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

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Dadektin Combo 50 mg/60 mg Spot-on Solution for Cats
Amflee Combo 50 mg/60 mg spot-on solution for cats (CY, IE)
Fyperix Combo 50 mg/60 mg spot-on solution for cats (PT)
Fyperix Comp vet 50 mg/60 mg spot-on solution for cats (FI)
Fypermid Combo 50 mg/60 mg spot-on solution for cats (IT)

Date Created: May 2018

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0660/001/DC
Name, strength and pharmaceutical form	Dadektin Combo 50 mg/60 mg Spot-on Solution for Cats
Applicant	Krka, d.d., Novo Mesto, Smarjeska Cesta 6, 8501 Novo Mesto, Slovenia
Active substance(s)	Fipronil S-Methoprene
ATC Vetcode	QP53AX65
Target species	Cats
Indication for use	To be used against infestations with fleas, alone or in association with ticks and/or biting lice: - Treatment of fleas (*Ctenocephalides* spp.). Insecticidal efficacy against new infestations with adult fleas persists for 4 weeks. Prevention of the multiplication of fleas by inhibiting the development of eggs (ovicidal activity), larvae and pupae (larvicidal activity) originating from eggs laid by adult fleas for six weeks after application. - Treatment of ticks (*Ixodes ricinus, Dermacentor variabilis, Rhipicephalus sanguineus*). The product has a persistent acaricidal efficacy for up to 2 weeks against ticks (based on experimental data). - Treatment of biting lice (*Felicola subrostratus*).

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

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

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 conclusion of the decentralised procedure	28th February 2018
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Cyprus, Finland, Ireland, Italy, Portugal

I. SCIENTIFIC OVERVIEW

This application is for a generic product, submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended. The reference product, authorised in the UK since January 2004, is Frontline Combo Spot-On Cat. The legal basis for the application, that the proposed and reference products are pharmaceutically equivalent, is consistent with the principles underlying exemption from the requirement to provide in vivo bioequivalence studies outlined in section 7.1(d) of that guideline (EMA/CVMP/016/00-Rev.2). A biowaiver is therefore supported.

The product is to be used against infestations with fleas, alone or in association with ticks and/or biting lice:

For the treatment of fleas (*Ctenocephalides* spp.). For insecticidal efficacy against new infestations with adult fleas, persistant for 4 weeks. For the prevention of the multiplication of fleas by inhibiting the development of eggs (ovicidal activity), larvae and pupae (larvicidal activity), originating from eggs laid by adult fleas for six weeks after application.

For the treatment of ticks (*Ixodes ricinus, Dermacentor variabilis, Rhipicephalus sanguineus*). The product has a persistent acaricidal efficacy for up to 2 weeks against ticks (based on experimental data). For the treatment of biting lice (*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.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains 50 mg fipronil and 60 mg s-methoprene per 0.5 ml pipette and the excipients butylhydroxyanisole (E320), butylhydroxytoluene (E321), povidone (K25), polysorbate 80, ethanol 96 per cent and diethylene glycol monoethyl ether.

The container/closure system consists of white polypropylene single-dose pipette packaged in aluminium foil sachets. The product is provided in a cardboard box containing 1, 3 or 6 pipettes. 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. The manufacturing method consists of a series of dissolution and mixing steps, followed by filtration of the final solution and filling of pipettes.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

II.C. Control of Starting Materials

The active substances are fipronil and S-methoprene, established active substances not described in the European Pharmacopoeia. Active Substance Master Files (ASMF) have been provided for both of the active substances. The active substances are 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

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

specification have been provided. Acceptable assurances of suitability were provided.

All excipients are monographed in the Ph. Eur, and the quality of packaging materials is suitably controlled.

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 sites have been provided demonstrating compliance with the specification. Control tests on the finished product are: appearance, density, uniformity of dosage form, Identification of active substances and related substances, content of active substances and key excipients and microbiological quality.

II.F. Stability

Stability data on the active substances have been provided in accordance with applicable European guidelines, under VICH[3] conditions, demonstrating the stability of the active substance when stored under the approved conditions. Results showed that the product was generally stable and was not affected by freezing and thawing.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 2 years

Store below 30°C.

Store in the original package in order to protect from light and moisture.

[3] VICH – International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

For generics, insert in the relevant sections as appropriate:

III.A Safety Documentation

Due to the nature of the application, no data were required for toxicological or pharmacological assessment.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that the product is safe to use when used as recommended. The recommendations are the same as those of the reference product, with additional advice.

Warnings and precautions as listed on the SPC and the product literature are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

- This product can cause mucous membrane, skin and eye irritation. Therefore, contact of the product with mouth, skin and eyes should be avoided.
- People with a known hypersensitivity (allergy) to insecticides or alcohol 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 in clean water.
- If the product is accidentally swallowed, seek medical advice immediately and show the package leaflet to the physician.
- Wash hands after use.
- Do not smoke, drink or eat during application.
- Treated animals should not be handled until the application site is dry, and children should not be allowed to play with treated animals until the application site 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.
- Keep pipettes in original packaging until ready to use.

Environmental Safety

Phase I:

The product will only be used in non-food animals and as a result environmental exposure will be low. A Phase II ERA was not required. The product is not expected to pose a risk the environment when used as recommended in the SPC and product literature.

IV CLINICAL DOCUMENTATION

Due to the nature of the application, no pharmacological data were required.

Tolerance in the Target Species

Due to the nature of the application, no animal safety studies were required.

Resistance

A literature review was conducted. At present, there is no clinically-significant resistance amongst the target parasites which impacts on the benefit:risk balance of the product.

IV.II. Clinical Documentation

Due to the nature of the application, no efficacy studies were 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 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 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)