ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Ectofly 12.5 mg/ml Pour-On Solution for Sheep (UK, IE, FR, EL, ES, PT, IT, RO)
FlyEcto 12.5 mg/ml Pour-on Solution for Sheep (SE)

PuAR correct as of 06/07/2018 when RMS was transferred to FR.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0426/001/MR
Name, strength and pharmaceutical form	Ectofly 12.5 mg/ml Pour-On Solution for Sheep
Applicant	Cross Vetpharm Group Ltd Broomhill Road Tallaght Dublin Ireland
Active substance(s)	Cypermethrin High:Cis (80:20) 12.5 mg
ATC Vetcode	QP53AC08
Target species	Sheep
Indication for use	For the treatment and control of headflies, and treatment of tick infestation and biting lice. For the prevention and treatment of blowfly strike.

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 mutual recognition procedure	22 February 2012.
Date product first authorised in the Reference Member State (MRP only)	05 April 2011.
Concerned Member States for original procedure	France, Greece, Ireland, Italy, Portugal, Romania, Spain, Sweden

I. SCIENTIFIC OVERVIEW

Ectofly 12.5 mg/ml Pour-On Solution for Sheep is authorised for use in sheep for the treatment and control of headflies, and treatment of tick infestations and biting lice. The product can also be used for the prevention and treatment of blowfly strike in sheep.

The application was for a mutually recognised Marketing Authorisation for a generic product, and was submitted in accordance with Article 13 (1) of Directive 2001/82/EC, as amended by 2004/28/EC. The applicant claimed exemption from bioequivalence studies in accordance with exemption 4.c) of the Guidelines for the Conduct of Bioequivalence Studies for Veterinary Medicinal Products. The reference product is Crovect 1.25% pour-on solution for sheep, a product marketed by Novartis. Crovect 1.25% was first authorised in the UK in March 2001 as a National Informed Consent product. The reference product for Crovect 1.25% was Young's Vector, which is now discontinued.

The product is supplied in white high-density polyethylene flat bottom containers with polypropylene closures and induction heat-sealed wadding, in 1 litre, 2.5 litre and 5 litre pack sizes. The product must be applied only with the recommended applicator's gun, as the product may have a detrimental effect on certain components of conventional dosing guns.

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, the consumer of foodstuffs from treated animals and for the environment, when

[1] SPC - Summary of Product Characteristics.

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

The product contains cypermethrin high:cis (80:20) 1.25 %w/v., and the excipients are green dye (E142) and diethylene glycol monobutyl ether.

The container/closure system consists of white, high-density polyethylene flat bottom containers with polypropylene closures and induction heat-sealed wadding, in 1 litre, 2.5 litre, 5 litre and 7.5 litre (2.5 litre plus 5 litre) pack sizes 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 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. The manufacturing process is simple solubilisation process, with active substance an excipients being mixed as appropriate. In-process analyses are performed at various time points, before the product is filled into containers.

C. Control of Starting Materials

The active substance cypermethrin high:cis (80:20) is an established active substance and supporting data have been provided in the form of a Drug Master File. It is considered that the manufacturing process is adequately controlled and the active substance specification has been suitable justified. The active substance is manufactured in accordance with the principles of good manufacturing practice and the specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

A declaration was received from Cross Vetpharm Group Ltd, stating that the finished product complies with the latest version of the CVMP guideline on TSEs (EMEA/410/01 Rev. 2 of October 2003). A UK Format 3 statement was supplied

which indicated the active substance and excipients are sourced from non-animal origin.

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.

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. Data have been provided which indicate that the active substance is stable when stored in the appropriate container under appropriate conditions. The retest period of 2 years is justified.

For the finished product, data have been provided which indicate that the finished product is stable for 2 years when stored at a temperature below 25°C.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

An in-use shelf life of 3 months was justified.

- Do not store above 25°C.
- Protect from direct sunlight.
- Store in tightly closed original container in a safe place.
- Store away from food, drink and animal feeding stuffs.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmacological, toxicological and residues tests were not required.

The quantitative and qualitative aspects of this product are identical to the reference product. 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, the environment and consumers.

III.A Safety Testing

Ecotoxicity

The applicant provided a Phase II environmental risk assessment in compliance with the relevant guidelines. The PNEC[2] values derived from several studies were acceptable and in accordance with VICH guidelines.

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 product literature highlights the fact that the product is extremely dangerous to aquatic vertebrates, and that care must be taken not to contaminate ponds, waterways or ditches with the product or used container.

Withdrawal Periods

The withdrawal period is same as the reference product, meat and offal 8 days. A withdrawal period for milk of 5 days has been established.

IV CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

Pharmacodynamics
Cypermethrin is a neuropoison acting on the axons in the peripheral and central nervous system of insects by interacting with sodium channels.

[2] Predicted no effect concentration

Pharmacokinetics
Synthetic pyrethroids are generally metabolised in mammals through ester hydrolysis, oxidation and conjugation, and there is no tendency to accumulate in tissues.

Tolerance in the Target Species of Animals

Ectofly 1.25% w/v Pour-On Solution for Sheep was demonstrated as being quantitatively and qualitatively same as the reference product, Crovect 1.25% w/v. The applicant claimed for exemption under item 4c) of the Guidelines for the Conduct of Bioequivalence Studies for Veterinary Medicinal Products from providing bioequivalence studies, and, in accordance with Article 13(1), exemption from providing any data on this section. This was considered acceptable.

Resistance

Ectofly 1.25% w/v Pour-On Solution for Sheep was demonstrated as being quantitatively and qualitatively same as the reference product, Crovect 1.25% w/v. The applicant claimed for exemption under item 4c) of the Guidelines for the Conduct of Bioequivalence Studies for Veterinary Medicinal Products from providing bioequivalence studies, and, in accordance with Article 13(1), exemption from providing any data on this section. This was considered acceptable. Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

Ectofly 1.25% w/v Pour-On Solution for Sheep was demonstrated as being quantitatively and qualitatively the same as the reference product, Crovect 1.25% w/v. The applicant claimed for exemption under item 4c) of the Guidelines for the Conduct of Bioequivalence Studies for Veterinary Medicinal Products from providing bioequivalence studies, and, in accordance with Article 13(1), exemption from providing any data on this section. This was considered acceptable

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)