1. NAME OF THE VETERINARY MEDICINAL PRODUCT

PULSIX 100 mg/500 mg spot-on solution for dogs over 4 kg up to 10 kg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pipette of 1.0 ml contains:

Active substances:

Imidacloprid: 100.0 mg
Permethrin (40/60): 500.0 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Butylhydroxytoluene (E321)	1.0 mg
N-Methylpyrrolidone	482 mg
Miglyol 812	
Citric acid monohydrate	

Clear yellowish to brownish solution.

3. CLINICAL INFORMATION

3.1 Target species

Dogs (over 4 kg up to 10 kg).

3.2 Indications for use for each target species

For dogs with, or at risk from mixed infestations by fleas, biting lice, ticks, sand flies, mosquitos and stable flies. The veterinary medicinal product is only indicated when use against all the following parasite species is required at the same time.

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

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

The veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal 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 the veterinary medicinal product's activity against the vector.

3.3 Contraindications

In the absence of available data, the veterinary medicinal product should not be used on puppies of less than 7 weeks of age or dogs of 1.5 kg of weight or less.
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 3.5 – Other precautions).

3.4 Special warnings

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the veterinary medicinal product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features for each animal.

Resistance to permethrin has been reported in fleas, ticks (*Rhipicephalus sanguineus*), in stable flies (*Stomoxys calcitrans*), mosquitoes (*Culex pipiens, Aedes aegypti*) and sandflies (*P. papatasi*).

The use of this veterinary medicinal product should take into account local information about susceptibility of the target parasites, where available. It is recommended to further investigate cases of suspected resistance, using an appropriate diagnostic method. Confirmed resistance should be reported to the marketing authorisation holder or to the competent authorities.
In the absence of risk of co-infection with fleas, ticks and/or sandflies, a narrow spectrum product should be used.

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 veterinary medicinal 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.

The possibility that other animals in the same household can be a source of re-infection with fleas, ticks or biting lice should be considered, and these should be treated as necessary with an appropriate 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 veterinary medicinal 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 the veterinary medicinal product or at least 2 weeks after application, to optimise efficacy of the veterinary medicinal product.

3.5 Special precautions for use

Special precautions for safe use in the target species:

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 veterinary medicinal product correctly as described under section 3.9. In particular, oral uptake due to the licking of the application site by treated or in-contact animals should be avoided.

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

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

This veterinary medicinal product contains butylhydroxytoluene which may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.
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.
Avoid contact between the veterinary medicinal product and skin, eyes or mouth.
Do not eat, drink or smoke during application. Do not ingest.
Wash hands thoroughly after use.
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.
In case of accidental spillage onto skin, wash off immediately with soap and water.
People with known hypersensitivity to permethrin should avoid contact with the veterinary medicinal product.
If the veterinary medicinal 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.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Treated dogs must not be handled especially by children for at least 12 hours after application of the veterinary medicinal product. It is therefore recommended to treat the dogs e.g. in the evening. Recently treated dogs should not be allowed to sleep together with their owner, especially children.

Special precautions for the protection of the environment:

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

Other precautions:

Do not use on cats.



This veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal product. Seek veterinary advice immediately if this occurs.

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

3.6 Adverse events

Uncommon (1 to 10 animals / 1,000 animals treated):	Application site itching, application site hair change (e.g. greasy fur). Vomiting.
Rare (1 to 10 animals / 10,000 animals treated):	Application site erythema, application site inflammation, application site hair loss. Diarrhoea.
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Increased skin sensitivity (scratching, rubbing).[1,2] Lethargy.[2] Agitation[1,2,3], restlessness[1,2,3], whining[1,2,3], rolling.[1,2,3] Hypersalivation[1,2,3], decreased appetite.[1,2,3] Neurological disorder (e.g. abnormal movement, twitching).[1,2,3]

[1] transient
[2] self-resolving
[3] in dogs susceptible to permethrin

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

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established in dogs during pregnancy, lactation, or in animals intended for breeding. Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects. Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Spot-on use. For external use only. Apply only to undamaged skin. Animals should be weighed accurately prior to treatment.

Underdosing could result in ineffective use and may favour resistance development.

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

Dosing Scheme for the veterinary medicinal product:

Dogs (kg body weight)	**Volume (ml)**	**Content of imidacloprid / permethrin**	**Imidacloprid (mg/kg body weight)**	**Permethrin (mg/kg body weight)**
> 1.5 kg ≤ 4 kg	0.4 ml	40 mg/200 mg	10 - 26	50 - 133
> 4 kg ≤ 10 kg	1.0 ml	100 mg/500 mg	10 - 25	50 - 125
> 10 kg ≤ 25 kg	2.5 ml	250 mg/1250 mg	10 - 25	50 - 125
> 25 kg ≤ 40 kg	4.0 ml	400 mg/2000 mg	10 - 16	50 - 80
> 40 kg ≤ 60 kg	6.0 ml	600 mg/3000 mg	10 - 15	50 - 75

For dogs > 60 kg the appropriate combination with other sized pipettes should be used.

