IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Bimacox 2.5 mg/ml Oral Suspension for Sheep and Cattle

PRODUCT SUMMARY

EU Procedure number	IE/V/0784/001/DC
Name, strength and pharmaceutical form	Bimacox 2.5 mg/ml Oral Suspension for Sheep and Cattle
Active substance(s)	Diclazuril
Applicant	Bimeda Animal Health Limited 2, 3 & 4 Airton Close Airton Road, Tallaght Dublin 24 Ireland
Legal basis of application	Hybrid application in accordance with Article 19(1) of Regulation (EU) 2019/6
Date of completion of procedure	12th June 2024
Target species	Sheep (lambs), cattle (calves)
Indication for use	Lambs: Prevention of clinical signs of coccidiosis caused by *Eimeria crandallis* and *Eimeria ovinoidalis*. Calves: Prevention of clinical signs of coccidiosis caused by *Eimeria bovis* and *Eimeria zuernii*.
ATC vet code	QP51BC03
Concerned Member States	AT, BE, CZ, DE, EE, ES, FR, IT, LV, LT, PL, PT, UK(NI)

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 (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.
It has been shown that the VMP can be safely used in the target species; the reactions observed are indicated in the SPC.
The VMP 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 VMP was demonstrated according to the claims made in the SPC.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

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A. Qualitative and Quantitative Particulars

The product contains the active substance diclazuril at 2.5 mg/ml and the excipients methyl parahydroxybenzoate, propyl parahydroxybenzoate, microcrystalline cellulose and carmellose sodium, citric acid monohydrate, polysorbate 20, sodium hydroxide and purified water.
The container/closure system consists of high density polyethylene container with polypropylene tamper-evident cap with an aluminium seal.

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 is diclazuril, an established substance described in the European Pharmacopoeia. 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
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 has been provided demonstrating compliance with the specification.

F. Stability
Stability data on the active substance 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.

G. Other Information
Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This application has been submitted in accordance with Article 19(1) of Regulation (EU) 2019/6 (hybrid veterinary medicinal product).
The reference product is Vecoxan 2.5 mg/ml Oral Suspension for lambs and calves (VPA 10996/285/001, Intervet Ireland Limited).
Warnings and precautions as listed on the product literature are similar to those of the reference product and are adequate to ensure safety of the product to users, consumers and the environment.

III.A Safety Testing
Pharmacological Studies
No pharmacodynamic data were presented. Given the legal basis of the application (hybrid VMP) cross-reference to the data of the reference product was accepted.
The applicant has conducted *in vivo* bioequivalence studies in lambs and calves. In the case of bioequivalence in lambs, diclazuril values fell outside the pre-determined confidence intervals for the ratio of the two treatment means for both Cmax (152.8 – 186.6%) and AUCt (148.2 – 192.2%). Similarly, for cattle, the assessment of bioequivalence demonstrated that the confidence intervals for both Cmax (167.9 – 214.6%) and AUCt (157.2 – 195.9%) were outside the pre-determined limits. Based on the available information, it was concluded that the test article is suprabioavailable and that bioequivalence with the reference product has not been demonstrated in lambs or calves.

Toxicological Studies
The applicant has referred to the toxicology data detailed in the CVMP Diclazuril MRL Summary Reports. It was accepted that adequate information on the toxicology of diclazuril is available.

User Safety

The applicant has provided a user safety assessment. The VMP and the reference product are of the same qualitative and quantitative composition in terms of active substance. The VMP is intended to be administered by the oral route of administration, at the same dose, and for the same indications for use in the same species as the reference product. Given no difference in terms of active substance and qualitatively similar excipients as in the reference product, it was accepted that the risk posed to the user by the VMP is not expected to differ to that posed by 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

An environmental risk assessment (ERA) has not been provided, instead the applicant has cited the approach detailed in the 'Reflection paper on the interpretation of Article 18(7) of Regulation (EU) 2019/6' (EMA/CVMP/ERA/622045/2020) as a means to justify why an ERA should not be required. It was accepted that an ERA according to VICH GL38 has been performed by a competent authority for a sufficiently similar product and that the applicant should not be required to provide an ERA under Article 18(7) of Regulation (EU) 2019/6.

III.B Residues Documentation

Residue Studies

No residue depletion studies were conducted. The VMP and the reference product are of the same qualitative and quantitative composition in terms of active substance. The excipients are qualitatively the same. In addition, the VMP is intended to be administered by the oral route of administration, at the same dose, and for the same indications for use in the same species as the reference product.
Diclazuril is listed in Table 1 of the Annex to Commission Regulation (EU) No. 37/2010 as "No MRL required" for all ruminants, and the excipients are also allowed substances with "No MRL required" status. Noting that the entry for diclazuril was, in part, based on the consumer intake of residues representing less than 3% of the acceptable daily intake (ADI) 24 hours post-treatment, following administration of 5 mg/kg bw to cattle and 1 mg/kg bw to lambs it was accepted that residue depletion studies were not required and that the VMP will not pose a risk to consumer safety.

MRLs

Diclazuril is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active substance	**Marker residue**	**Animal species**	**MRL**	**Target tissue**	**Other provisions**
Diclazuril	Not applicable	All ruminants, porcine	No MRL required	Not applicable	For oral use only
	Diclazuril	Poultry	500 µg/kg 500 µg/kg 1500 µg/kg 1000 µg/kg	Muscle Skin and fat in natural proportions Liver Kidney	Not for use in animals from which eggs are produced for human consumption
		Rabbit	150 µg/kg 300 µg/kg 2500 µg/kg 1000 µg/kg	Muscle Fat Liver Kidney	

Withdrawal Periods

Based on the data provided, the following withdrawal periods are justified.
Meat and offal:
Sheep (lambs): zero days
Cattle (calves): zero days
Not authorised for use in animals producing milk for human consumption.

IV. CLINICAL ASSESSMENT

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has not been demonstrated, information to support efficacy has been considered.

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

No target animal tolerance studies in the target species were conducted. Bibliographical data have been provided which shows that diclazuril is of low toxicity and that increased bioavailability is unlikely to pose a safety concern for either target species. The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance
Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies
The applicant provided information to show that increased bioavailability will not affect the efficacy profile of the VMP. The efficacy claims for this VMP are equivalent to those of the reference product. Appropriate restrictions and a range of warnings and advice to support the prudent use of anticoccidials are included in the product information.

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.