IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

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Fasinex 240 mg/ml oral suspension for cattle

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Fasinex 240 mg/ml oral suspension for cattle
Active substance(s)	Triclabendazole
Applicant	Elanco GmbH Heinz-Lohmann-Strasse 4 27472 Cuxhaven Germany
Legal basis of application	Full application in accordance with Article 12(3) of Directive 2001/82/EC as amended.
Date of Authorisation	5th September 2008
Target species	Cattle
Indication for use	For the treatment of acute, subacute and chronic infection due to early immature, immature, and mature stages of *Fasciola hepatica*.
ATCvet code	QP52AC01

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, 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 triclabendazole (240 mg/ml) and the excipients microcrystalline cellulose and carmellose sodium, povidone K30, methyl parahydroxybenzoate, propyl paraphydroxybenzoate, benzyl alcohol, simethicone emulsion, propylene glycol and purified water.

The container/closure system consists of high density polyethylene containers of 0.8 L, 2.2 L, 5 L and 12 L.

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 triclabendazole, an established active 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 have 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 have been provided.
Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

F.Stability

Stability data on the active substance have 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 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

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.ASafety Testing

Pharmacological Studies

No new data presented. The applicant refers to data submitted for the original product, Fasinex 10% Oral Suspension

The applicant has conducted pharmacokinetic studies and has provided bibliographical data which show that the product can be considered bioequivalent to the reference product, Fasinex 10% suspension.

About 75% of the orally administered dose of triclabendazole is absorbed from the gastrointestinal tract. Very rapidly absorbed, triclabendazole is almost completely oxidised to its sulfoxide and sulfone. Peak plasma concentrations are reached within 3 days. Both metabolites bind strongly to plasma proteins, particularly albumin. Metabolites are excreted via the bile mainly as conjugates. More than 90% of the total dose of Fasinex is excreted in the faeces, about 2% in the urine and less than 1% in the milk. The elimination is virtually complete by 10 days after administration.

Toxicological Studies

No new data presented. The applicant refers to data submitted for the original product, Fasinex 10% Oral Suspension

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that there is no unacceptable health risk to users of the 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 applicant has provided a Phase 1 environmental risk assessment in compliance with the relevant guideline which shows that a phase II assessment was required. The assessment concluded that the environmental risks are acceptable.No special warnings are required.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.BResidues Documentation

Residue Studies

No tissue residue depletion study was conducted because the applicant has provided original and bibliographic data to show that the product is essentially bioequivalent to the original product, Fasinex 10% Oral Suspension.Residue depletion in tissues is therefore equivalent. Following the establishment of an MRL for milk, residue depletion studies using the final formulation have also been conducted in dairy cows. Samples of milk were taken from animals at several timepoints. Results show that residues depleted to below the MRL in milk before the end of the withdrawal period.

MRLs

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

	All ruminants
Muscle	225 µg/kg
Liver	250 µg/kg
Kidney	150 µg/kg
Fat	100 µg/kg
Milk	10 µg/kg

Withdrawal Periods

Based on the data provided above, a withdrawal period of 56 days for meat is justified. In relation to milk, milk for human consumption may only be taken from 48 hours after calving. If calving occurs before 35 days after treatment, milk for human consumption may only be taken after 35 days plus 48 hours after the treatment.

IV. CLINICAL ASSESSMENT

IV.APre-Clinical Studies

Tolerance in the Target Species of Animals

The applicant has provided original and bibliographic data to show that the product is essentially bioequivalent to the original product, Fasinex 10% Oral Suspension.Target animal tolerance is therefore equivalent.

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

Resistance

The bibliography and information provided indicates that *Fasciola hepatica* may develop resistance to triclabendazole.

Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

Laboratory Trials

The applicant has provided original and bibliographic data to show that the product is essentially bioequivalent to the original product, Fasinex 10% Oral Suspension.Efficacy is therefore equivalent.

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:

Summary of change	Approval date
Establishment of a milk withdrawal period (HPRA case reference number 7012857)	24/08/2012