Institute for State Control of Veterinary Biologicals and Medicines
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(Reference Member State - CZ)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Oriverm 10 mg/mL solution for injection for cattle, sheep and pigs.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	CZ/V/0150/001/DC
Name, strength and pharmaceutical form	Oriverm 10 mg/mL solution for injection for cattle, sheep and pigs
Applicant	actrevo GmbH, Neuer Wall 54, 20354 Hamburg Germany
Active substance(s)	Ivermectin
ATC vet code	QP54AA01
Target species	Cattle, sheep and pigs
Indication for use	The product is indicated for the effective treatment and control of the spread of parasitic disease caused by a number of parasites – see SPC.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	18/12/2019
Date product first authorised in the Reference Member State (MRP only)	NA
Concerned Member States for original procedure	PL

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 claims for this product are equivalent to those of the reference product.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains 10 mg of ivermectin per 1 ml and excipients propylene glycol and glycerol formal.

The container/closure system consists of amber (brown) Ph. Eur. Type II glass vials containing either 50 ml or 100 ml of solution. The vials are closed with chlorobutyl rubber stoppers and sealed with aluminium caps.

The choice of the formulation is sufficiently justified.

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 ivermectin 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.

Scientific data and certificate of suitability issued by the EDQM have been provided.

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

The tests performed during production are described and the results conforming to the specifications are provided.

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 are covered by the relevant certificate of suitability issued by the EDQM.

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 as stated in SPC when stored under the approved conditions.

The in-use shelf-life of the product is supported by relevant data.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and exemption from bioequivalence is claimed on the basis of the product being completely identical to the reference product, results of pharmacological and toxicological tests are not required.

Warnings and precautions as listed on the product literature are adequate to ensure safety of the product to users / the environment / consumers.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline. Due to known cases of propylene glycol hypersensitivity in human medicine and maternal toxicity in animals and in compliance with the human medicine product with the same active substance, the warning sentences considering hypersensitivity and risk for pregnant women have been added.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

A Phase I and Phase II environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines. The product is antiparasitics, solution for injection intended to treat intensively reared animals (cattle, pigs) and also pasture animals (cattle, sheep).

Phase I:

The initial predicted environmental concentrations in soil ($PEC_{soil\ initial}$) were less than 100 µg/kg but the product is an antiparasitic and therefore the potential for ivermectin to adversely affect the environment was anticipated.

For pasture animals (cattle and sheep) ERA Phase II was required.

Phase II:

A Phase II data set was provided according to the requirements of the CVMP/VICH guideline GL38 and the CVMP guideline on the Environmental Impact Assessment for Veterinary Medicinal Products in support of the VICH guidelines GL6 and GL38 (EMEA/CVMP/ERA/418282/2005-Rev.1-Corr.,2016). Risk for the product was identified and appropriate RMM and safety information were included in the product literature. Nevertheless the data were not considered to be complete therefore, a post-authorisation commitment via a variation was agreed at the end of an authorization procedure.

The following mitigation measures and safety warnings were included on the SPC and product literature.

- The product is very toxic to aquatic organisms and dung insects. Treated animals should not have direct access to ponds, streams or ditches for 14 days after treatment. Long term effects on dung insects caused by continuous or repeated use cannot be excluded. Therefore repeated treatment of animals on a pasture with an ivermectin-containing product within a season should only be given in the absence of alternative treatments or approaches to maintain animal/flock health, as advised by a veterinarian.
- Extremely dangerous for fish and aquatic life. Do not contaminate surface waters or ditches with this product or used container.

III.B Residues documentation

This application is for a generic product, submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended, using the decentralised procedure. The reference product is Ivomec 10 mg/ml solution for injection, marketed by Merial SAS, France (Mevet

spol. s r.o., Czech Republic), which has been authorised in the Czech Republic since 12/12/1987.
The formulation of the generic product is essentially similar to formulation of the reference product.

Residue Studies

No residue depletion studies were conducted by the applicant.

MRLs

The active substance ivermectin is an allowed substance as described in table 1 of the annex to Commission Regulation (EU) No 37/2010:

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs (µg/kg)	Target tissues	Other provisions
Ivermectin	22, 23-Dihydro-avermectin B 1a	All mammalian food producing species	30 µg/kg 100 µg/kg 100 µg/kg 30 µg/kg	Muscle Fat Liver Kidney	Not for use in animals from which milk is produced for human consumption

The excipients propylene glycol and glycerol formal are classified as allowed substances with no MRL required in the European Union.

Withdrawal Periods

The formulation of the generic product is essentially similar to formulation of the reference product, therefore the withdrawal periods approved for the reference product can be applied to the generic product.

The text of the withdrawal period(s) is following:

Cattle:
Meat and offal: 49 days.
Milk: Do not use in cattle producing milk for human consumption.

Sheep:
Meat and offal: 28 days.
Milk: Do not use in sheep producing milk for human consumption.

Pigs
Meat and offal: 28 days.

IV. CLINICAL ASSESSMENT (EFFICACY)

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 risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

None

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