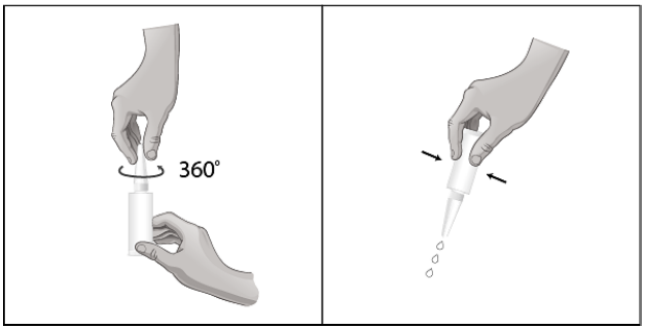
In case of biting louse infestation, a further veterinary examination 30 days after treatment is recommended as some animals may require a second treatment.

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

For infestations with fleas, ticks, mosquitos and stable flies, the need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

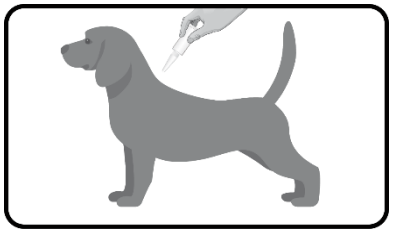
Method for administration

Remove one pipette from the package. Hold applicator pipette in an upright position for opening it. The cap should be rotated clockwise or counter clockwise one full turn. The cap will stay on the pipette; it is not possible to remove it. The pipette is open and ready for application. The entire content of the pipette has to be applied to the animal's skin.

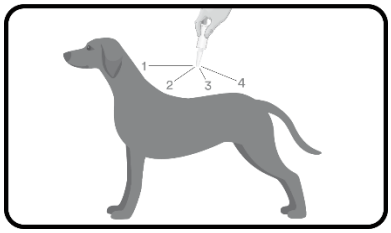


Veterinary medicinal product for dogs over 1,5 kg up to 4 kg and veterinary medicinal product for dogs over 4 kg up to 10 kg:

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.



Veterinary medicinal product for dogs over 10 kg up to 25 kg, veterinary medicinal product for dogs over 25 kg up to 40 kg, and veterinary medicinal product for dogs over 40 kg up to 60 kg:
With the dog standing still, the entire contents of the 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.



3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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 veterinary medicinal product.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance.

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code

QP53AC54

4.2 Pharmacodynamics

This veterinary medicinal product is an ectoparasiticide for topical use containing imidacloprid and permethrin. This combination acts as an insecticide, acaricide and as a repellent.

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 veterinary medicinal 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.

Resistance to permethrin may develop and it is known that resistance manifests in single or multiple mutations of its primary target site, the voltage-gated sodium channels (VGSC), commonly referred to as knockdown resistance (kdr- or skdr-mutation). Other mechanisms of resistance development include cuticle thickening and metabolic resistance via over expression of metabolizing P450 mono-oxygenases, esterases, and glutathione-S-transferases.

4.3 Pharmacokinetics

The veterinary medicinal 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.

Environmental properties
The veterinary medicinal 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 3.5.

Imidacloprid and permethrin containing veterinary medicinal products are toxic to honey bees.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months.

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

5.4 Nature and composition of immediate packaging

Type of container:	White laminated PP/aluminium/PP single use pipette closed with a polyethylene cap.
Material of the secondary packaging:	Pipette individually pouched: PET/aluminium/PP three-layer pouch(es) in a cardboard box.
Pack sizes:	Cardboard box containing 1 pipette of 1.0 ml with pouch.

Cardboard box containing 2 pipettes of 1.0 ml with pouch.
Cardboard box containing 3 pipettes of 1.0 ml with pouch.
Cardboard box containing 4 pipettes of 1.0 ml with pouch.
Cardboard box containing 6 pipettes of 1.0 ml with pouch.
Cardboard box containing 12 pipettes of 1.0 ml with pouch.
Cardboard box containing 24 pipettes of 1.0 ml with pouch.

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.
This veterinary medicinal product should not enter water courses as permethrin/imidacloprid may be dangerous for fish and other aquatic organisms.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Ab7 Santé

7. MARKETING AUTHORISATION NUMBER(S)

VPA23263/001/002

8. DATE OF FIRST AUTHORISATION

20/09/2024

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

01/09/2026

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).