
- the treatment of infections with gastrointestinal nematodes (L4 larvae, immature adults and adults of *Toxocara canis*, *Ancylostoma caninum* and *Uncinaria stenocephala*, adults of *Toxascaris leonina* and *Trichuris vulpis*). The product can be used as part of a treatment strategy for flea allergy dermatitis (FAD).

Dosage and administration

Dosage schedule

The recommended minimum doses for cats are 10 mg/kg body weight imidacloprid and 1.0 mg/kg body weight moxidectin, equivalent to 0.1ml/kg body weight Advocate for cats.

Dosage schedule for ferrets: one pipette of Advocate spot-on solution for small cats and ferrets (0.4 ml) should be administered per animal. Do not exceed the recommended dose.

The recommended minimum doses for dogs are 10 mg/kg body weight imidacloprid and 2.5 mg/kg body weight moxidectin, equivalent to 0.1ml/kg body weight Advocate for dogs.

The treatment schedule for all species should be based on individual veterinary diagnosis and on the local epidemiological situation.

Cats (Refer to Table 1)

Table 1:

Weight of CAT [kg]	Pipette size to be used	Volume (ml)	Imidacloprid [mg/kg bw]	Moxidectin [mg/kg bw]
≤4kg	Advocate for small cats and ferrets	0.4	minimum of 10	minimum of 1
>4-8kg	Advocate for large cats	0.8	10-20	1-2
>8kg	the appropriate combination of pipettes			

Dogs(Refer to Table 2)

Table 2:

Weight of DOG [kg]	Pipette size to be used	Volume (ml)	Imidacloprid [mg/kg bw]	Moxidectin [mg/kg bw]
≤4kg	Advocate for small dogs	0.4	minimum of 10	minimum of 2.5
>4-10kg	Advocate for medium dogs	1.0	10-25	2.5-6.25
>10-25kg	Advocate for large dogs	2.5	10-25	2.5-6.25
>25-40kg	Advocate for extra-large dogs	4.0	10-16	2.5-4
>40kg	the appropriate combination of pipettes			

Flea treatment and prevention (*Ctenocephalides felis*)(Cats & Dogs)

One treatment prevents future flea infestation for 4 weeks. Existing pupae in the environment may emerge for 6 weeks or longer after treatment is initiated, depending upon climatic conditions. Therefore, it may be necessary to combine Advocate treatment with environmental treatments aimed at breaking the flea life cycle in the surroundings. This can result in a more rapid reduction in the household flea population. The product should be administered at monthly intervals when used as part of a treatment strategy for flea allergy dermatitis.

Flea treatment and prevention (*Ctenocephalides felis*) (Ferrets)

One treatment prevents future flea infestation for 3 weeks. Under heavy flea pressure it may be necessary to repeat the dose after 2 weeks.

Treatment of ear mite infestation (*Otodectes cynotis*) (Cats & Dogs)

A single dose of the product should be administered. In dogs, loose debris should be gently removed from the external ear canal at each treatment. For both cats and dogs, a further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment. Do not apply directly to the ear canal.

Treatment of biting lice (*Trichodectes canis*) (Dogs)

A single dose should be administered. A further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment.

Treatment of sarcoptic mange (caused by *Sarcoptes scabiei* var. *canis*) (Dogs)

A single dose should be administered twice 4 weeks apart.

Treatment of notoedric mange (*Notoedres cati*) (Cats)

A single dose of the product should be administered.

Treatment of the lungworm *Eucoleus aerophilus* (syn. *Capillaria aerophila*) (adults) (Cats)

A single dose of the product should be administered.

Prevention of *Aelurostrongylus abstrusus* (Cats)

The product should be administered monthly.

Treatment of *Aelurostrongylus abstrusus* (Cats)

Advocate should be administered monthly for three consecutive months.

Treatment of *Eucoleus* (syn. *Capillaria*) *boehmi* (adults)(Dogs)

The product should be administered monthly for two consecutive months. It is advisable to prevent auto-coprophagia between the two treatments in order to prevent possible reinfection.

Treatment of the eye worm *Thelazia callipaeda* (adults)(Cats & Dogs)

A single dose of the product should be administered.

