MINISTERIO
DE SANIDAD, POLÍTICA SOCIAL
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agencia española de
medicamentos y
productos sanitarios

SUBDIRECCIÓN GENERAL
DE MEDICAMENTOS
DE USO VETERINARIO

Agencia Española de Medicamentos y Productos Sanitarios

Parque Empresarial Las Mercedes
Edificio 8
C/Campezo 1,
28022 – Madrid
España
(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

TOLCOX 50 mg/ml Oral Suspension for pigs

CORREO ELECTRÓNICO

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0194/001/DC
Name, strength and pharmaceutical form	TOLCOX 50 mg/ml Oral Suspension for pigs
Applicant	Vetpharma Animal Health, S.L. C/ Les Corts, 23. 08028 Barcelona. Spain.
Active substance(s)	Toltrazuril
ATC Vet code	QP 51AJ01
Target species	Pigs
Indication for use	For the prevention of clinical signs of coccidiosis in neonatal piglets (3 – 5 days old) on farms with a confirmed history of coccidiosis caused by *Isospora suis.*

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 13 (3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	25/09/2013
Date product first authorised in the Reference Member State (MRP only)	
Concerned Member States for original procedure	CZ, DE, DK, EE, FR, HU, LT, LV, PL, PT, SE, SK, UK.

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 risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains toltrazuril (50 mg) and excipients (sodium docusate, simethicone emulsion, sodium propionate, sodium benzoate, bentonite, citric acid, anhydrous, xanthan gum, propylene glycol and purified water).

The container/closure system is a 250 ml white HDPE bottle with HDPE stopper. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation is 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 from 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 toltrazuril, an established active substance. 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.

An ASMF is included.

D. 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.

F. 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.

G. 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.

The claim of an in use stability of 3 months is based on the demonstration of stability for a batch.

H. Genetically Modified Organisms

J. Other Information

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACOTOXICOLOGICAL)

This is a hybrid application according to Article 13 (3) of Council Directive 2001/82/EC. In accordance with the cited Directive, when bio-equivalence between the reference product and the test product cannot be demonstrated through bioavailability studies, the results of the appropriate safety and residue test shall be provided.

III.A Safety Testing

Pharmacological Studies

The applicant has provided a bibliographical overview which include the main pharmacokinetic and pharmacodinamic properties of the active substance.

Toxicological Studies

The applicant has provided a bibliographical overview which show relevant toxicity aspects of the active substance.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the product does not pose an unacceptable risk to the user.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that the use of the product as recommended in the SPC does not present an unacceptable risk for the environment.
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

A Residue depletion study using the final formulation have also been conducted in piglets. Samples of kidney, liver, fat plus skin and muscle were taken from animals at several time points. Results show that residues depleted to below the MRL in all tissues before the end of the withdrawal period. Alternative approach was used to set the withdrawal period of 73 days.

MRLs

Toltrazuril is included in Table 1 of the Annex of Commission Regulation (EU) No. 37/2010 in accordance with the following table:

Active substance	Marker residue	Animal species	MRL	Target tissues
Toltrazuril	Toltrazuril sufone	Porcine	100 µg/kg 150 µg/kg 500 µg/kg 250 µg/kg	Muscle Skin+fat Liver Kidney

Withdrawal Periods

Based on the data provided above, a withdrawal period of 73 for meat in piglets is justified.

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IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a hybrid application according to Article 13.(3). of Council Directive 2001/82/EC, as amended, and equivalence with a reference product has been demonstrated, the efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

Both the Pharmacodynamic properties and the Pharmacokinetic characteristics are adequately described in the SPC, sections 5.1. and 5.2.

Tolerance in the Target Species of Animals

See also “IV.B: Clinical studies”.

Resistance

Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

The applicant has conducted an equivalence trial, which demonstrated that the product is equivalent to the reference product. An adequate tolerance by the target species was also shown.

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

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 veterinary Heads of Agencies website (www.hma.eu).

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.

<None>