IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Exidot 400 mg Spot-on solution for Extra Large Dogs

PRODUCT SUMMARY

EU Procedure number	IE/V/0414/005/DC
Name, strength and pharmaceutical form	Exidot 400 mg Spot-on solution for Extra Large Dogs
Active substance	Imidacloprid
Applicant	Chanelle Pharmaceuticals Manufacturing Limited
Legal basis of application	Hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of Authorisation/ completion of procedure	13/03/2019
Target species	Dogs
Indication for use	For the prevention and treatment of flea infestations and for the treatment of biting lice (*Trichodectes canis*) on dogs weighing 25 kg and greater. 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 the control of Flea Allergy Dermatitis (FAD) where this has been previously diagnosed by a veterinary surgeon.
ATCvet code	QP53AX17
Concerned Member States	BE, DE, FR, HU, IT, NL, PL, PT

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the 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 Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC 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 slight 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 4.0 ml pipette contains 400 mg imidacloprid and the excipients butylhydroxytoluene (E321), benzyl alcohol (E1519) and propylene carbonate.
The product is presented as a white pipette composed of a heat-formed shell of a polypropylene/cyclic olefin copolymer/polypropylene layer and a polyethylene/ethylene vinyl alcohol/polyethylene layer.
Cardboard box containing 1, 2, 3, 4, 6, 8, 9, 10, 12, 15, 18, 20, 21, 24, 30, 60, 90, 150 or 160 pipettes.

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 on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials
The active substances is imidacloprid an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.
The active substance specification is considered adequate to control the quality of the materials. Batch analytical data demonstrating compliance with this specifications have been provided.
Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies
There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

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 have been provided.
Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

F. Stability
Stability data on the active substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substances when stored under the approved conditions.
Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

The application has been submitted in accordance with article 13(3) of Directive 2001/82/EC, as amended (a hybrid application).
The reference veterinary medicinal products are Advantage Spot-on Solutions for Dogs, containing imidacloprid.

III.A Safety Testing
Pharmacological Studies
The Applicant claimed that the product has the same qualitative and quantitative composition of active ingredient and excipients as the reference veterinary medicinal product, Advantage spot-on solution (i.e. it is claimed to be identical). Both products are spot-on solutions and they are used in the same species, for the same indications, in the same doses and using the same administration method.
Based upon the results of comparative studies conducted using the reference product and the candidate formulation, comparing the qualitative and quantitative composition of candidate and reference products, it was accepted that the formulation of the candidate product is sufficiently similar to that of the reference product in terms of the active substance (imidacloprid) and the excipients to be considered the same.
Hence bioequivalence can be assumed and in vivo bioequivalence studies are not required. Given that bioequivalence with the authorised reference product can be accepted and that the test product is intended to be administered to the same target species, using the same routes of administration at the same dose rates as already approved for the reference product, the applicant is not required to provide the results of safety and residue tests or of pre-clinical and clinical trials.

Toxicological studies
This is a hybrid application according to Article 13(3), and as bioequivalence with a reference product is accepted, results of toxicological tests are not required. The safety aspects of this product are expected to be identical to those of the reference product. Warnings and precautions as listed on the product literature are broadly in line with those of the reference product.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the risk to the user associated with this product is identical to that of the reference product. The proposed user safety statements are broadly in line with those of the reference product and are generally acceptable.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product:

- This product contains benzyl alcohol and may cause skin sensitisation or transient skin reactions in rare cases (for example, irritation, tingling) and/or eye irritation.
- Avoid contact between the product and skin, eyes or mouth.
- People with known hypersensitivity to the active ingredient or any of the excipients should avoid contact with the veterinary medicinal product.
- Do not eat, drink or smoke during application. Wash hands thoroughly after use.
- Do not massage the application site. After application, do not stroke or groom animals until application site is dry.
- 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.

Environmental Risk Assessment
Phase I
The environmental risk assessment can stop in Phase I, because the medicine will be used only in non-food animals. It is acknowledged that imidacloprid may be toxic to aquatic organisms and appropriate environmental safety statements are included in the product information.

Conclusion
Based on the data provided, the ERA can stop at Phase I. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

IV. CLINICAL ASSESSMENT

See **Part III.A**
As this is a hybrid application according to Article 13(3), and bioequivalence with a reference product is accepted, efficacy studies are not required. The efficacy claims for this product are expected to be equivalent to those of the reference product. In addition, it is considered that the risk to the target species will be similar for both the test and the reference products. The product literature accurately reflects the type and incidence of adverse effects which might be expected.

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 benefit/risk 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 veterinary medicinal product. The current SPC is available on the HPRA website.
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.