Treatment of demodicosis (caused by *Demodex canis*) (Dogs)

The administration of a single dose every 4 weeks for 2 to 4 months is efficacious against *Demodex canis* and leads to a marked improvement of clinical signs particularly

in mild to moderate cases. Especially severe cases may require more prolonged and more frequent treatment. To achieve the best possible response in these severe cases, at the discretion of the veterinarian, Advocate can be applied once a week and for a prolonged time. In all cases it is essential that the treatment should be continued until skin scrapings are negative on at least 2 consecutive monthly occasions. Treatment should be stopped in dogs that show no improvement or do not respond in mite count after 2 months treatment. Alternative treatment should be administered. Seek the advice of your veterinarian.

As demodicosis is a multi-factorial disease, where possible, it is advisable to also treat any underlying disease appropriately.

Prevention of heartworm disease (*D.immitis*) (Cats, Ferrets & Dogs) and cutaneous dirofilariosis (*D. repens*) (Dogs)

Cats, ferrets and dogs in areas endemic for heartworm, or those which have travelled to endemic areas, may be infected with adult heartworms. Therefore prior to treatment with Advocate, the advice provided in Contra-Indications and Warnings etc should be considered. For prevention of heartworm disease and cutaneous dirofilariosis, the product must be applied at regular monthly intervals during the time of the year when mosquitoes (the intermediate hosts which carry and transmit *D. immitis* and *D. repens* larvae) are present. The product may be administered throughout the year or at least 1 month before the first expected exposure to mosquitoes. Treatment should continue at regular monthly intervals until 1 month after the last exposure to mosquitoes. To establish a treatment routine, it is recommended that the same day or date be used each month. When replacing another heartworm preventative product in a heartworm prevention programme, the first treatment with Advocate must be given within 1 month of the last dose of the former medication. In non-endemic areas there should be no risk of animals having heartworm. Therefore they can be treated without special precautions.

Treatment of microfilariae (*D. immitis*) (Dogs)

Advocate should be administered monthly for two consecutive months.

Treatment of cutaneous dirofilariosis (skin worm) (adult stages of *Dirofilaria repens*) (Dogs)

Advocate should be administered monthly for six consecutive months.

Reduction of microfilariae (skin worm) (*D. repens*) (Dogs)

The product should be administered monthly for four consecutive months.

Roundworm and hookworm treatment (*Toxocara cati* and *Ancylostoma tubaeforme*) (Cats)

In areas endemic for heartworm, monthly treatment may significantly reduce the risk of re-infection caused by the respective roundworms and hookworms. In areas non-endemic for heartworm, the product can be used as part of a seasonal prevention programme against fleas and gastrointestinal nematodes.

Roundworm, hookworm and whipworm treatment (*Toxocara canis*, *Ancylostoma caninum*, *Uncinaria stenocephala*, *Toxascaris leonina* and *Trichuris vulpis*) (Dogs)

In areas endemic for heartworm, monthly treatment may significantly reduce the risk of re-infection caused by the respective round-, hook- and whipworms. In areas non-endemic for heartworm, the product can be used as part of a seasonal prevention programme against fleas and gastrointestinal nematodes. Studies have shown that monthly treatment of dogs will prevent infections caused by *Uncinaria stenocephala*.

Treatment and Prevention of *Angiostrongylus vasorum* (Dogs)

A single dose should be administered. A further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment.

In endemic areas regular four weekly application will prevent angiostrongylosis and patent infection with *Angiostrongylus vasorum*.

Treatment of *Crenosoma vulpis* (Dogs)

A single dose should be administered

Prevention of spirocercosis *Spirocerca lupi* (Dogs)

The product should be administered monthly.

Method of administration

For external use only.

Remove one pipette from the package. Then hold the pipette in an upright position, and twist and pull off the cap. Reverse the cap and use it to twist and remove the seal from the pipette, as shown. See Figure 1.

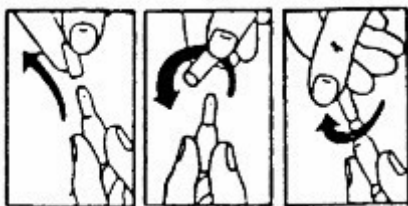


Figure 1: Opening a pipette

Cats and Ferrets

Part the fur on the animal's neck at the base of the skull until the skin is visible. Place the tip of the pipette on the skin and squeeze the pipette firmly several times to empty its contents directly onto the skin. Application at the base of the skull will minimise the opportunity for the animal to lick the product. Apply only to undamaged skin. See Figure 2.

