IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

Levatum Super Solution for Injection.

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Levatum Super Solution for Injection.
Active substances	Ivermectin Clorsulon
Applicant	Chanelle Pharmaceuticals Manufacturing Ltd., Loughrea, Co. Galway, Ireland.
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of Authorisation	21st December 2010
Target species	Cattle
Indication for use	For the treatment and control of gastrointestinal roundworms, lungworms, liver fluke, eye worms, warbles, mange mites and sucking lice. Also as an aid in the control of some biting lice.
ATCvet code	QP54AA51

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 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 substances ivermectin (10 mg/ml) and clorsulon (100 mg/ml) and the excipients glycerol formal and propylene glycol.

The container/closure system consists of 50 ml, 250 ml and 500 ml HDPE containers with siliconised bromobutyl rubber stoppers.

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 substances are ivermectin and clorsulon, established active substances described in the European Pharmacopoeia. The active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substance specifications are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with these specifications 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(s) have been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substances 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

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.

A bioequivalence study was conducted demonstrating that this product was bioequivalent to the reference product, Ivomec Super, when administered by the subcutaneous route to cattle at a dose of 200 µg/kg ivermectin and 2 mg/kg clorsulon.

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

Warnings and precautions as listed on the product literature reflect those agreed for the reference product and are adequate to ensure safety to users of the product.

Environmental Risk Assessment

The Applicant has conducted a detailed ERA for the product Levatum Super Solution for Injection. Based on the data provided, it is accepted that this product is unlikely to represent an unacceptable risk to the environment when used in accordance with the recommended posology.

III.B Residues Documentation

Residue Studies

A confirmatory residue depletion study using the final formulation was conducted in cattle. Samples of tissues were taken from animals at several time points up to 49 days following treatment. Results show that residues depleted to below the MRL in the relevant target tissues before the end of the study.

The analytical method was a fully validated HPLC (high performance liquid chromatography) with fluorescence detection.

MRLs

Ivermectin and clorsulon are listed in Table 1 of the Annex of Council Regulation 37/2010. The marker substance for ivermectin is 22, 23-dihydroavermectin B1a. The marker substance for clorsulon is clorsulon.

	IVERMECTIN (microg/kg)	**CLORSULON** (microg/kg)
Muscle	30	35
Liver	100	100
Kidney	30	200
Fat / skin	100	-
Milk	-	16

Withdrawal Periods

A Commission Decision relating to the Article 35 referral for ivermectin was published on 1st October 2009. This decision gave effect to the Opinion of the Committee for Medicinal Products for Veterinary Use reached on 5th June 2009 which concluded that a withdrawal period of 66 days for cattle should be established for products containing ivermectin in combination with clorsulon as a second active substance.

In line with the outcome of this referral procedure, a withdrawal period of 66 days was established for meat in cattle for this product.

IV CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13(1), 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 applicant has conducted a controlled target animal tolerance study using multiples of the recommended dose in the target species. All doses were administered by the subcutaneous route. An authorised reference product containing the same active substances and a negative control were included.
Parameters evaluated were clinical observation, including injection site assessment.

The product was well tolerated at the recommended treatment dose: mild, transient reactions at the injection site only were observed. Adverse effects at the injection site were more severe (characterised by tissue necrosis, fibrosis and inflammation) following administration of five times the recommended dose.

Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

As this is a generic application according to Article 13(1), 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:
None.