SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advantage 40 mg Spot-on Solution for Small Cats, Small Dogs and Pet Rabbits

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance	**mg per 0.4 ml tube**
Imidacloprid	40
Excipients	
Benzyl alcohol	332.8
Butylated hydroxytoluene (antioxidant)	0.4

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Spot-on solution.

Clear yellow to slightly brownish solution

4. CLINICAL PARTICULARS

4.1 Target species

For cats, dogs and pet rabbits

4.2 Indications for use, specifying the target species

For the prevention and treatment of flea infestations and for the treatment of biting lice *(Trichodectes canis)* on dogs of less than 4 kg. For dogs of 4 kg body weight and greater see section 4.9.

For the prevention and treatment of flea infestations oncats of less than 4 kg body weight. For cats of 4 kg body weight and greater see section 4.9.

For the treatment of flea infestations on pet rabbits. For rabbits of 4 kg body weight and greater see section 4.9.

Fleas are killed within one day following treatment. One treatment prevents further flea infestation for up to four weeks on dogs, three to four weeks on cats and up to one week on pet rabbits. The product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD) in cats and dogs, where this has been previously diagnosed by a veterinary surgeon.

4.3 Contraindications

Do not treat unweaned puppies or kittens of less than 8 weeks of age.
Do not use on pet rabbits of less than 10 weeks of age.
Do not use in animals that are known to be hypersensitive to the active substance or any of the excipients.

4.4 Special warnings for each target species

There are no special warnings required for the target species.
Apply only to undamaged skin.

4.5 Special precautions for use

i. Special precautions for use in animals

Care should be taken to avoid the contents of the tube coming into contact with the eyes or mouth of the recipient animal.
Do not allow recently treated animals to groom each other.
For external use only.

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

This product contains benzyl alcohol and may cause skin sensitisation or transient skin reactions (for example, irritation, tingling).
Avoid contact between the product and skin, eyes or mouth.
Do not eat, drink or smoke during application.
Wash off any skin contamination with soap and water.
If the product gets into eyes accidentally, the eyes should be thoroughly flushed with water.
If skin or eye irritation persists, obtain medical attention.
If the product is accidentally swallowed, obtain medical attention immediately.
Wash hands thoroughly after use.
After application, do not stroke or groom animals until application site is dry.
Store away from food, drink and animal feedingstuffs.

iii. Other precautions

The solvent in this product 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)

The product is bitter tasting and salivation may occasionally occur if the animal licks the application site immediately after treatment. This is not a sign of intoxication and disappears within a few minutes without treatment (see also section 4.9 Amounts to be administered and administration route).

In very rare occasions skin reactions such as hair loss, redness, itching and skin lesions may occur. Agitation has also been reported. Excessive salivation and nervous signs such as incoordination, tremors and depression have been reported exceptionally in cats.

4.7 Use during pregnancy, lactation or lay

No reproductive toxic effects have been observed in rats and no primary embryotoxic or teratogenic toxic effects have been observed during the studies on rats and rabbits. Studies on pregnant and lactating bitches, queens and does together with their offspring are limited. Evidence so far suggests that no adverse effects are to be expected in these animals.

4.8 Interaction with other medicinal products and other forms of interaction

No incompatibility has been observed between this product at twice the recommended dose and the following commonly used veterinary products: lufenuron, febantel, pyrantel and praziquantel (dogs) and lufenuron, pyrantel and praziquantel (cats). The compatibility of the product was also demonstrated with a wide range of routine treatments under field conditions including vaccination.

4.9 Amount(s) to be administered and administration route

Dosage and Treatment Schedule

Cat/Dog	**Product**	**Number of Tubes**	**mg/kg bw**
Less than 4 kg bodyweight	Advantage 40 mg Spot-On Solution for Small Cats, Small Dogs and Pet Rabbits	1 x 0.4 ml	Minimum of 10
Cats of 4 kg body weight and greater receive 1 tube Advantage 80 mg Spot-On Solution for Large Cats & Pet Rabbits Dogs of 4 kg body weight and greater receive the appropriate Advantage for Dogs product.			

Rabbit	Product	Number of Tubes	mg/kg bw
Adult (greater than 10 weeks)	Advantage 40 mg Spot-On Solution for Small Cats, Small Dogs and Pet Rabbits	1 x 0.4 ml	Minimum of 10
Rabbits of more than 4 kg body weight should receive 1 tube Advantage 80 mg Spot-On Solution for Large Cats & Pet Rabbits			

Treatment should be repeated after 4 weeks. Treatment of nursing bitches and queens controls flea infestations on both dam and offspring.

Fleas are killed within one day following treatment. One treatment prevents further flea infestation on dogs and cats for up to 4 weeks and on rabbits for up to one week. Should re-treatment become necessary earlier than 4 weeks, do not re-treat more frequently than weekly.

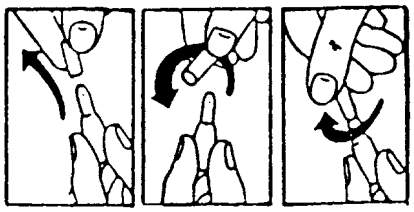
Re-infestation from emergence of new fleas in the environment may continue to occur for six weeks or longer after treatment is initiated. More than one treatment may therefore be required, depending on the level of fleas in the environment. To aid reduction in environmental challenge, the additional use of a suitable environmental treatment against adult fleas and their developing stages is recommended. In order to reduce further the environmental challenge, it is recommended that all dogs, cats and rabbits in the household are treated.

