IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

Zeromectin 5 mg/ml Pour-on Solution for beef and dairy cattle

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PRODUCT SUMMARY

EU Procedure number	IE/V/0356/001/MR
Name, strength and pharmaceutical form	Zeromectin 5 mg/ml Pour-on Solution for beef and dairy cattle
Active substance(s)	Eprinomectin
Applicant	Chanelle Pharmaceuticals Manufacturing Ltd. Loughrea Co. Galway Ireland
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of Authorisation	22nd May 2015
Target species	Cattle (beef and dairy cattle)
Indication for use	The product is indicated for effective treatment and control of gastrointestinal roundworms (adults and fourth-stage larvae), lungworms, warbles (parasitic stages), mange mites, lice and horn flies.
ATCvet code	QP54AA04
Concerned Member States	DE, UK

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 product is safe for the user, the consumer of foodstuffs from treated animals 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.

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II QUALITY ASPECTS

A. Qualitative and Quantitative Particulars

The product contains the active substance eprinomectin 5 mg/ml and the excipients propylene glycol dicarprylocaprate and butylated hydroxytoluene.
The containers are high density polyethylene containers with a tamper evident cap which consist of the 1 L 'Squeeze pour' packs and 2.5 L, 3 L and 5 L 'Flexi' packs.
The 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 in accordance with European guidelines is provided.

C. Control of Starting Materials

The active substance is eprinomectin. 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 has been provided.

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

Compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated. **D. Control tests 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 has been provided demonstrating compliance with the specification.

F. Stability

Stability data has 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 has been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

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G. Other Information

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application. The product is the same as the reference product Eprinex 0.5% w/v pour-on solution for beef and dairy cattle (VPA 10857/003/001, Merial Animal Health Ltd.) in terms of qualitative and quantitative composition of the active substance (eprinomectin) and has the same pharmaceutical form (pour-on solution). In addition, the product contains the same excipients as the reference product and it is accepted that any differences between products in terms of quantity of excipients are minor and will not influence bioavailability. Therefore, an exemption from the conduct of an *in vivo* bioequivalence study is justified. It is accepted that the test product is bioequivalent to the reference product.

As bioequivalence with an authorised reference product is accepted, specific pharmacological data relating to the active substance have not been presented.

Toxicological Studies

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application. As bioequivalence with an authorised reference product is accepted, specific toxicological data relating to the active substance have not been presented.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the user safety profile will be the same as that of the reference product.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

Phase I

The Phase I assessment showed that the trigger of 100 µg/kg was not exceeded. However, as this is an endectoparasiticide, a Phase II ERA was required.

Phase II

The applicant provided a comprehensive data package on the environmental fate and toxicity of eprinomectin. Using those study data, the applicant presented a detailed ERA. The risk assessment highlights potential risks for aquatic organisms in surface water and sediment and for dung dwelling organisms. Eprinomectin is considered to be very toxic to dung fauna and aquatic organisms. Faeces containing eprinomectin excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on dung degradation.

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A PBT assessment was conducted, it was determined that eprinomectin is persistent in soils and may accumulate in sediments.

The available data indicated that the risk to aquatic ecosystems and dung fauna can be reduced by avoiding too frequent and repeated use of eprinomectin in cattle. The risk to aquatic ecosystems will be further reduced by keeping treated cattle away from water bodies for three weeks after treatment.

The environmental risks identified for this product are as expected for this class of compound (macrocyclic lactones) and, with a view to reducing the risks identified, risk mitigation measures similar to those accepted for related products have been included in the SPC and on product labelling.

III.B Residues Documentation

Residue Studies

No residue depletion studies were conducted because the product is essentially similar to the reference product. As bioequivalence is accepted the withdrawal periods approved for the reference product can be applied to this product.

MRLs

Eprinomectin is listed in Table I of the Annex to Commission Regulation (EU) No 37/2010 as follows:

	Bovine
Muscle	50 µg/kg
Liver	1500 µg/kg
Kidney	300 µg/kg
Fat	250 µg/kg
Milk	20 µg/kg

Withdrawal Periods

Based on the information presented, a withdrawal period of 15 days for meat in cattle and zero hours for milk are justified.

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IV CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

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Tolerance in the Target Species of Animals

A target animal safety study specific to the test product has not been presented with the application, as the product is essentially similar to the reference product containing 5 mg/ml eprinomectin. On this basis it may be concluded that the same tolerance profile is expected.

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

IV.B Clinical Studies

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application. No proprietary efficacy studies have been carried out. Given the nature of the application, this is accepted.

It is accepted that the efficacy profile of the test product is the same as that of the reference product.

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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