SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advantix Spot-on solution for dogs over 25 kg up to 40 kg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pipette of 4.0 ml contains:

Active substances:

Imidacloprid: 400.0 mg
Permethrin (40/60): 2000.0 mg Excipient(s):

N-Methylpyrrolidone: 1936 mg
Butylhydroxytoluene (E321): 4.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Spot-on solution
Clear yellowish to brownish solution

4. CLINICAL PARTICULARS

4.1 Target species

Dogs (over 25 kg up to 40 kg)

For dogs less than or equal to 25 kg or more than 40 kg body weight, use the appropriate Advantix Spot-on solution product (see section 4.9).

4.2 Indications for use, specifying the target species

For the treatment and prevention of flea (*Ctenocephalides canis*, *Ctenocephalides felis*) infestation.

Fleas on dogs are killed within one day following treatment. One treatment prevents further flea infestation for four weeks. The product can be used as part of a treatment strategy for flea allergy dermatitis (FAD).

For the treatment of biting lice (*Trichodectes canis*).

The product has persistent acaricidal and repellent efficacy against tick infestations (*Rhipicephalus sanguineus* and *Ixodes ricinus* for four weeks, and *Dermacentor reticulatus* for three weeks).
By repelling and killing the tick vector *Rhipicephalus sanguineus,* the product reduces the likelihood of transmission of the pathogen *Ehrlichia canis,* thereby reducing the risk of canine ehrlichiosis. The reduction in risk has been shown in studies to commence from 3 days following application of the product and to persist for 4 weeks.
Ticks already on the dog may not be killed within two days after treatment and may remain attached and visible. Therefore the removal of ticks already on the dog at the time of treatment is recommended, in order to prevent them from attaching and having a blood meal.

One treatment provides repellent (anti-feeding) activity against sand flies (*Phlebotomus papatasi* for two weeks and *Phlebotomus perniciosus* for three weeks), against mosquitoes (*Aedes aegypti* for two weeks and *Culex pipiens* for four weeks) and against stable flies (*Stomoxys calcitrans*) for four weeks.

Reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies (*Phlebotomus perniciosus*) for up to 3 weeks. The effect is indirect due to product's activity against the vector.

4.3 Contraindications

In the absence of available data the product should not be used on puppies of less than 7 weeks of age or 25 kg of weight.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.
Do not use on cats. (Refer to section 4.5 – Special precautions for use).

4.4 Special warnings for each target species

There may be an attachment of single ticks or bites by single sand flies or mosquitoes. For this reason, a transmission of infectious diseases by these parasites cannot be completely excluded if conditions are unfavourable.

It is recommended to apply the treatment at least 3 days before expected exposure to *E. canis*. With regard to *E. canis*, studies have demonstrated a reduced risk of canine ehrlichiosis in dogs exposed to *Rhipicephalus sanguineus* ticks infected with *E. canis* from 3 days following application of the product and to persist for 4 weeks.

Immediate protection against sandflies bites is not documented. Treated dogs for the reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies *P. perniciosus* should be kept in a protected environment during the first 24 hours after the initial treatment application.

4.5 Special precautions for use

i) Special precautions for use in animals

Care should be taken to avoid the content of the pipette coming into contact with the eyes or mouth of the recipient dogs.

Care should be taken to administer the product correctly as described under section 4.9. In particular oral uptake due to the licking of the application site by treated or in-contact animals should be avoided.

Do not use on cats.

This product is extremely poisonous to cats and could be fatal due to the unique physiology of cats which is unable to metabolise certain compounds including permethrin. To prevent cats from being accidentally exposed to the product, keep treated dogs away from cats after treatment until the application site is dry. It is important to ensure that cats do not groom the site of application on a dog, which has been treated with this product. Seek veterinary advice immediately if this occurs.

Consult your veterinary surgeon before using the product on sick and debilitated dogs.

ii) Special precautions to be taken by the person administering the veterinary medicinal product to animals

Avoid contact between the product and 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. People with known skin sensitivity may be particularly sensitive to this product.
The predominant clinical symptoms that in extremely rare case may be shown are transient sensory irritations of the skin like tingling, burning sensation or numbness.
If the product gets accidentally into the eyes, they should be thoroughly flushed with water. If skin or if eye irritation persists obtain medical attention immediately and show the package insert to the physician.
Do not ingest. In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.
Treated dogs should not be handled especially by children until the application site is dry. This may be ensured by treating the dogs e.g. in the evening. Recently treated dogs should not be allowed to sleep together with their owner, especially children.
In order to prevent children from getting access to pipettes, keep the pipette in the original packaging until ready for use and dispose of used pipettes immediately.