The product remains effective if the animal becomes wet, for example after exposure to heavy rain or after swimming (dogs). However, re-treatment may become necessary, depending on the presence of fleas in the environment. In these cases do not treat more frequently than once weekly.

In case of biting lice infection in dogs, a veterinary examination 30 days after treatment is recommended as some animals may require a second treatment.

Method of Administration

Remove one tube from the package. Hold tube in an upright position, twist and pull off cap. Use reversed cap to twist and remove seal from tube.



Administration to the Cat

Part the hair on the cat's neck at the base of the skull until the skin is visible.

Place the tip of the tube on the skin and squeeze firmly several times to empty the contents directly onto the skin.

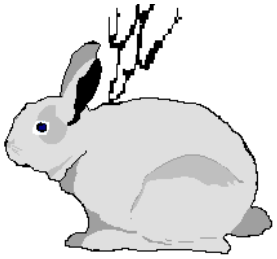
Administration to the Dog

With the dog in the standing position, part the coat between the shoulder blades until the skin is visible.

Place the tip of the tube on the skin and squeeze firmly several times to empty the contents directly onto the skin.

Administration to the Rabbit

Part the hair on the rabbit’s neck at the base of the skull until the skin is



visible.

Place the tip of the tube on the skin and squeeze firmly several times to empty the contents directly onto the skin.

All Species

Correct application will minimise the opportunity for the animal to lick off the product.
Apply only to undamaged skin. Do not allow recently treated animals to groom each other.

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

In cats, no adverse clinical signs were produced using doses of five times the therapeutic level for eight consecutive weeks.

In dogs, no adverse clinical signs were produced by individual doses of up to 200 mg/kg body weight (five to eight times the therapeutic dose), daily treatments at 100 mg/kg body weight for five consecutive days or weekly treatments at five times the maximum dose rate for eight consecutive weeks.

In rabbits, no adverse clinical signs were seen using doses of up to 45 mg/kg body weight (4 times the therapeutic level) weekly for 4 consecutive weeks.

Poisoning following inadvertent oral uptake in either man or animals is unlikely. In this event, treatment should be symptomatic. There is no known specific antidote but administration of activated charcoal may be beneficial.

4.11 Withdrawal period(s)

Do not use on rabbits intended for human consumption.

5. PHARMACOLOGICAL PROPERTIES

The Active Ingredient

Imidacloprid, 1-(6-Chloro-3-pyridylmethyl)-N-nitro-imidazolidin-2-ylideneamine is an ectoparasiticide belonging to a new group of chloronicotinyl compounds. Chemically, it is more accurately described as a chloronicotinyl nitroguanidine.

ATC VetCode: QP53AX17

5.1 Pharmacodynamic properties

The pharmacological properties of imidacloprid are novel. The substance has a high affinity for the nicotinergic acetylcholine receptors in the post-synaptic region of the central nervous system (CNS). The ensuing inhibition of cholinergic transmission in insects results in paralysis and death. Due to the weak nature of the interaction with mammalian nicotinergic receptor sites and the postulated poor penetration through the blood/brain barrier in mammals, it has virtually no effect on the mammalian CNS. The minimal pharmacological activity in mammals is supported by safety studies involving systemic administration of sub-lethal doses to rabbits, mice and rats.
In further studies, in addition to the adulticide flea efficacy of imidacloprid, a larvicidal flea efficacy in the surroundings of the treated cat or dog has been demonstrated. Larval stages in the cat’s and dog's surroundings are killed following contact with a treated animal.

5.2 Pharmacokinetic particulars

Oral studies in the rat show imidacloprid to be absorbed rapidly from the gastro-intestinal tract. Almost complete absorption (95%) occurs within 48 hours. Peak plasma concentrations are observed within 2.5 hours following administration. Tissue distribution is also rapid with the lowest levels recorded in the brain. The active ingredient undergoes extensive metabolism with only 10-16% remaining as parent compound. Almost complete (96%) elimination occurs within 48 hours, approximately 75% being removed by the kidneys and 21% with the faeces.

The solution is indicated for cutaneous administration. Following topical application, the product is quickly distributed over the animal. Acute dermal studies in the rat and target animal overdose and serum kinetic studies have established that systemic absorption is very low, transient and not relevant for clinical efficacy. This has been further demonstrated by a study in which fleas were not killed after having fed on previously treated animals once the animal's skin and fur had been cleaned of all active material.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Butylated hydroxytoluene
Propylene carbonate

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 5 years

6.4 Special precautions for storage

Store away from food, drink and animal feedingstuffs.

6.5 Nature and composition of immediate packaging

Packaging style	Blister packs containing either 2, 3, 4 or 6 unit dose tubes or a single unit dose tube without blister.
Pack Size	Carton contains 1 tube or 1, 5, 10 or 20 blisters each with 2, 3, 4 or 6 tubes
Container material	White polypropylene tube; White polypropylene cap 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, if appropriate

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

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER

Vm 00010/4117

9. DATE OF FIRST AUTHORISATION

14 August 2001

10. DATE OF LAST REVISION OF THE TEXT

May 2017

Approved: 05 May 2017