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

Fiprocat 50 mg spot-on solution for cats

Date: 28th February 2022

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0138/001/DC
Name, strength and pharmaceutical form	Fiprocat 50 mg spot-on solution for **cats**
Applicant	Domes Pharma 3 Rue André Citroën 63430 Pont-du-Château France
Active substance(s)	Fipronil
ATC Vetcode	QP53AX15
Target species	Cat
Indication for use	For the treatment of cats against flea infestations (Ctenocephalides spp.). Insecticidal efficacy against new infestation with fleas persists for up to 4 weeks. The product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD), where this has been previously diagnosed by a veterinary surgeon. Although the product has not demonstrated an immediate acaricidal effect, acaricidal efficacy for up to 1 week against the tick Ixodes ricinus has been shown. If ticks of Ixodes ricinus are present when the product is applied, all the ticks may not be killed within the first 48 hours, but they may be killed within a week.

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 13.2 of Directive 2001/82/EC as amended.
Date of completion of the original Decentralised procedure	24 November 2010
Date product first authorised in the Reference Member State (MRP only)	n.a.
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DK, EE, EL, ES, FI, FR, HU, IE, IT, IS, LU, LV, LT, NL, NO, PL, PT, RO, SE, SI, SK, UK

I. SCIENTIFIC OVERVIEW

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 extremely rare suspected adverse reactions observed are indicated in the SPC.
Warnings and precautions as indicated in the SPC are adequate to ensure safety to the users and the environment when the product is used as recommended.
The efficacy and safety aspects of this product are identical to Frontline spot-on. The initial application for Frontline spot-on was assessed before there was a requirement to have a public assessment report; therefore no details in this section are available.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains fipronil 100 mg/ml and butylhydroxyanisole 0.2 mg/ml, butylhydroxytoluene 0.1 mg/ml and diethylene glycol monoethyl ether.

For primary packaging the product is packed in pipettes made of:

bottom foil: PP/PET
lidding foil: ALU/PET
(PP = polypropylene, PET = polyethylene terephthalate, ALU = aluminium)

For secondary packaging and to protect the content of the pipettes from moisture and light the pipettes are packed in:
blister foils made of:
cold - form foil: PVC/OPA/ALU/PVC
lidding foil: PET/ALU
(PVC = polyvinyl chloride, OPA = (biaxially) oriented polyamide, ALU = aluminium, PET = polyethylene terephthalate)

The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation 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.

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. 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.

For the quality of the active ingredient reference is made to an Active Substance Master File (ASMF).

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> *(pharmaceuticals)*

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 sites 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.

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.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Bioequivalence cannot be demonstrated through bioavailability studies due to the nature of the products. Therefore, the applicant has submitted conclusive bibliographical data on pharmacology and toxicity of fipronil.

Pharmacological Studies

Please be referred to IV.A.

Toxicological Studies

The applicant has provided comprehensive bibliographical data on toxicity that show essential similarity with the reference product.

Observations in Humans

The applicant has provided information which show that accidental ingestion, inhalation, or exposure of the skin / eye may lead to conjunctivitis, oro-pharyngeal pain, vomiting, headache, dizziness, abdominal pain, cough, drowsiness, nausea, vertigo, headache and weakness. Symptoms were reported mild at contamination and reported to subside spontaneously.

Studies on Metabolites, Impurities, Other Substances and Formulation.

The applicant has provided bibliographical data regarding metabolites which show that the toxicity of most of the metabolites is comparable to or less than that of fipronil with the exception of fipronil desulfinyl, a metabolite which only occurs through exposure of fipronil to direct sunlight.

Excipients are commonly used veterinary medicinal products.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the risks for children and adults petting treated animals can be considered acceptable taking into account the proposed user warning phrases. 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 risk mitigation measurements are required. The assessment concluded that fipronil is extremely toxic for aquatic invertebrates. Warnings regarding the ecotoxicity and consecutive risk mitigation measurement are required.

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 application according to Article 13, where bioequivalence with a reference product could not be demonstrated through bioavailability studies because of the nature of the product. The efficacy claims for this product are also claimed for the reference product.

The applicant has provided a clinical assessment in compliance with the relevant guidelines which showed the efficacy of the product concerning the indications listed in the product literature and that the safety for the treated animals can be considered acceptable. No adverse effects have been observed in the clinical studies which could be related to treatment. The safety information including precautions for use in animals is considered adequate.

IV.A Pre-Clinical

Studies Pharmacology

The products are essentially similar to the reference products with respect to the pharmaceutical form and the composition with regard to the active ingredient and the proposed use. Bioequivalence based on blood concentrations was considered inappropriate to demonstrate the safety and efficacy of the generic product compared to the reference product.

Tolerance in the Target Species of Animals

The products have the same composition in active substance and in the major excipients as an authorised reference product. The differences in excipients were adequately addressed.

The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance

Although fipronil has been widely used all over the world in different pharmaceutical forms since more than 15 years resistance of flea or tick species towards fipronil has not yet been reported. This might be explained by its mode of action (blocking the chloride channels in the target organisms by inhibiting the GABA complex).

IV.B .B Clinical

Studies Laboratory

Trials

The applicant has conducted dose confirmation studies with fleas which show in accordance with the recommended guideline that the product is effective for treatment of flea infestations (fleas are killed within 24 hours) with a residual protection period of 5 weeks against *Ctenocephalides felis* and can be used as a part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD).
However, in the product literature a residual protection period of 4 weeks could be accepted only as for the reference product.
In addition, the applicant conducted a dose confirmation study with this product which showed persistent acaricidal efficacy for up to 1 week against *I. ricinus* on cats. A treatment claim against ticks could not be confirmed.
Studies demonstrating acaricidal efficacy against ticks *Dermacentor variabilis* and *Rhipicephalus sanguineus* on cats have not been provided.

V . OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The benefit of the indication on ticks on cats is marginal. Based on the submitted data only 1 week persistent acaricidal efficacy against *I. ricinus* could be demonstrated.

However, the data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the risk benefit 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 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.

Safety/efficacy changes

Summary of change **(Type II VAR; application number)**	**Section updated in Module 3**	**Approval date**
Addition of a new indication on ticks on cats (DE/V/0138-0139/001/II/001)	IV.B, V	04/11/2011

Quality changes

Summary of change **(Type II VAR; application number)**	**Section updated in Module 3**	**Approval date**
New active substance manufacturer Change in active substance specification Change in test procedure of the active substance (DE/V/xxxx/WS/005)	B.I.a.1.b B.I.b.1.f B.I.b.2.e	24/08/2012
Deletion of an active substance manufacturer (DE/V/0138/001-005/IA/003)	A.7	06/07/2017
Change in test procedure for the finished product (DE/V/0138/001-005/IB/004)	B.II.d.2	09/01/2018
Change in the name of the MAH from Laboratoire TVM to Domes Pharma SC (FR/V/xxxx/IA/155/G)	A.1	12/03/2021

Transfer of the Marketing Authorisation from Domes Pharma SC to Domes Pharma (national procedure)		28.02.2022