IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Norbrook Fipronil and (S)-Methoprene 402 mg / 361.8 mg spot-on solution for very large dogs

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PRODUCT SUMMARY

EU Procedure number	IE/V/0366/005/DC
Name, strength and pharmaceutical form	Norbrook Fipronil and S-Methoprene 402 mg / 361.8 mg spot-on solution for very large dogs
Active substances	Fipronil and S-Methoprene
Applicant	Norbrook Laboratories (Ireland) Limited Rossmore Industrial Estate Monaghan Ireland
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of procedure	22nd February 2017
Target species	Dogs
Indication for use	For the treatment of dogs weighing over 40 kg bodyweight: 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 persists for 8 weeks. Prevention of the multiplication of fleas by inhibiting of 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	UK

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PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the 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 Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. 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 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. 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

A. Composition

Each pipette contains 402 mg fipronil and 361.8 mg S-methoprene and the excipients ethanol, polysorbate 80, povidone (K17), butylhydroxyanisole, butylhdroxytoluene and diethylene glycol monoethyl ether. The product is presented in a:
4.02 ml pipette, moulded from a film composed of 3 layers: a polypropylene/COC/polypropylene, solvent free lacquer laminate and a copolymer of polyethylene/EVOH/polyethylene. The pipettes are sealed within a child resistant 4-ply foil sachet composed of LDPE/nylon/aluminium foil/polyester film and presented in an outer box.

Pipettes are presented in boxes containing 1, 2, 3, 4 or 6 pipettes. Each pipette is individually sealed in a foil sachet.

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 on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substances are fipronil and S-methoprene both of which are established active substances. 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.

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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.

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)

This was a generic application submitted in accordance with Article 13 (1) of Directive 2001/82/EC, as amended. The reference veterinary medicinal products are Frontline Combo Spot-On for Dogs/Cats – containing fipronil and S-methoprene.

III.ASafety Testing

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 (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 claim that PestiGon Combo can be considered identical to the reference product was based on a comparison of the qualitative and quantitative composition of both products, including a comparison of physicochemical properties. Based on these data, the applicant argued that an exemption from the requirement to conduct an in vivo bioequivalence study was justified in accordance with current guidance, EMA/CVMP/016/00-Rev2 ("Guideline on the conduct of bioequivalence studies for veterinary medicinal products"), Chapter 7.1 (d):
The formulations are identical (identical active substances and excipients as well as physicochemical properties [e.g. identical concentration, dissolution profile, crystalline form, pharmaceutical form and particle size distribution with identical manufacturing process]).
Based on the data/information provided, the test product can be accepted as a generic of the reference product and, consequently, the applicant is not required to provide the results of safety tests or of pre-clinical and clinical trials.

Toxicological Studies

As this is a generic application according to Article 13 (1), 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. In case of accidental eye contact, immediately and thoroughly rinse the eyes with clean water. If eye irritation persists seek medical advice and show the package leaflet or the label to the physician. If contact with the skin occurs, wash hands with soap and water.

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- People with a known hypersensitivity to insecticides or alcohol should avoid contact with the veterinary medicinal product.
- Wash hands after use.
- Ingestion of the product is 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.

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

See **Part III.A**
As this is a generic application according to Article 13 (1), and bioequivalence with a 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

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 HPRA website.
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.

Changes:
None.

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