Laboratory studies in rabbits and rats with the excipient N-Methylpyrrolidone have shown evidence of foetotoxic effects. The veterinary medicinal product should not be administered by pregnant women and women suspected of being pregnant. Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product by women of childbearing age.

iii) Other precautions

As the product is dangerous to aquatic organisms, treated dogs must not under any circumstances be allowed into any type of surface water for at least 48 hours after treatment.

The solvent in Advantix Spot-on solution may stain certain materials including leather, fabrics, plastics and finished surfaces. Allow the application site to dry before permitting contact with such materials.

4.6 Adverse reactions (frequency and seriousness)

Application site itching and hair change (e.g. greasy fur) and vomiting were uncommonly observed in clinical studies. Other reactions like redness, inflammation and hair loss at the application site and diarrhoea were reported rarely.

On very rare occasions reactions in dogs including transient skin sensitivity (scratching and rubbing) or lethargy were reported in spontaneous (pharmacovigilance) reports. These reactions are generally self-resolving.

In very rare cases dogs may show behaviour changes (agitation, restlessness, whining or rolling), gastro-intestinal symptoms (hypersalivation, diminished appetite) and neurological signs such as unsteady movement and twitching in dogs susceptible to the ingredient permethrin. These signs are generally transient and self-resolving.

Poisoning following inadvertent oral uptake in dogs is unlikely but may occur in very rare cases. In this event, neurological signs such as tremor and lethargy can occur. Treatment should be symptomatic. There is no known specific antidote.

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).

4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

The recommended minimum dose is:
10 mg/kg body weight (bw) imidacloprid and 50 mg/kg body weight (bw) permethrin.

Dosing Scheme for Advantix Spot-on:

Dogs (kg body weight)	Trade name	Volume (ml)	Imidacloprid (mg/kg body weight)	Permethrin (mg/kg body weight)
≤ 4 kg	Advantix Spot-on for dogs up to 4 kg	0.4 ml	minimum of 10	minimum of 50
>4 kg ≤ 10 kg	Advantix Spot-on for dogs over 4 kg up to 10 kg	1.0 ml	10 - 25	50 - 125
>10 kg ≤ 25 kg	Advantix Spot-on for dogs over 10 kg up to 25 kg	2.5 ml	10 - 25	50 - 125
>25 kg ≤ 40 kg	Advantix Spot-on for dogs over 25 kg up to 40 kg	4.0 ml	10 - 16	50 - 80

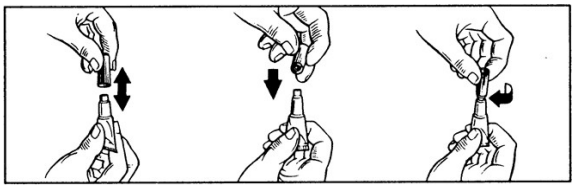
To reduce re-infestation from emergence of new fleas, it is recommended to treat all dogs in a household. Other animals living in the same household should also be treated with a suitable product. To aid further in reducing environmental challenge, the additional use of a suitable environmental treatment against adult fleas and their developmental stages is recommended.

The product remains effective if the animal becomes wet. However, prolonged, intense exposure to water should be avoided. In cases of frequent water exposure the persistent efficacy may be reduced. In these cases do not retreat more frequently than once weekly. If a dog requires a shampoo, it should be administered before applying Advantix or at least 2 weeks after application, to optimise efficacy of the product.

In case of biting louse infestation, a further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment.

To protect a dog over the whole sand fly season, treatment should be compliantly continued throughout.

For dermal use only. Apply only to undamaged skin. Method for administration:
Remove one pipette from the package. Hold applicator pipette in an upright position, twist and pull cap off. Turn the cap around and place the other end of cap back on pipette. Twist cap to break seal, then remove cap from pipette.



For dogs 10 kg body weight or less:

With the dog standing still, part the coat between the shoulder blades until the skin is visible. Place the tip of the pipette on the skin and squeeze firmly several times to empty the contents directly onto the skin.

For dogs of more than 10 kg body weight:

With the dog standing still, the entire contents of the Advantix pipette should be applied evenly to four spots on the top of the back from the shoulder to the base of the tail. At each spot, part the hair until the skin is visible. Place the tip of the pipette on the skin and gently squeeze to expel a portion of the solution on the skin. Do not apply an excessive amount of solution at any one spot that could cause some of the solution to run off the side of the dog.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No adverse clinical signs were noted in healthy puppies or adult dogs exposed to 5x overdosage or for puppies whose mothers were treated with 3x overdosage of the product.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antiparasitic agent, ATC vet code: QP53AC54

Advantix Spot-on is an ectoparasiticide for topical use containing imidacloprid and permethrin. This combination acts as an insecticide, acaricide and as a repellent.

