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Publicly Available Assessment Report for a Veterinary Medicinal Product

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FLUKIVER BOVIS 50 mg/ml Solution for Injection for cattle

PRODUCT SUMMARY

EU Procedure number	IE/V/0244/001/DC
Name, strength and pharmaceutical form	Flukiver Bovis 50 mg/ml Solution for Injection
Active substance(s)	Closantel sodium
Applicant	Elanco GmbH Heinz-Lohmann-Str.4 27472 Cuxhaven Germany
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of procedure	30th June 2010
Target species	Cattle
Indication for use	For the treatment and control of liver fluke, gastro-intestinal nematodes and arthropods.
ATCvet code	QP52AG09
Concerned Member States	AT, NL, 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 50 mg/ml closantel (as the sodium dihydrate) and the excipients propylene glycol, povidone K12, citric acid monohydrate, sodium hydroxide and purified water.
The product is packaged in 250 ml amber type I glass vials sealed with a siliconized bromobutyl rubber stopper and an aluminium overseal. 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 on the product have been presented in accordance with the relevant European guidelines.

C.Control of Starting Materials

The active substance is closantel sodium dihydrate 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 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

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

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

The pharmacological aspects of this product are identical to the reference product.

Toxicological Studies

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

The toxicological aspects of this product are identical to the reference product.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the risk to the user is comparable to that of the reference product. Given that there is a potential risk associated with accidental self-administration, a warning to this effect is included on the product literature. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that further assessment was required. The assessment concluded that the risk to dung organisms and sediment dwelling organisms posed by the administration of the product is acceptable and that the impact on populations of dung fauna species and sediment dwelling organisms will be negligible.

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.B Residues Documentation

Residue Studies

Residue depletion studies using the final formulation have also been conducted in

cattle.Samples of tissues were taken from animals at several time points. Results showed that residues depleted to below the MRL in all tissues before the end of the withdrawal period. Statistical analysis of the results was used to set the withdrawal period.

The analytical method was an LC-MS/MS method. The method was fully validated.

MRLs

Closantel sodium is listed in Table I of the Annex of Council Regulation (EU) 37/2010 (O.J. 20.1.2010, L 15/22).The marker substance is closantel.
MRLs are listed below:

	BOVINE	**OVINE**
Muscle	1000 µg/kg	1500 µg/kg
Liver	1000 µg/kg	1500 µg/kg
Kidney	3000 µg/kg	5000 µg/kg
Fat/ skin	3000 µg/kg	2000 µg/kg
Milk	-	-

Withdrawal Periods

Based on the data provided above, a withdrawal period of 77 days for meat in cattle is justified.
Milk: Not authorised for use in cattle producing milk for human consumption including during the dry period. Do not use during the last trimester of pregnancy in heifers which are intended to produce milk for human consumption.

IV. CLINICAL ASSESSMENT

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

Tolerance in the Target Species of Animals

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

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. 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:

Description of change	**Date issued**
C.I.1.A Update to section 4.11 of SPC to include the following text: Milk: Not authorised for use in cattle producing milk for human	14th March 2013

consumption including during the dry period. Do not use during the last trimester of pregnancy in heifers which are intended to produce milk for human consumption. IE/V/0244/001/IA/004	