Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Fypryst 2.5 mg/ml Cutaneous Spray Solution for Cats and Dogs

PuAR correct as of 26/02/2018 when RMS was transferred to HU. Please contact the RMS for future updates

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0407/001/DC
Name, strength and pharmaceutical form	Fypryst 2.5 mg/ml Cutaneous Spray Solution for Cats and Dogs
Applicant	KRKA, d.d., Novo mesto Šmarješka cesta 6 8501 Novo mesto Slovenia
Active substance	Fipronil
ATC Vetcode	QP53AX15
Target species	Cats and Dogs
Indication for use	The treatment and prevention of flea and tick infestations in cats and dogs, and as part of a treatment strategy for Flea Allergy Dermatitis in cats and dogs. The product is active against *Ixodes* spp. including *Ixodes ricinus*, important as the vector of Lyme disease. The product controls infestations with *Trichodectes canis* biting lice on dogs, and *Felicola subrostratus* biting lice on cats. The product is active for up to 3 months against fleas in dogs, and up to 2 months in cats, depending on the environmental challenge. It is effective against tick infestations for up to one month in dogs and cats, 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 application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	25th July 2012.
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Bulgaria, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia, Slovenia.

I. SCIENTIFIC OVERVIEW

This was a generic application according to Article for which the reference product is Frontline Spray 0.25% w/v Cutaneous Spray Solution, marketed in the UK for more than 10 years. The product is for the treatment and prevention of flea and tick infestation in cats and dogs and may be used as part of a treatment strategy for Flea Allergy Dermatitis in these animals. The product has efficacy against *Ixodes* spp. including *Ixodes ricinus* and controls infestation caused by *Trichodectes canis* in dogs and *Felis subrostratus* in cats. Fipronil exhibits insecticidal and acaricidal activity against fleas (*Ctenocephalides* spp), ticks (*Rhipicephalus* spp., *Ixodes* spp.) and lice (*Trichodectes* spp. and *Felicola* spp.) in the dog and cat.

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 2.5 mg/ml fipronil and the excipients copovidone, isopropyl alcohol and purified water.

The container/closure system consists of opaque, white, high density polyethylene bottles fitted with a pump sprayer, and comes in 100 ml, 250 ml or 500ml sizes, delivering respectively 0.5 ml, 1.5 ml or 3.0 ml of product. 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. 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 fipronil, an established active substance not 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 material. Batch analytical data demonstrating compliance with this specification have been provided. Suitable data were provided in the form of an Active Substance Master File.

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

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. 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 on the finished product include those for fill volume, identification of fipronil, related substances and microbiological quality.

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. Validation batches were analysed after storage at various time points at 25°C/60% RH, 30°C/65% RH, and 40°C/75% RH. A freeze-thaw cycling test and photostability test were also performed. Some stability test continued post-approval. Testing of in-use shelf-life was also performed over a twelve months period, at 25°C/60% RH.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

The shelf-life of the product as packaged for sale was determined from stability studies to be two years. Shelf-life after opening of the immediate packaging is one year.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product was accepted via pharmaceutical similarity, results of pharmacological and toxicological tests are not required. The applicant provided a user risk assessment and an environmental risk assessment.

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 Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which concluded that as the product has been shown to be pharmaceutically equivalent to the reference product, any hazards and risks

from the product are the same. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

- This product can cause mucous membrane and eye irritation. Therefore, contact of the product with mouth and eyes should be avoided.
- Operators 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.
- After accidental ocular exposure the eye should be rinsed carefully with plain 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.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required beyond an investigation of the possible risk to aquatic life, should the product be passed from dogs to water courses. This information was subsequently provided. The assessment concluded that warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed. The SPC reflects the warnings as defined by the reference product.

IV CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with a reference product was accepted via pharmaceutical similarity, efficacy studies were not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13, and bioequivalence with a reference product was accepted via pharmaceutical similarity, pharmacological studies were not required. The efficacy claims for this product are equivalent to those of the reference product.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13, and bioequivalence with a reference product was accepted via pharmaceutical similarity, tolerance studies were not required.

Resistance

As this is a generic application according to Article 13, and bioequivalence with a reference product was accepted via pharmaceutical similarity, resistance studies were not required.

IV.B Clinical Studies

Laboratory Trials

As this is a generic application according to Article 13, and bioequivalence with a reference product was accepted via pharmaceutical similarity, laboratory studies were not required.

Field Trials

As this is a generic application according to Article 13, and bioequivalence with a reference product was accepted via pharmaceutical similarity, field studies were 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.

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