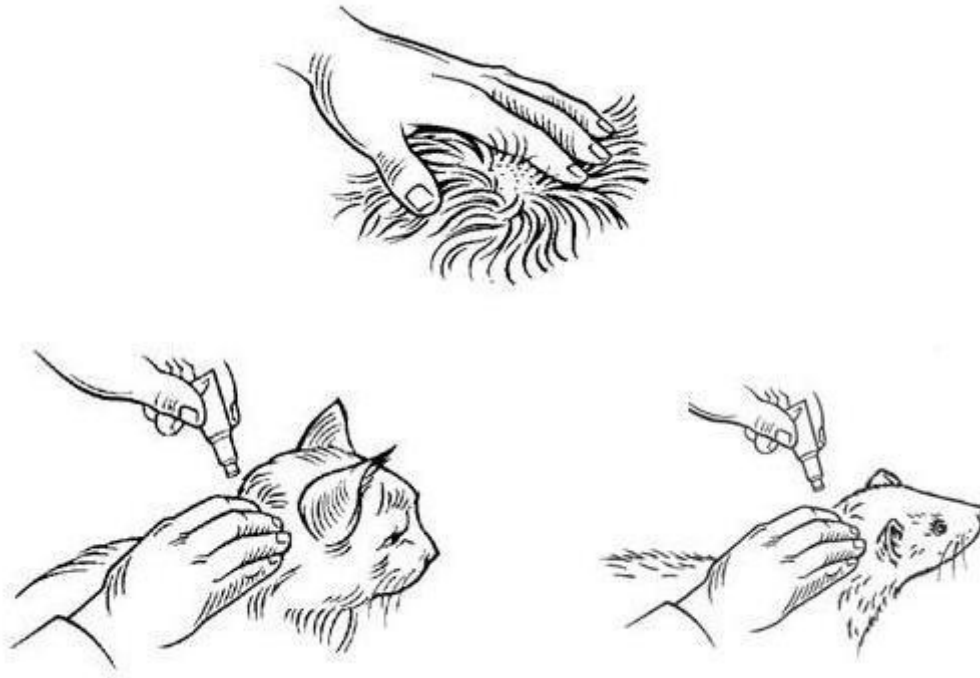


Figure 2: Administration to the Cat or Ferret

For dogs up to 25kg

With the dog in a standing position, part the coat between the shoulder blades until the skin is visible. Wherever possible apply to undamaged skin. Place the tip of the pipette on the skin and squeeze the pipette firmly several times to empty its contents directly onto the skin. See Figure 3.



Figure 3: Administration to dogs up to 25kg

For dogs of more than 25 kg

For easy application the dog should be standing. The entire contents of the pipette should be applied evenly as 3 or 4 spots along the top of the back, from between the shoulders to the base of the tail. At each spot, part the coat until the skin is visible. Wherever possible apply to undamaged skin. Place the tip of the pipette on the skin and gently squeeze the pipette to expel a portion of its contents directly onto the skin. Do not apply an excessive amount of solution at any one spot, as that could cause some of the product to run down the animal's side. See Figure 4.

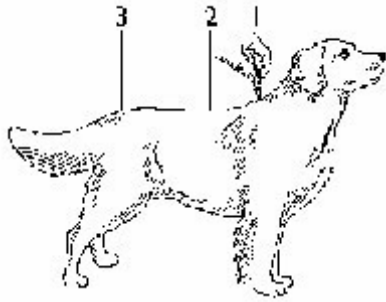


Figure 4: Administration to dogs over 25kg

Use During Pregnancy and Lactation

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Laboratory studies with either imidacloprid or moxidectin in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects. Use only according to the risk-benefit assessment by the responsible veterinarian.

Contra-indications, warnings, etc

Do not use in kittens under 9 weeks of age.

Do not use in puppies under 7 weeks of age.

Treatment of cats or dogs weighing less than 1 kg, and ferrets weighing less than 0.8 kg should be based on a risk-benefit assessment.

Do not use in the cases of hypersensitivity to the active substances or to any of the excipients.

There is limited experience on the use of the product in sick and debilitated animals, thus the product should only be used based on a risk-benefit assessment for these animals.

For cats, the corresponding "Advocate spot-on solution for cat" product, which contains 100 mg/ml imidacloprid and 10 mg/ml moxidectin, must be used.

For ferrets: Do not use Advocate for large cats (0.8ml) or Advocate for dogs (any size), only "Advocate for small cats and ferrets" (0.4 ml) must be used. The product's efficacy has not been tested in ferrets weighing over 2 kg and therefore the duration of effect might be shorter in these animals.

For dogs, the corresponding "Advocate for dog" product, which contains 100 mg/ml imidacloprid and 25 mg/ml moxidectin, must be used.

Do not use on canaries.