Pharmacodynamic properties

Imidacloprid is an ectoparasiticide belonging to the chloronicotinyl group of compounds. Chemically, it can be classified as a chloronicotinyl nitroguanidine. Imidacloprid is effective against adult fleas and larval flea stages. In addition to the adulticide flea efficacy of imidacloprid, a larvicidal flea efficacy in the surroundings of the treated pet has been demonstrated. Larval stages in the dog`s immediate surroundings are killed following contact with a treated animal. It has a high affinity for the nicotinergic acetylcholine

receptors in the post-synaptic region of the central nervous system (CNS) in insects. The ensuing inhibition of cholinergic transmission in insects results in paralysis and death of the parasite.

Permethrin belongs to the type I class of pyrethroid acaricides and insecticides and also acts as repellent. Pyrethroids affect the voltage-gated sodium channels in vertebrates and non-vertebrates. Pyrethroids are so called “open channel blockers” affecting the sodium channel by slowing both the activation and the inactivation properties thus leading to hyperexcitability and death of the parasite.

In the combination of both substances, it has been shown Imidacloprid functions as the activator of arthropod ganglion and therefore increases the efficacy of permethrin.

The product provides repellent (anti-feeding) activity against ticks, sand flies and mosquitoes, thus preventing the repelled parasites from taking a blood meal and thus reducing the risk of Canine Vector-Borne Disease (CVBD) transmission (e.g. borreliosis, rickettsiosis, ehrlichiosis, leishmaniosis). However, there may be an attachment of single ticks or bites by single sand flies or mosquitoes. For this reason, a transmission of infectious diseases by these parasites cannot be completely excluded if conditions are unfavourable. The product provides repellent (anti-feeding) activity against stable flies thereby assisting in the prevention of fly-bite dermatitis.

The product provides repellent activity (anti-feeding activity) against *Phlebotomus perniciosus* (> 80% for 3 weeks), mosquitoes and ticks. Field data from an endemic area showed that the product indirectly reduces the risk of transmission of *Leishmania infantum* from infected sandflies (*Phlebotomus perniciosus*) for up to 3 weeks, thereby reducing the risk of canine leishmaniosis in treated dogs.

5.2 Pharmacokinetic particulars

The product is indicated for dermal administration. Following topical application in dogs, the solution rapidly distributes over the body surface of the animal. Both active substances remain detectable on the skin and hair of the treated animal for 4 weeks.

Acute dermal studies in the rat and target animal, overdose and serum kinetic studies have established that systemic absorption of both active substances after application on intact skin is low, transient and not relevant for the clinical efficacy.

5.3 Environmental properties

The product should not be allowed to enter water courses as this may be dangerous for fish and aquatic organisms. For treated dogs, please see section 4.5.

Permethrin containing products are toxic to honey bees.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene (E321) N-Methylpyrrolidone Miglyol 812

Citric acid (E330)

6.2 Major incompatibilities

None known.

6.3 Shelf life

Shelf-life of product in foil pouch: 5 years.

Shelf life of product after opening foil pouch: 2 years
(all pipettes should be used within 2 years after opening the foil pouch or before expiry date on the pipette whichever is shorter).

Shelf-life of the broached pipette: Not applicable, once opened, the entire content of the pipette has to be applied to the animal's skin.

6.4 Special precautions for storage

Do not freeze.
After opening the foil pouch store in a dry place at a temperature not above 30°C.

6.5 Nature and composition of immediate packaging

Fill volume: 4.0 ml clear yellowish to brownish, non-aqueous solution per 4 ml pipette
(400 mg imidacloprid, 2000 mg permethrin).

Type of the container: White polypropylene pipette.
White polypropylene cap.

Material of the secondary packaging: Polychlorotrifluoroethylene PCTFE/PVC heat sealed blister packs in one or more aluminium pouch(es) and a cardboard box.

Package sizes: Packs containing 1, 2, 3, 4, 6 and 24 unit dose pipettes. Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

After use, replace cap on tube. Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

Vm 00879/4108

9. DATE OF FIRST AUTHORISATION

23 December 2003

10. DATE OF REVISION OF THE TEXT

December 2024

Gavin Hall

Approved: 22 January 2025