IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Rumenil 34 mg/ml oral suspension for cattle

PRODUCT SUMMARY

EU Procedure number	IE/V/0369/001/MR
Name, strength and pharmaceutical form	Rumenil 34 mg/ml oral suspension for cattle
Active substance(s)	Oxyclozanide
Applicant	Chanelle Pharmaceuticals Manufacturing Ltd. Loughrea Co. Galway
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of Authorisation	19th February 2016
Target species	Cattle
Indication for use	This product is indicated for the treatment and control of fascioliasis in cattle. It removes practically all adult flukes (*Fasciola*spp.) present in the bile ducts of the liver. Tapeworm segments (*Moniezia*) are also removed.
ATCvet code	QP52AG06
Concerned Member States	BG, ES, HU, LT, 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 slight reactions observed are indicated in the SPC.

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 the active substance oxyclozanide (34 mg/ml) and the excipients sodium laurilsulfate, propylene glycol, methyl parahydroxybenzoate, propyl parahydroxybenzoate, disodium edetate, carmellose sodium, aluminium magnesium silicate, simeticone, sodium citrate and purified water.

The container/closure system consists of 1 L, 2.5 L or 5L HDPE flexi pack containers with polypropylene caps with tamper evident seals or 10 L HDPE containers with HDPE caps with aluminium seals.

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 oxyclozanide, an established active substance described in the British Veterinary 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)

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 applicant has conducted a bioequivalence study in cattle. Comparable rates and extent of oxyclozanide absorption/systemic exposure for Rumenil 34 mg/ml oral suspension for cattle and the reference product, Zanil Fluke Drench following oral administration at a dose rate of 10 mg oxyclozanide/kg bodyweight to calves were observed. The results of the study indicate that the 90% confidence intervals for both AUC and C_{max} lie within the narrower limits of 80-125%. For plasma oxyclozanide, the products can be considered bioequivalent with respect to AUC and C_{max}.

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results on pharmacodynamics are not required.

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 are not required.

User Safety

The applicant has provided a user safety assessment which shows that the 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
A Phase II ERA is required as the Phase I assessment showed that the product is an endoparasiticide.

Phase II Tier A
A Phase II Tier A assessment was conducted.

The applicant provided studies which show that the product does not pose a risk to soil microbes, terrestrial plants and earthworms. However, potential risks for the following organisms were identified:

- algae, daphnids and fish following direct excretion into a water body,
- sediment-dwelling organisms in case of direct excretion into a water body, and
- dung dwelling organisms exposed to dung produced by treated pasture animals.

Based upon the data provided, a risk for the environment could not be excluded and a Tier B assessment was performed.

Phase II Tier B

In order to further characterise the risk for the environment, a refinement of predicted exposures was undertaken. Based on information on the excretion pattern of oxyclozanide in faeces it was calculated that the risk to aquatic and sediment-dwelling organisms from direct excretion will be acceptable after five days.

In relation to dung dwelling organisms exposed to dung produced by treated pasture animals, no refinement of the risk was possible. However, it is accepted that the risk needs to be considered in conjunction with factors that serve to mitigate potential risk on a population level (such as dung fly/bettle behavioural patterns and compensatory strategies).

As the results of the tier B assessment indicate that a risk for the environment cannot be excluded, appropriate measures to mitigate the identified risks are required for this product.

Conclusion

Based on the data provided in the ERA, a risk to the aquatic environment and dung organisms following direct excretion cannot be excluded. Therefore suitable risk mitigation measures and advice were included in the SPC for this product.

III.B Residues Documentation

Residue Studies

As bioequivalence with the reference product is accepted and taking into account that this product is administered orally,it is reasonable to expect that there will be no difference between products with respect to residue depletion from the primary target tissues, including milk.

A milk residue depletion study using the final formulation has been conducted in cattle.The analytical method was LC-MS/MS. The method was fully validated. Results of the study confirm that residues depleted to below the MRL in milk before the end of the withdrawal period.

MRLs

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

	All ruminants
Muscle	20 µg/kg
Liver	500 µg/kg
Kidney	100 µg/kg
Fat	20 µg/kg
Milk	10 µg/kg

Withdrawal Periods

Based on the information provided, a withdrawal period of 28 days for meat in cattle and 72 hours for milk are justified.

IV. CLINICAL ASSESSMENT

IV.A Pre-Clinical 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 bioequivalent with the reference product Zanil Fluke Drench (VPA 10996/262/001, Intervet Ireland Ltd.)
As bioequivalence with the reference product has been demonstrated, the results of pre-clinical and clinical trials are not required.

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 bioequivalent with the reference product. 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.

Resistance

Adequate warnings and precautions appear on the product literature.

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 Rumenil 34 mg/ml oral suspension for cattle 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.