The product tastes bitter. Salivation may occasionally occur if the animal licks the application site immediately after treatment. This is not a sign of intoxication and disappears within some minutes without treatment. Correct application will minimise licking of the application site.

In case of accidental oral uptake, symptomatic treatment should be administered. There is no known specific antidote. The use of activated charcoal may be beneficial. After accidental oral ingestion (e.g. licking at the site of application) or overdose, neurological

signs (most of which are transient) such as ataxia, generalised tremors, ocular signs (dilated pupils, little pupillary reflex, nystagmus), abnormal respiration, salivation and vomiting may be observed in very rare cases.

The use of the product may result in transient pruritus in the animal. On rare occasions greasy fur, erythema and vomiting can occur. These signs disappear without further treatment. The product may, in rare cases cause local hypersensitivity reactions. The product may in very rare cases cause at the application site a sensation resulting in transient behavioural changes such as lethargy, agitation, and inappetence.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

Care should be taken that the contents of the pipette or the applied dose does not come into contact with the eyes or mouth of the recipient and/or other animals.

Do not allow recently treated animals to groom each other.

When the product is applied in 3 to 4 separate spots in larger dogs, specific care should be taken to prevent the animal licking the application sites. Oral uptake by Collies, Old English Sheepdogs and related breeds or crossbreeds should be prevented.

During treatment with Advocate no other antiparasitic macrocyclic lactone should be administered. This product contains moxidectin (a macrocyclic lactone), therefore special care should be taken with Collies, Old English Sheepdogs and related breeds or crossbreeds, to correctly administer the product as described above. In particular, oral uptake by the recipient and/or other animals in close contact should be prevented.

Ivermectin-sensitive Collie dogs tolerated up to 5 times the recommended dose repeated at monthly intervals without any adverse effects, but the safety of application at weekly intervals has not been investigated in ivermectin-sensitive Collie dogs. When 40% of the unit dose was given orally, severe neurological signs were observed. Oral administration of 10% of the recommended dose produced no adverse effects.

Up to 10 times the recommended dose was tolerated in adult dogs with no evidence of adverse effects or undesirable clinical signs. Five times the recommended minimum dose applied at weekly intervals for 17 weeks was investigated in dogs aged over 6 months and tolerated with no evidence of adverse effects or undesirable clinical signs.

Up to 10 times the recommended dose was tolerated in cats with no evidence of adverse effects or undesirable clinical signs.

The product was administered to kittens and puppies at up to 5 times the recommended dose, every 2 weeks for 6 treatments, and there were no serious safety concerns. Transient mydriasis, salivation, vomiting and transient rapid respiration were observed.

The product was administered to ferrets at 5 times the recommended dose, every 2 weeks for 4 treatments, and there was no evidence of adverse effects or undesirable clinical signs.

It is recommended that cats and ferrets living in, or travelling to areas endemic for heartworm are treated monthly with the product to protect them from heartworm disease. Whilst the accuracy of diagnosis of heartworm infection is limited, it is recommended that attempts be made to check the heartworm status of any cat and ferret aged over 6 months, before beginning prophylactic treatment, as use of the product on cats or ferrets which have adult heartworms may cause serious adverse effects, including death. If adult heartworm infection is diagnosed, the infection should be treated in accordance with current scientific knowledge.

Although experimental overdosage studies have shown that the product may be safely administered to dogs infected with adult heartworms, it has no therapeutic effect against adult *Dirofilaria immitis*. It is therefore recommended that all dogs 6 months of age or more, living in areas endemic for heartworm, should be tested for existing adult heartworm infection before being treated with the product. At the discretion of the veterinarian, infected dogs should be treated with an adulticide to remove adult heartworms. The safety of Advocate has not been evaluated when administered on the same day as an adulticide.

Dogs infected with adult heartworms tolerated up to 5 times the recommended dose, every 2 weeks for 3 treatments, without any adverse effects.

The safety of the product has only been evaluated in dogs classified as either Class 1 or 2 for heartworm disease in laboratory studies and in a few Class 3 dogs in a field study. Therefore the use in dogs with obvious or severe symptoms of the disease should be based on a careful benefit risk assessment by the treating veterinarian.

Do not use in dogs classified as Class 4 for heartworm disease as the safety of the product has not been evaluated in this animal group.

A field study has shown that in heartworm positive dogs with microfilaraemia there is a risk of severe respiratory signs (coughing, tachypnoea and dyspnoea) that may require prompt veterinary treatment. In the study these reactions were common (seen in 2 of 106 treated dogs). Gastrointestinal signs (vomiting, diarrhoea, inappetence) and lethargy are also common adverse reactions following treatment in such dogs.

