Bundesamt für Verbraucherschutz und Lebensmittelsicherheit

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
10117 Berlin
(Germany)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Amflee 2.5 mg/ml Cutaneous Spray. Solution for Cats and Dogs (BE, DE, IT, NL, ES, PT, UK
Fypryst 2.5 mg/ml cutaneous spray, solution for cats and dogs (GR)
Fyperix 2.5 mg/ml cutaneous spray, solution for cats and dogs (FR)

Date: 08 March 2018

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0187/001
Name, strength and pharmaceutical form	Amflee 2.5 mg/ml Cutaneous Spray. Solution for Cats and Dogs
Applicant	TAD Pharma GmbH Heinz-Lohmann-Str. 5 27472 Cuxhaven Germany
Active substance(s)	Fipronil
ATC Vetcode	QP53AX15
Target species	Cats and Dogs
Indication for use	Treatment of flea (*Ctenocephalides* spp.) and tick (*Ixodes ricinus*, *Rhipicephalus sanguineus*) infestations in dogs and cats. Treatment of biting lice infestations 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 2 months 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 Veterinary Medicinal Agencies website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	29 August 2014
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Belgium, France, Greece, Italy, The Netherlands, Portugal, Spain, United Kingdom (former RMS)

I. SCIENTIFIC OVERVIEW

This was a generic application made in accordance with Article 13 (1) of Directive 2001/82/EC as amended. The reference veterinary medicinal product is Frontline Spray 0.25% w/v Cutaneous Spray Solution, which has been marketed in the UK for more than 10 years. Bioequivalence with the reference product was confirmed.

The product is a cutaneous spray containing 2.5 mg/ml of fipronil, indicated for the treatment of flea and tick infestations, and for use as a treatment for flea allergy dermatitis. The product may be used to treat flea *(Ctenocephalides* spp.) and tick (*Ixodes ricinus*, *Rhipicephalus sanguineus*) infestations in dogs and cats, and biting lice infestations in dogs (*Trichodectes canis*) and cats (*Felicola subrostratus*).

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto the market. It has been shown that the product can be safely used in the target species, any 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 [2] 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.
[2] Efficacy – The production of a desired or intended result.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTIUENTS

II.A. Composition

The product contains 2.5 mg/ml fipronil and excipients copovidone, isopropyl alcohol and purified water.

The container/closure system consists of the following:

Opaque, white 100 ml high density polyethylene bottle fitted with a low density polyethylene/polypropylene pump sprayer capable of delivering 0.5 ml per spray.

Opaque, white 250 ml high density polyethylene bottle fitted with a low density polyethylene/polypropylene pump sprayer capable of delivering 1.5 ml per spray.

Opaque, white 500 ml high density polyethylene bottle fitted with a low density polyethylene/ polypropylene pump sprayer capable of delivering 3.0 ml per spray.

Not all pack sizes may be marketed. The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the formulation and the 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.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. Process validation data on the product have been presented in accordance with the relevant European guidelines. The manufacturing method is a simple dissolution process.

II.C. Control of Starting Materials

The active substance is fipronil an established active substance not described in the European Pharmacopoeia, with appropriate data provided in an Active Substance Master File. The active substance is manufactured in accordance with the principles of good manufacturing practice, and the substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

II.C.4. Substances of Biological Origin

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.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. Tests include those relevant for the pharmaceutical form.

II.F. 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. In accordance with VICH requirements, under which the active substance was tested at 25ºC/60% RH, and 40ºC/75% RH, no adverse effect was noted. Photostability studies were also conducted which showed no adverse effect on the active substance. A retest period of 3 years was agreed.

G. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.

Shelf-life after first opening the immediate packaging: 1 year.

Store below 25°C.

Highly flammable.

Protect from direct sunlight.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13 .(1), and bioequivalence with a reference product has been demonstrated, results of pharmacological and toxicological tests were not required. Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users and the environment.

III.A Safety Documentation

User Safety

A user risk assessment was provided in compliance with the relevant guideline. The SPC carries the following warnings, which are the same as those of the reference product. No further assessment was required:

- This product can cause mucous membrane and eye irritation. Therefore, contact of the product with mouth and eyes should be avoided. After accidental ocular exposure the eye should be rinsed carefully with plain water.
- People with a known hypersensitivity to the active substance or alcohol or with asthma should avoid contact with the product. Avoid contents coming into contact with the fingers. If this occurs, wash hands with soap and water.
- Treated animals should not be handled until the fur is dry, and children should not be allowed to play with treated animals until the fur is dry. It is therefore recommended that animals are not treated during the day, but should be treated during the early evening, and that recently treated animals are not allowed to sleep with owners, especially children.
- Spray animals in the open air or a well ventilated room.
- Do not breathe spray. Do not smoke, drink or eat during application.
- Wear PVC or nitrile gloves during treatment of animals. It is recommended to wear a waterproof apron for the protection of clothing. If clothing becomes heavily wetted with the product, it should be removed and washed before re-use
- Dispose of gloves after use and then wash hands with soap and water.
- Wash splashes from skin with soap and water immediately. If irritation occurs, seek medical advice. People with known sensitivity or asthma may be particularly sensitive to the product. Do not use product if you have previously experienced a reaction to it.

- Treatment of multiple animals: Good ventilation is particularly important where several animals are to be treated. Treat multiple animals outside, or reduce the build up of vapour by removing the animals from the treatment room while the alcohol is evaporating and ensure that the treatment room is well ventilated between individual treatments. In addition, ensure that the drying room is well ventilated and avoid housing several recently treated animals within the same air space.

Environmental Safety

A Phase I Risk Assessment was provided which satisfactorily addressed any environmental concerns associated with the product:

- Fipronil may adversely affect aquatic organisms. Dogs should not be allowed to swim in watercourses for 2 days after application.

IV CLINICAL DOCUMENTATION

As this was a generic application according to Article 13 (1), and bioequivalence with a reference product has been demonstrated, efficacy studies were not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.I. Pre-Clinical Studies

As this was a generic application according to Article 13 (1), and bioequivalence with a reference product has been demonstrated, efficacy studies were not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.II. Clinical Documentation

As this was a generic application according to Article 13 (1), and bioequivalence with a reference product has been demonstrated, efficacy studies were not required. The efficacy claims for this product are equivalent to those of the reference product.

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 of the product(s) is favourable.

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 Heads of Veterinary Medicinal Agencies website (www.hma.eu).

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.

•	08 March 2018	Change of RMS from UK to DE
•	22 February 2018	Change in contact details for local representative.
•	26 May 2017	Increase in batch size (including batch size range*) of the finished product.
•	03 March 2016	Addition of a site of manufacture for the active substance
•	15 December 2014	Change in the invented name of the medicinal product in France only.
•	09 October 2014	Change of MAH from KRKA d.d. NOVO mesto to TAD Pharma GmbH