Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Dycoxan 2.5 mg/ml Oral Suspension for Sheep and Cattle
Rumicox 2.5 mg/ml Oral Suspension for sheep and cattle (ES, IT, PT)

Date Created: 15th August 2018

PuAR correct as of 26/03/2019 when RMS was transferred to ES. Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0637/001/DC
Name, strength and pharmaceutical form	Dycoxan 2.5 mg/ml Oral Suspension for Sheep and Cattle
Applicant	Chanelle Pharmaceuticals Manufacturing Ltd. Loughrea Co Galway Ireland
Active substance(s)	Diclazuril
ATC Vetcode	QP51AJ03
Target species	Sheep (lambs),Cattle (calves)
Indication for use	In lambs: Prevention of clinical signs of coccidiosis caused by *Eimeria crandallis* and *Eimeria ovinoidalis* sensitive to diclazuril. In calves: Prevention of clinical signs of coccidiosis caused by *Eimeria bovis* and *Eimeria zuernii* sensitive to diclazuril.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

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 conclusion of the decentralised procedure	31st January 2018
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Hungary, Ireland, Luxembourg, The Netherlands, Poland, Portugal, Romania, Slovakia, Spain

I. SCIENTIFIC OVERVIEW

This was a generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended. The reference product is Vecoxan 2.5 mg/ml Oral Suspension, authorised in the UK since February 1999. The product is indicated in lambs for the prevention of clinical signs of coccidiosis caused by *Eimeria crandallis* and *Eimeria ovinoidalis* sensitive to dicalzuril. In calves the product is indicated for the prevention of clinical signs of coccidiosis cause by *Eimeria bovis* and *Eimeria zuernii* sensitive to diclazuril. The product is an oral suspension and should be administered with a drenching gun. In lambs, dosage is a single oral administration of 1 mg diclazuril per kg bodyweight or 1 ml of the product oral suspension per 2.5 kg bodyweight at about 4-6 weeks of age at the time that coccidiosis can normally be expected on the farm. Under conditions of high infection pressure, a second treatment may be indicated about 3 weeks after the first dosing. In calves, dosage is a single administration of 1 mg diclazuril per kg bodyweight or 1 ml of the product oral suspension per 2.5 kg bodyweight, administered as a single dose, 14 days after moving into a potentially high risk environment. If animals are to be treated collectively they should be grouped according to their bodyweight and dosed accordingly. The product is authorised in pack sizes of 200 ml, 1 litre, 2.5 litre and 5 litre bottles.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto the market. It has been shown that the product can be safely used in the target species, any 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 used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy [2] 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. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains 2.5 mg/ml diclazuril and the excipients methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate, microcrystalline cellulose, carmellose sodium, polysorbate 20, sodium hydroxide and purified water.

The container/closure system consists of a 200 ml PET bottle with child resistant tamper evident high density polyethylene cap with a low density polyethylene lining, or a 1, 2.5 or 5 litre high density polyethylene bottle with polypropylene tamper evident cap with an aluminium seal seal The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the presence of preservative are justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method is a standard process involving the sequential addition and mixing of the components, followed by settling and making to batch volume with purified water. Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is diclazuril, an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice and in accordance with an Active Substance Master File.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

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.

All excipients are manufactured in accordance with the European Pharmacopoeia.

II.C.4. Substances of Biological Origin

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.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 sites have been provided demonstrating compliance with the specification. Control tests on the finished product are those for: appearance, pH, viscosity, density, assay of the active substance, identification of active, identification of preservative, related substances, assay of the preservative, microbiological purity, uniformity of fill, resuspendability and particle size

II.F. Stability

Stability data on the active substance have been provided within the Active Substance Master File 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.

G. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf-life after first opening the immediate packaging: 6 months

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

This was an application for a generic product in accordance with Article 13(1) of Directive 2001/82/EC. Due to the nature of the application pharmacological and toxicological data are not required. Bioequivalence to the reference product has been demonstrated and is discussed in Part IV.

User Safety

A user risk assessment was provided in compliance with the relevant guideline. Warnings and precautions as listed on the product literature are the same as for the reference product and are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

- Wash hands after use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:

The initial predicted environmental concentration (PEC) in soil is less than 100 µg/kg. A Phase II ERA was not required. The applicant provided data to show that the active substance is very persistent in soil but is not bioaccumulative. Soil persistence is highlighted in the SPC. The product is not expected to pose a risk for the environment when used as recommended.

III.B.2 Residues documentation

Residue Studies

Due to the nature of the application and bioequivalence with the reference product has been demonstrated, residue depletion study data are not required. As the product is not intended for administration by intramuscular, subcutaneous or transdermal routes, no further evidence to demonstrate equivalent depletion of residues from the administration site is necessary.

MRLs

Diclazuril is listed in Table 1 of Regulation 37/2010 with no MRL required for all ruminants and porcine species.

Withdrawal Periods

Based on the data provided, a withdrawal period of zero days for meat and offal in sheep (lambs) and cattle (calves) are justified.

IV CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

This was an application for a generic product in accordance with Article 13(1) of Directive 2001/82/EC. Due to the nature of the application the results of pre-clinical and clinical studies are not required. Bioequivalence to the reference product has been demonstrated and is discussed below.

Pharmacology

The applicant conducted and presented two *in vivo* bioequivalence studies, one in lambs and one in calves comparing the test product with the reference product Vecoxan 2.5 mg/ml Oral Suspension for Lambs and Calves. The studies were GLP compliant and block randomized. The animals were fasted before treatment. The test and the reference product were administered orally as a single dose. The parameters for statistical analysis were AUC_t and $C_{max.}$ Non-compartmental statistical methods were applied using EquivTest/PK software. Bioequivalence between the test formulation and reference product was tested with the 90% confidence intervals of the parameters. The 90% confidence intervals are within the pre-specified acceptance limits of 80 – 125% for $AUC_{t.}$ For $C_{max,}$ the the 90% confidence intervals70 – 143%, justified by expected variability in this parameter following oral dosing and a high tolerability of the active substance in calves and lambs. Both studies showed bioequivalence, with 90% confidence intervals for ratios for $C_{max,\ ,}$ $AUC_{t\ ,}$ and AUC_{inf} and therefore bioequivalence can be concluded.

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 of the product is favourable.

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.

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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.

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