ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Johnson's 4fleas 40 mg Spot-on Solution for Kittens and Small Cats
Johnson's 4fleas 80 mg Spot-on Solution for Cats
(United Kingdom)

Advantage Flea Control 40 mg Spot-on Solution for Small Cats
Advantage Flea Control 80 mg Spot-on Solution for Large Cats
(Ireland)

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0507/001/DC UK/V/0507/002/DC
Name, strength and pharmaceutical form	Johnson's 4fleas 40 mg Spot-on Solution for Kittens and Small Cats Johnson's 4fleas 80 mg Spot-on Solution for Cats
Applicant	Bayer plc Animal Health Division Bayer House Strawberry Hill Newbury Berkshire RG14 1JA
Active substance(s)	Imidacloprid
ATC Vetcode	QP53AX17
Target species	Cats
Indication for use	For the prevention and treatment of flea infestations on cats. One treatment prevents further flea infestations for three to four weeks.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	26th March 2014
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Ireland

I. SCIENTIFIC OVERVIEW

Johnson's 4fleas 40 mg and 80 mg Spot-on Solutions for use in kittens and small cats and cats have been developed as generics of Advantage 40 mg and 80 mg Spot-on Solutions for cats. The reference products have been authorised in the UK since March 1997. Bioequivalence has been claimed to the reference product on the basis that the products are identical in composition and posology.

The products have been developed as spot-on solutions indicated for the prevention and treatment of flea infestations in cats weighing below 4 kg (0.4 ml pipette) and cats weighing 4 kg or greater (0.8 ml pipette). The dosage is 10 mg/kg and treatment should not be repeated more frequently than once weekly. The products are contraindicated in unweaned kittens less than 8 weeks old and in animals where there is known hypersensitivity to the active or any of the excipients.

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[1].

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.

[1] SPC – Summary of Product Characteristics

II. QUALITY ASPECTS

A. Composition

The product contains imidacloprid as the active substance and the excipients butylhydroxytoluene E321, benzyl alcohol E1519 and propylene carbonate.

The container/closure system consists of white polypropylene pipettes with caps containing either 0.4 ml or 0.8 ml of solution. The pipettes are supplied in blisters containing 1, 2, 3, 4 or 6 pipettes and packaged in a cardboard carton. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and absence of preservative are 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 from a licensed manufacturing site. The product is manufactured by mixing the excipients before adding the imidacloprid and stirring until fully dissolved. The solution is then filtered and filled into large containers before transfer into the single-dose pipettes which are then heat sealed. 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 not described in the European Pharmacopoeia. An in-house specification has been provided for the active substance manufacturer. 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.

The excipients butylhydroxytoluene and benzyl alcohol comply with their respective Ph. Eur. monographs. Propylene carbonate is not described in a pharmacopeia and the specification has been submitted. Certificates of analysis have been provided for all excipients.

D. 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.

E. Control on intermediate products

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

F. 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. The tests include those for identification and assay of the active substance and excipients, clarity, colour, density, refractive index, extractable volume and content uniformity.

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.

G. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. The stability studies show imidacloprid is very stable and a retest period of 2 years has been established.

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. Data have been provided for the product stored at 25°C/60%RH, 30°C/50%RH and 30°C/80%RH for 60 months as well as batches stored at 40°C for 3 months and 4°C for 12 months. A shelf life of 5 years is supported.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

- The shelf life of the finished product as packaged for sale is 5 years.
- This product does not require any special temperature storage conditions.
- Keep the blister in the outer carton.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

As this is a generic application submitted according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed due to the nature of the product, the results of pharmacological studies are not required.

Toxicological Studies

As this is a generic application submitted according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed due to the nature of the product, the results of toxicological studies are not required.

User Safety

The applicant has not provided a user safety assessment in compliance with the relevant guideline as the application has been submitted as a generic according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed due to the nature of the product. The user risks are the same as those identified for the reference product and therefore the same warnings and precautions are listed on the product literature and are adequate to ensure safety to users of the product.

- Wash hands thoroughly after use.
- Wash off any skin contamination with soap and water.
- People with known skin sensitivity may be particularly sensitive to this product.
- Avoid contact of the product with the eyes or mouth.
- After application, do not stroke or groom pets until application site is dry.
- If the product gets into eyes accidentally, the eyes should be thoroughly flushed with water. If skin or eye irritation persists, or the product is accidentally swallowed, obtain medical attention.
- Do not eat, drink or smoke during application.

Ecotoxicity

The applicant provided a Phase I environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that as the product is for use in non-food animals only it will pose minimal risk to the environment. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

IV CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application submitted according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed due to the nature of the product, the results of pharmacological studies are not required.

Tolerance in the Target Species of Animals

As this is a generic application submitted according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed due to the nature of the product, the results of tolerance studies are not required.

Resistance

The information provided suggests that there is no indication of a recent change to the susceptibility patterns of fleas to the active substance. As such the same warnings and precautions as cited on the reference product appear on the product literature.

IV.B Clinical Studies

Laboratory Trials

As this is a generic application submitted according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed due to the nature of the product, the results of laboratory trials are not required.

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.

MODULE 4

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 Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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