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

Vetflea 2.5 mg/ml cutaneous spray, Solution for cats and dogs

PuAR correct as of 17/09/2018 when RMS was transferred to HU.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0397/006/DC
Name, strength and pharmaceutical form	Vetflea 2.5 mg/ml cutaneous spray, Solution for cats and dogs
Applicant	Alfamed 13ème rue – L.I.D. 06517 Carros Cedex France
Active substance(s)	Fipronil
ATC Vetcode	QP53AX15
Target species	Cats and dogs
Indication for use	Treatment of flea infestation (*Ctenocephalides* spp.) in dogs and cats. Treatment of tick infestation (*Ixodes ricinus, Rhipicephalus sanguineous*) in dogs and cats. Treatment of biting lice infestation in dogs (*Trichodectes canis*) and cats (*Felicola subrostratus*). The product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD). Insecticidal efficacy against new infestations with adult fleas persists for up to 6 weeks in cats and up to 3 months in dogs, depending on environmental challenge. The product has a persistent acaricidal efficacy for up to 4 weeks against ticks, depending on the level of environmental challenge.

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 hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	21 March 2012
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Belgium, Hungary, Romania

I. SCIENTIFIC OVERVIEW

This was a generic hybrid application for which the reference product is Frontline spray, 2.5 mg/ml cutaneous spray, solution by Merial Animal Health Ltd, authorised in the UK since 1994.

Bioequivalence to the reference product cannot be demonstrated through bioavailability studies due of the nature of the product (a cutaneous spray with little to no trans-cutaneous absorbsion).

The indications for Vetflea 2.5 mg/ml cutaneous spray, Solution for cats and dogs are for the treatment of flea infestation (*Ctenocephalides* spp.) in dogs and cats, treatment of tick infestation (*Ixodes ricinus, Rhipicephalus sanguineous*) in dogs and cats, and treatment of biting lice infestation in dogs (*Trichodectes canis*) and cats (*Felicola subrostratus*). The product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD). Insecticidal efficacy against new infestations with adult fleas persists for up to 6 weeks in cats and up to 3 months in dogs, depending on environmental challenge. The product has a persistent acaricidal efficacy for up to 4 weeks against ticks, depending on the level of environmental challenge.

The product is recommended to be administered at 3 to 6 ml per kg bodyweight (7.5 to 15 mg of active ingredient per kg bodyweight), depending on the length of hair. The product is administered by mechanical pump spray for external use only by spraying the entire body of the animal. The product comes in three presentations of 100 ml, 250 ml, and 500 ml. The recommended dosage can be achieved with 6 to 12 pump applications per kg bodyweight of the 100 ml presentation, or 2 to 4 pump applications of the 250 ml presentation, or 1 to 2 pump application(s) of the 500 ml presentation.

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; any adverse 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 risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains fipronil and excipients copovidone, isopropyl alcohol and water (purified).

The container for this product is a white opaque high-density polyethylene bottle sealed with a mechanical trigger pump. The product is presented in 100 ml, 250 ml, and 500 ml pack sizes. The particulars of the containers and controls performed are provided and conform to the regulation. The absence of preservative 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 from a licensed manufacturing site.

The product is manufactured using a simple mixing method. At a maintained temperature in a suitable vessel, fipronil, copovidone and purified water are mixed together. The solution is then filled into bottles and sealed with the dose delivery device.

Process validation data on three batches of the product, filled into all bottle sizes, have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is fipronil and is manufactured in accordance with the manufacturer's specification. The active substance specification is considered adequate to control the quality of the material. Batch analytical data on three batches demonstrating compliance with this specification have been provided. The excipients copovidone, isopropyl, and purified water are described in the European Pharmacopoeia

[1] Summary of Product Characteristics.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

The applicant has stated that 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

Not applicable.

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. Batch analytical data on 3 batches of each presentation manufactured at the proposed manufacturing site have been provided demonstrating compliance with the specification. Tests include those for appearance, clarity, identification and microbiological quality. Satisfactory validation data for the analytical methods have been provided.

G. Stability

Stability data on 3 batches of 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. Tests include those for appearance, solubility, melting point and related substances.

Stability data on 3 batches of each presentation of the product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product when stored under the approved conditions. Tests include those for appearance of solution, clarity, assay of fipronil content, and microbiological quality.

J. Other Information

The application was supported with regard to quality. The following precautions are included on the SPC and product literature:

Highly flammable.
Do not store above 25°C.
Protect from direct sunlight.

The finished product has a shelf-life of 3 years, and an in-use shelf-life of 1 year.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This is a generic hybrid application according to Article 13(3) where bioequivalence cannot be demonstrated through bioavailability studies. However, the product has been shown to be pharmaceutically equivalent to the reference product, Frontline Spray 0.25% w/v Cutaneous Spray Solution. Both products are solutions and they are used in the same species, for the same indications, in the same doses and using the same administration method and therefore bioequivalence can be assumed. Therefore it is considered justified that the applicant has not provided pharmacological or toxicological data in support of this application.

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

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline. The assessment states that the product is clinically equivalent to the reference product, and that it is quantitatively and qualitatively the same in terms of composition and it is intended for use in the same target species, with the same indication claims and dose rate. Given that the product is pharmaceutically equivalent to the reference product and the risk management measures proposed are also the same as for the reference product, these are considered to be acceptable. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

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 it is unlikely that the product would directly enter the environment when used as directed. 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)

This is a generic hybrid application according to Article 13(3) where bioequivalence cannot be demonstrated through bioavailability studies. However, the product has been shown to be pharmaceutically equivalent to the reference product, Frontline Spray 0.25% w/v Cutaneous Spray Solution. Both products are solutions and they are used in the same species, for the same indications, in the same doses and using the same administration method and therefore bioequivalence can be assumed. Therefore no data have been

presented for the clinical assessment (efficacy) and this is considered to be acceptable.

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.

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