Efficacy against adult *Dirofilaria repens* has not been tested under field conditions.

In certain individual cats *Notoedres cati* infestation may be severe. In these severe cases concomitant supportive treatment is necessary as treatment with the product alone may not be sufficient to prevent death of the animal.

Imidacloprid is toxic to birds, especially canaries.

No interactions between Advocate and routinely used veterinary medicinal products or medical or surgical procedures have been observed.

Safety of Advocate when administered on the same day as an adulticide to remove adult heartworms has not been evaluated.

Brief contact of the animal with water on one or two occasions between monthly treatments is unlikely to significantly reduce the efficacy of the product. However, frequent shampooing or immersion of the animal in water after treatment may reduce the efficacy of the product.

Parasite resistance to any particular class of anthelmintic may develop following frequent, repeated use of an anthelmintic of that class. Therefore, the use of this product should be based on the assessment of each individual case and on local epidemiological information about the current susceptibility of the target species in order to limit the possibility of a future selection for resistance.

The use of the product should be based on the confirmed diagnosis of mixed infection (or risk of infection, where prevention applies) at the same time.

The solvent in Advocate may stain or damage certain materials including leather, fabrics, plastics and finished surfaces. Allow the application site to dry before permitting contact with such materials.

User Safety

Avoid contact with skin, eyes or mouth.

Do not eat, drink or smoke during application.

Wash hands thoroughly after use.

In case of accidental spillage onto skin, wash off immediately with soap and water.

After application do not stroke or groom animals until the application site is dry.

People with a known hypersensitivity to benzyl alcohol, imidacloprid or moxidectin should administer the product with caution. In very rare cases the product may cause skin sensitisation or transient skin reactions (for example numbness, irritation or burning/tingling sensation). In very rare cases the product may cause respiratory irritation in sensitive individuals.

If the product accidentally gets into eyes, they should be thoroughly flushed with water.

If skin or eye symptoms persist, or the product is accidentally swallowed, seek medical advice immediately and show the package leaflet or the label to the physician.

Environmental Safety

Advocate should not be allowed to enter water courses as it has harmful effects on aquatic organisms: moxidectin is highly toxic to aquatic organisms. Dogs should not be allowed to swim in surface waters for 4 days after treatment.

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

Pharmaceutical precautions

Do not store above 30°C.

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years

Legal category

Legal category: POM-V

Packaging quantities

White polypropylene unit dose pipette with screw cap.

<i>Product name</i>	<i>Pack</i>
Advocate Spot-on solution for Small Cats and Ferrets	Blister pack containing 3, 6 or 21 unit dose pipettes: 0.4 ml per pipette
Advocate Spot-on solution for Large Cats	Blister pack containing 3, 6 or 21 unit dose pipettes: 0.8 ml per pipette
Advocate Spot-on solution for Small Dogs	Blister pack containing 3 or 21 unit dose pipettes: 0.4 ml per pipette
Advocate Spot-on solution for Medium Dogs	Blister pack containing 3, 6 or 21 unit dose pipettes: 1.0 ml per pipette
Advocate Spot-on solution for Large Dogs	Blister pack containing 3, 6 or 21 unit dose pipettes: 2.5 ml per pipette
Advocate Spot-on solution for Extra-Large Dogs	Blister pack containing 3, 6 or 21 unit dose pipettes: 4.0ml per pipette

Further information

Pharmacotherapeutic group: therapeutic antiparasitic agent; ATCvet code: QP54AB52.

Imidacloprid, 1-(6-Chloro-3-pyridylmethyl)-N-nitro-imidazolidin-2-ylideneamine is an ectoparasiticide belonging to the chloronicotinyl group of compounds. Chemically, it is more accurately described as a chloronicotinyl nitroguanidine. Imidacloprid is effective against larval flea stages and adult fleas. Flea larvae in the pet's surroundings are killed after contact with a pet treated with the product. Imidacloprid has a high affinity for the nicotinic acetylcholine receptors in the post-synaptic region of the central nervous system (CNS) of the flea. The ensuing inhibition of cholinergic transmission in insects results in paralysis and death. Due to the weak nature of the interaction with mammalian nicotinic receptors and the postulated poor penetration through the blood-brain barrier in mammals, it has virtually no effect on the mammalian CNS. Imidacloprid has minimal pharmacological activity in mammals.

