IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

PULSIX 250 mg/1250 mg spot-on solution for dogs over 10 kg up to 25 kg

PRODUCT SUMMARY

EU Procedure number	IE/V/0667/003/DC
Name, strength and pharmaceutical form	PULSIX 250 mg/1250 mg spot-on solution for dogs over 10 kg up to 25 kg
Active substance(s)	Imidacloprid, permethrin (40/60)
Applicant	AB7 Santé
Legal basis of application	Hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of procedure	07/08/2024
Target species	Dogs (over 10 kg up to 25 kg)
Indication for use	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.
ATCvet code	QP53AC54
Concerned Member States	AT, BE, DE, FR, ES, EL, HU, IT, SK, NL, PL, PT, RO, UK(NI)

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Regulation 2019/6 for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland. The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

The product is produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.
It has been shown that the product can be safely used in the target species; the reactions observed are indicated in the SPC.
The product is safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.
The efficacy of the product was demonstrated according to the claims made in the SPC.
The overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Qualitative and Quantitative Particulars
Each pipette contains imidacloprid 250 mg and permethrin (cis:trans 40:60) 1250 mg and the excipients miglyol 812, butylhydroxytoluene, citric acid monohydrate, and N-methylpyrrolidone. The container/closure system consists of a white laminated PP/aluminium/PP single use pipette closed with a polyethylene cap in PET/aluminium/PP three-layer pouch(es) in a cardboard box.
The choice of the formulation is justified. The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.
B. Method of Preparation of the Product
The product is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site. Process validation data for the manufacturing process has been presented in accordance with the relevant European guidelines.
C. Control of Starting Materials
The active substances imidacloprid and permethrin (cis:trans 40:60) are established active substances. The active substances are manufactured in accordance with the principles of good manufacturing practice.
The active substance specifications are considered adequate to control the quality of the materials. Batch analytical data demonstrating compliance with the specifications has been provided.
Compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.
D. Control on Intermediate Products
Not applicable.
E. Control Tests on the Finished Product
The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product.
Satisfactory validation data for the analytical methods has been provided.
Batch analytical data from the proposed production site has been provided demonstrating compliance with the specification.
F. Stability
The active substances are fully tested to ensure compliance with the specifications immediately prior to use in manufacture of the product.
Stability data on the finished product has been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.
G. Other Information
Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

The application has been submitted in accordance with Article 13(3) of Directive 2001/82/EC (a "hybrid" veterinary medicinal product). The reference veterinary medicinal product cited is Advantix Spot-on solution for dogs (VPA22020/048/001-005, Elanco GmbH), which was first granted a marketing authorisation on 02/04/2004.

III.A Safety Testing

Pharmacological Studies

Based on the information provided it is accepted that the formulation of the product can be considered sufficiently similar in terms of the qualitative and quantitative composition of active substances and excipients and physico-chemical characteristics as that of the reference product. Also, as the product is to be administered at the same dose and route of administration as the reference product the omission of pharmacological data is accepted.

Toxicological Studies

Based on the information provided it is accepted that the formulation of the product can be considered sufficiently similar in terms of the qualitative and quantitative composition of active substances and excipients and physico-chemical characteristics as that of the reference product. Also, as the product is to be administered at the same dose and route of administration as the reference product the omission of toxicological data is accepted.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline.
Given the similarity in formulations and the fact that this product is intended to be administered by the same route of administration at the same dose and for the same indications for use in the same species as the reference product no greater risk to the user is anticipated following use of the product than that which already exists for the reference product.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the VMP will only be used in non-food animals. Adequate warnings and precautions appear on the product literature.

IV. CLINICAL ASSESSMENT

In accordance with the CVMP 'Guideline for the testing and evaluation of the efficacy of antiparasitic substances for the treatment and prevention of tick and flea infestation in dogs and cats (EMEA/CVMP/EWP/005/2000-Rev.4), "efficacy or tolerance studies are not considered necessary in the case that the composition (i.e. quality and quantity of the active substance(s) and excipient(s)) and the physico-chemical properties of the generic product and the reference product are identical and the generic is to be administered at the same dose and route of administration as the reference product".
Based on the information provided it is accepted that the formulation of the product can be considered sufficiently similar in terms of the qualitative and quantitative composition of active substances and excipients and physico-chemical characteristics as that of the reference product. Also, as the product is to be administered at the same dose and route of administration as the reference product, the requirements set out in the aforementioned guideline (EMEA/CVMP/EWP/005/2000-Rev.4), have been satisfactorily met. It is considered that the tolerance in the target species and efficacy claims for this product are equivalent to those of the reference product. The omission of tolerance, pre-clinical and clinical data can be accepted.

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

No pre-clinical studies were performed.
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

IV.B Clinical Studies

No clinical trials were performed.

V. OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

VI. POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the product. The current SPC is available in the Union Product Database (UPD).
This section contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

Changes:
None.