IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Diclazuril Karizoo 2.5 mg/ml Oral Suspension for lambs and calves

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Diclazuril Karizoo 2.5 mg/ml Oral Suspension for lambs and calves
Active substances(s)	Diclazuril
Applicant	Laboratorios Karizoo S.A. Pol. Ind. La Borda Mas Pujades, 11-12 08140 Caldes de Montbui Barcelona Spain
Legal basis of application	Hybrid application (Article 19(1)(b) of Regulation (EU) 2019/6)
Date of completion of procedure	12/02/2024
Target species	Sheep (lambs) and cattle (calves)
Indication for use	In lambs: Prevention of clinical signs of coccidiosis caused by *Eimeria crandallis* and *Eimeria ovinoidalis*. In calves: Prevention of clinical signs of coccidiosis caused by *Eimeria bovis* and *Eimeria zuernii*.
ATCvet code	QP51AX03
Concerned Member States	N/A

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 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.

II. QUALITY ASPECTS

A. Qualitative and Quantitative Particulars
The product contains 2.5 mg/ml diclazuril as the active substance and the excipients methyl parahydroxybenzoate, propyl parahydroxybenzoate, microcrystalline cellulose and carmellose sodium, polysorbate 20, citric acid monohydrate, sodium hydroxide and purified water.
The container/closure system consists of high density bottles of 1 L, 2.5 L and 5 L closed with polypropylene screw caps with induction disk.

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 is a hybrid application according to Article 19 of Regulation (EU) 2019/6, and the applicant has cited a suitable reference product ('Vecoxan 2,5 mg/ml suspension terneros y corderos' as authorised in ES). The safety aspects of this product are accepted as being the same as those of the reference product.
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, the environment and consumers.

III. SAFETY ASSESSMENT

Pharmacological Studies

Two pivotal *in vivo* bioequivalence studies in the target animal species lambs and calves have been provided in support of this application. In these studies, the candidate product was compared to the reference product ('Vecoxan 2,5 mg/ml suspension terneros y corderos' as authorised in ES) when administered *per os* at the authorised posology of 1 mg/ kg bodyweight. The studies were performed to GLP standard. In all animals studied, the candidate product was well tolerated.
Based on the results of these studies, the candidate and reference products were not demonstrated to be bioequivalent in accordance with guideline requirements, however it is accepted based on supporting information presented that any differences observed are not anticipated to negatively impact on the safety profile of the candidate product in the target animal species lambs and calves. The safety profile of the reference product can therefore be extrapolated to the candidate product in the context of this application, and the results of further pharmacological and toxicological studies are not required.

User Safety

It is accepted that risk posed to a user by the candidate product will not differ from that posed by the approved reference product. The following warnings and precautions as listed on the product literature are considered adequate to ensure safety to users of the product:

- Esters of parahydroxybenzoic acid may cause allergic reactions (possibly delayed). People with known hypersensitivity to parabens should administer the veterinary medicinal product with caution.

- Wash hands after administration of the veterinary medicinal product.

Environmental Risk Assessment

Phase I

The applicant has presented an environmental risk assessment that is compliant with current guidance. The environmental risk assessment can stop in Phase I and no Phase II assessment is required as calculated PEC_{soil} values for use in intensively reared calves and pasture-reared lambs are <100 µg/kg.

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, however based on publicly available information, text highlighting the classification of diclazuril as very persistent in soil has been included in the SPC of the candidate product.

III.B Residues Documentation

Residue Studies

No residue depletion studies were conducted in support of this application as extrapolation of the withdrawal period for the approved reference product to the candidate product can be accepted.

MRLs

Diclazuril is listed in Table I of the Annex to Commission Regulation (EU) No 37/2010 as 'No MRL required' in all ruminants (for oral use only).

Withdrawal Periods

A withdrawal period of zero days for meat and offal in sheep (lambs) and cattle (calves) is accepted. The candidate product is not authorised for use in animals producing milk for human consumption.

IV. CLINICAL ASSESSMENT

This is a hybrid application according to Article 19 of Regulation (EU) 2019/6. Based on the results of two pivotal *in vivo* bioequivalence studies, the candidate and reference products were not demonstrated to be bioequivalent in accordance with guideline requirements, however it is accepted based on supporting information presented that any differences observed are not anticipated to negatively impact on the efficacy profile of the candidate product in the target animal species lambs and calves. As such, efficacy studies are not required, and the efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacological Studies

The applicant has proposed inclusion of the same information in sections 4.2 and 4.3 of the SPC 'Pharmacodynamics' and 'Pharmacokinetics' as that contained in the equivalent sections of the SPC of the approved reference product, which is considered acceptable.

Tolerance in the Target Species of Animals

It is accepted that the target animal safety profile of the candidate product will not differ from that of the reference product. The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance

The applicant has provided a summary of published literature concerning reported resistance to diclazuril. The SPC for the candidate product contains similar warnings concerning the development of resistance as are included in the SPC of the reference product, and these have been suitably updated where necessary.

IV.B Clinical Studies

No clinical studies have been provided in support of this application and it is accepted that the efficacy claims for this product are equivalent to those 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.