Moxidectin, 23-(O-methyloxime)-F28249 alpha is a second-generation macrocyclic lactone of the milbemycin family. It is a parasiticide which is active against many internal and external parasites. Moxidectin is active against larval stages of *Dirofilaria immitis* (L1, L3, L4) and *Dirofilaria repens* (L1, L3). It is also active against gastrointestinal nematodes. Moxidectin interacts with GABA and glutamate-gated chloride channels. This leads to opening of the chloride channels on the postsynaptic junction, the inflow of chloride ions and induction of an irreversible resting state. The result is flaccid paralysis of affected parasites, followed by their death and/or expulsion.

The drug has a persistent action and protects dogs for 4 weeks after a single application against re-infection with the following parasites: *Dirofilaria immitis*, *Dirofilaria repens*, *Angiostrongylus vasorum*, and cats for 4 weeks after a single application against reinfection with *Dirofilaria immitis*.

After topical administration of the product, imidacloprid is rapidly distributed over the animal's skin within one day of application. It can be found on the body surface throughout the treatment interval. Moxidectin is absorbed through the skin, reaching maximum plasma concentrations approximately 1 to 2 days after treatment in cats and approximately 4 to 9 days after treatment in dogs. Following absorption from the skin,

moxidectin is distributed systemically throughout the body tissues but due to its lipophilicity it is concentrated mainly in the fat. It is slowly eliminated from the plasma as manifested by detectable moxidectin concentrations in plasma throughout the treatment interval of one month.

The mean T_½ in cats ranges between 18.7 and 25.7 days. The T_½ in dogs is about 28.4 days.

Studies evaluating the pharmacokinetic behaviour of moxidectin after multiple applications have indicated that steady state serum levels are achieved following approximately 4 consecutive monthly treatments in cats and dogs.

Marketing Authorisation Holder (if different from distributor)

Marketing Authorisation Holder

Bayer Animal Health GmbH, D-51368 Leverkusen, Germany

Distributed by

UK: Bayer plc, 400 South Oak Way, Green Park, Reading, Berkshire, RG2 6AD

Ireland: Bayer Ltd, The Atrium, Blackthorn Road, Sandyford Ind Est, Dublin 18

Marketing Authorisation Number

EU/2/03/039/001 - 005

EU/2/03/039/007 - 012

EU/2/03/039/019, EU/2/03/039/021, EU/2/03/039/023, EU/2/03/039/025,

EU/2/03/039/027, EU/2/03/039/029

Significant changes

GTIN

GTIN description: Advocate Spot-on solution for Small Cats and Ferrets (3 Pack)

GTIN:04007221016878

GTIN description: Advocate Spot-on solution for Small Cats and Ferrets (6 Pack)

GTIN:04007221020691

GTIN description: Advocate Spot-on solution for Small Cats and Ferrets (21 Pack)

GTIN:04007221039594

GTIN description: Advocate Spot-on solution for Large Cats (3 Pack)

GTIN:04007221016885

GTIN description: Advocate Spot-on solution for Large Cats (6 Pack)

GTIN:04007221020684

GTIN description: Advocate Spot-on solution for Large Cats (21 Pack)

GTIN:04007221039600

GTIN description: Advocate Spot-on solution for Small Dogs (3 Pack)

GTIN:04007221016892

GTIN description: Advocate Spot-on solution for Small Dogs (21 Pack)

GTIN:04007221039570

GTIN description:Advocate Spot-on solution for Medium Dogs (3 Pack)

GTIN:04007221016908

GTIN description:Advocate Spot-on solution for Medium Dogs (6 Pack)

GTIN:04007221020677

GTIN description:Advocate Spot-on solution for Medium Dogs (21 Pack)

GTIN:04007221039617

GTIN description:Advocate Spot-on solution for Large Dogs (3 Pack)

GTIN:04007221016915

GTIN description:Advocate Spot-on solution for Large Dogs (6 Pack)

GTIN:04007221020660

GTIN description:Advocate Spot-on solution for Large Dogs (21 Pack)

GTIN:04007221039587

GTIN description:Advocate Spot-on solution for Extra-large Dogs (3 Pack)

GTIN:04007221016922

GTIN description:Advocate Spot-on solution for Extra-large Dogs (6 Pack)

GTIN:04007221020653

GTIN description:Advocate Spot-on solution for Extra-large Dogs (21 Pack)

GTIN:04007221039563

Bayer plc

Telephone:0118 206 3000

Website:www.bayer.co.uk

Email:animal.health@bayer.com