IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

Clearspot 100 mg Spot-On Solution for Medium Dogs

PRODUCT SUMMARY

EU Procedure number	IE/V/0315/003/DC
Name, strength and pharmaceutical form	Clearspot 100 mg Spot-On Solution for Medium Cats
Active substance(s)	Imidacloprid
Applicant	Norbrook Laboratories Limited Station Works Newry Co. Down BT35 6JP United Kingdom
Legal basis of application	Generic-hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of procedure	25th September 2013
Target species	Dogs
Indication for use	For dogs of 4 kg to less than 10 kg: Prevention and treatment of flea (*Ctenocephalides felis*) infestations. The product shows immediate insecticidal effect and persistent insecticidal activity for up to 4 weeks in dogs. The product may 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	AT, BE, CZ, DE, DK, ES, FR, HU, IT, NL, PL, PT, SE, SK, UK.

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

The product contains imidacloprid 100 mg and the excipients butylhydroxytoluene (E321), benzyl alcohol and ethanol, anhydrous.

The product is presented in a 1.0 ml pipette, moulded from a film composed of 3 layers: a polypropylene/COC/polypropylene, solvent free lacquer laminate and a copolymer of polyethylene/EVOH/polyethylene. The pipettes are sealed within a child resistant 4-ply foil sachet composed of LDPE/nylon/aluminium foil/polyester film and presented in an outer box.

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 substance is imidacloprid, an established active substance. 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 material. Batch analytical data demonstrating compliance with this specification 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 substance has been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

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)

This is a generic-hybrid application submitted in accordance with Article 13(3) of Directive 2001/82/EC, as amended.

The applicant has cited Advantage 100 mg Spot-on (authorised to Bayer plc Animal Healthcare Division, UK) as reference product.

The product is qualitatively and quantitatively identical in terms of the active substance imidacloprid when compared with the reference product.

Consequently, the toxicological aspects of this product are considered identical to the reference product.

Warnings and precautions as listed on the product literature are in line with those of the reference product and are considered adequate to ensure safety of the product to users and the environment.

III.A Safety Testing

Toxicological Studies

The applicant conducted a review of the published literature in order to summarise the toxicological profile of the active substance imidacloprid in the target species and in humans.

User Safety

The applicant has presented a user risk assessment broadly in line with guideline requirements. The product is presented in the same volume sizes of pipettes as already approved for the reference product.

Given that the same amount of imidacloprid is included in the product when compared with the same size pipette of the reference product, total user exposure to the active substance imidacloprid is not expected to differ between candidate and reference product formulations.

The user warnings are in line with those approved for the reference product. It can be accepted that the product will not present an unacceptable risk for the user when stored, used and disposed of in accordance with the proposed SPCs.

Environmental Risk Assessment

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that the product will not present an unacceptable risk to the environment when used in accordance with the recommendations included in the SPC.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues Documentation

Residue Studies

Given that the product is only intended for use in non-food producing target species, no residue data were required.

IV CLINICAL ASSESSMENT (EFFICACY)

This is a generic-hybrid application submitted in accordance with Article 13(3) of Directive 2001/82/EC, as amended.

As systemic bioequivalence with the reference product cannot be demonstrated, results of a dose confirmatory studies in support of an indication against fleas were provided.

IV.A Pre-Clinical Studies

Pharmacology

The applicant conducted a review of published literature on the pharmacodynamics of imidacloprid. In summary, imidacloprid exerts its insecticidal properties via an agonist action on nicotinergic acetylcholine receptors on post-synaptic membranes of the central nervous system. This inhibits neuronal transmission in insects, leading to paralysis and death.

Tolerance in the Target Species of Animals

In support of target animal tolerance, the results of a target animal safety study conducted in dogs was provided. Based upon the data presented, an acceptable level of target animal tolerance has been demonstrated in pups from 8 weeks of age when the product is applied at up to 5 x the recommended treatment dose on three occasions at 14 day intervals.
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance

The applicant conducted a review of published literature detailing incidences of resistance development to imidacloprid. The majority of the information relates to use of imidacloprid for agricultural pest control. From the limited data relevant for this application, it is noted that *Ctenocephalides felis* is considered the most resistant cat flea to the greatest number of insecticides and surveys have yet to reveal the emergence of resistance to imidacloprid in cat fleas.

IV.B Clinical Studies
Laboratory Trials

In support of the efficacy of the product for the proposed indications, the applicant provided results of a dose confirmatory study conducted in dogs. The study investigated the efficacy of the product against experimentally induced flea *(Ctenocephalides felis)* infestations.

Based upon the findings from this study, immediate (within 48 hours) and persistent efficacy (for up to 28 days) in dogs has been demonstrated.

Field Trials

No field trial data was provided.

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.