IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

DV8FLEA COMBO M 134 mg / 120.6 mg spot-on solution for dogs

PRODUCT SUMMARY

EU Procedure number	N/A
Name, strength and pharmaceutical form	DV8FLEA COMBO M 134 mg / 120.6 mg spot-on solution for dogs
Active substances(s)	Fipronil,(S)-Methoprene
Applicant	Duggan Veterinary Supplies Limited Unit 9 Retail Park Thurles Tipperary E41 E7K7 Ireland
Legal basis of application	Hybrid application – bioavailability studies cannot be used to demonstrate bioequivalence (Article 19(1)(b) of Regulation (EU) 2019/6)
Date of completion of procedure	23/02/2024
Target species	Dogs
Indication for use	For the treatment of dogs: • To be used against infestations with fleas, alone or in association with ticks and/or biting lice. • Treatment of flea infestations *(Ctenocephalides spp.)*. Insecticidal efficacy against new infestations with adult fleas persist for 8 weeks. • Prevention of the multiplication of fleas by inhibiting the development of eggs (ovicidal activity) and larvae and pupae (larvicidal activity) originating from eggs laid by adult fleas for eight weeks after application. • Treatment of tick infestations *(Ixodes ricinus, Dermacentor variabilis, Dermacentor reticulatus, Rhipicephalus sanguineus)*. The product has a persistent acaricidal efficacy for up to 4 weeks against ticks. Treatment of infestations with biting lice *(Trichodectes canis*).
ATCvet code	QP53AX65
Concerned Member States	N/A

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in relevant articles of Regulation (EU) 2019/6. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland. The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

The veterinary medicinal 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 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.

II. QUALITY ASPECTS

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A. Qualitative and Quantitative Particulars

Each pipette contains 134 mg fipronil and 120.6 mg (S)-methoprene and the excipients butylhydroxyanisole (E320), butylhydroxytoluene (E321), ethanol (96 per cent), polysorbate 80, povidone K17 and diethylene glycol monoethyl ether.
The product is presented as a: 1.34 ml red pipette composed of a heat-formed shell (internal layer PE/EVOH/PE external layer PP/COC/PP) and a film (PET/PE/ALU/PE).
Carton box with 1 pipette.
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 at a licensed manufacturing site.
Process validation data for the manufacturing process has been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance fipronil is an established active substance described in the European Pharmacopoeia. The active substance (S)-methoprene is an established active substance. The active substances are manufactured in accordance with the principles of good manufacturing practice.
The active substance specifications are considered adequate to control the quality of the materials. Batch analytical data demonstrating compliance with these specifications have been provided.
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.

D. Control on Intermediate Products

Not applicable.

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 has been provided.
Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substances 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.

G. Other Information

None.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

The application has been submitted in accordance with Article 19(1)(b) of Regulation (EU) 2019/6, as amended (a hybrid veterinary medicinal product). The reference veterinary medicinal product is Frontline Combo Spot-on Dog M containing fipronil and (s)-methoprene.

III. SAFETY ASSESSMENT

Pharmacological Studies
It was claimed that the product has the same qualitative and quantitative composition of active ingredient and excipients as the reference veterinary medicinal product, Frontline Combo Spot-on Dog M (i.e. it is claimed to be identical). Both products are spot-on solutions, and they are used in the same species, for the same indications, in the same doses and using the same administration method. The applicant claimed that the candidate formulation is identical to that of the reference product, Frontline Combo Spot-on Dog M, based upon the results of comparative studies conducted using the reference product and the candidate formulation, including a comparison of physicochemical properties. The applicant has demonstrated that the candidate product is qualitatively and quantitatively similar enough to be considered the same as the reference product in terms of the active substances (fipronil and (S)-methoprene), and the excipients. Hence bioequivalence can be assumed, and *in vivo* bioequivalence studies are not required. Given that bioequivalence with the authorised reference product can be accepted and that the test product is intended to be administered to the same target species, using the same routes of administration at the same dose rates as already approved for the reference product, the applicant is not required to provide the results of safety and residue tests or of pre-clinical and clinical trials.

Toxicological Studies
This is a hybrid application in accordance with Article 19(1)(b) of Regulation (EU) 2019/6, and as bioequivalence with a reference product is accepted, results of toxicological tests are not required. The safety aspects of this product are expected to be identical to those of the reference product. Warnings and precautions as listed on the product literature are broadly in line with those of the reference product.

User Safety
The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the risk to the user associated with this product is identical to that of the reference product. The proposed user safety statements are broadly in line with those of the reference product and are generally acceptable. 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, skin and eye irritation. Therefore, contact of the product with mouth, skin and eyes should be avoided.*
People with a known hypersensitivity 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 exposure the eye should be rinsed carefully with pure water.
Wash hands after use.
Ingestion of the product may be harmful. Prevent children getting access to the pipettes and discard the used pipettes immediately after applying the product. In case of accidental ingestion of product seek medical advice immediately.
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.
Do not smoke, drink or eat during application.
The alcohol carrier may have adverse effects on painted, varnished or other household surfaces or furnishings."

Environmental Risk Assessment
Environmental Risk Assessment Phase I: The environmental risk assessment can stop in Phase I, Question No. 3, because the medicine will be used only in non-food animals. It is acknowledged that fipronil may be toxic to aquatic organisms and it is accepted that the environmental safety statements agreed for the reference product can be applied to this product.

Conclusion
Based on the data provided, the ERA can stop at Phase I. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

IV. CLINICAL ASSESSMENT

As this is a hybrid application in accordance with Article 19(1)(b) of Regulation (EU) 2019/6, and bioequivalence with the reference product is accepted, efficacy studies are not required. The efficacy claims for this product are expected to be equivalent to those of the reference product. In addition, it is considered that the risk to the target species will be similar for

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

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.

VI. POST-AUTHORISATION ASSESSMENTS

None.