College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
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The Netherlands

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

COCCINOX 25 mg/ml oral solution for use in drinking water for chickens, turkeys, pigeons and rabbits

NL/V/0272/001/DC

Created: March 2022

CMS: BE, FR

MODULE 1

PRODUCT SUMMARY

Dutch Registration number	REG NL 123781
EU Procedure number	NL/V/0272/001/DC
Name, strength and pharmaceutical form	COCCINOX 25 mg/ml oral solution for use in drinking water
Applicant	Avimedical B.V. Abbinkdijk 1 7255 LX Hengelo The Netherlands
Active substance(s)	Toltrazuril
ATC Vet code	QP51AJ01
Target species	Chickens (broilers, pullets and breeders), turkeys, pigeons and rabbits held as “hobby” animals.
Indication for use	For the treatment of coccidiosis in chickens, turkeys, pigeons and rabbits not intensively farmed for meat production (“hobby” animals), caused by infections with various species of *Eimeria*: Chickens*: E. acervulina, E. brunetti, E. maxima, E. mitis, E. necatri* and*, E. tenella.* Turkeys*: E. adenoides* and *E. meleagrimitis* Pigeons*: E. columbae, E. columbarum* and *E. labbeana* Rabbits*: E. intestinalis, E. flavescens, E. magna* and *E. stiedae*

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	Application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	25 September 2019
Concerned Member States for original procedure	BE, FR

I. SCIENTIFIC OVERVIEW

Coccinox is a generic application. The reference product is Baycox 2.5% oplossing voor orale toediening, authorized in the Netherlands with marketing authorisation number REG NL 9857 since 1 December 2005 by Bayer B.V. and withdrawn by the marketing authorisation holder in 2016.

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. Qualitative and quantitative particulars

The product contains toltrazuril 25 mg/ml and the excipients triethanolamine and macrogol 200.

The container/closure system consists of a type III amber glass bottle of 10 or 50 ml with a HDPE screw cap with ring and colourless LDPE syringe insert of 1 ml or 5 ml.

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 on 2 batches in accordance with the relevant European guidelines. Validation should be performed on one additional batch. The data does not need to be submitted to the competent authority but the data

should be held at the manufacturing location and made available for inspection upon request.

C. Control of Starting Materials

The active substance is toltrazuril, an established active substance not 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.

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.

The shelf life, in-use shelf life and shelf life of the medicated solutions are based on the studies provided in the dossier.

G. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmacological and toxicological tests are not required for chickens and turkeys. Coccinox can be considered as a product for minor use in minor species for pigeons and pet rabbits.

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

III.A Safety Testing

Pharmacological Studies

Bioequivalence has been demonstrated between Coccinox and the reference product Baycox 2.5% as registered in the Netherlands based on a biowaiver, since Coccinox is essentially similar to the reference product and both products are to be administered via drinking water.

Observations in Humans

The applicant has provided information which shows that the active substance is not used in human pharmaceutical preparations and the use of the excipients is sufficiently substantiated.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that exposure to toltrazuril through dermal exposure, accidental ingestion or hand-to-mouth contact may cause adverse effects in humans. The product may be irritating to the skin, eye or mucous membranes and the product may cause hypersensitivity reactions. Also, the product may be harmful for the unborn child.

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

Environmental Risk Assessment

The environmental risk assessment can stop in Phase I because Coccinox is intended to be used in animals held as a hobby; i.e. non-intensively reared chickens and turkeys and non-food pigeons and pet rabbits. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted because this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated. The withdrawal periods are identical to the withdrawal periods of the reference product for chickens and turkeys.

MRLs

Toltrazuril is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

	Poultry
Muscle	100 microgram/kilogram
Liver	600 microgram/kilogram
Kidney	400 microgram/kilogram
Fat / skin	200 microgram/kilogram
Eggs	Not for use in animals from which eggs are produced for human consumption.

Withdrawal Periods

Based on the data provided above, a withdrawal period of 16 days for meat in chickens and turkeys are justified. The products is not authorized for use in poultry producing eggs for human consumption and should not be used in pullets beyond the 15th week of life. The product is not authorized for use in pigeons or rabbits intended for human consumption.

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 for chickens and turkeys are equivalent to those of the reference product. Bibliographical data was provided by the applicant to support the efficacy in pigeons and pet rabbits.

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, pharmacology of Coccinox for chickens and turkeys is considered identical to the reference product. In support of the addition of non-food target species pigeons and pet rabbits, peer reviewed published data on pharmacokinetics in the target species rabbits was provided. This is reflected in the SPC.

Tolerance in the Target Species

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, pharmacology of Coccinox for chickens and turkeys is considered identical to the reference product. No target animals safety studies were conducted for pigeons and pet rabbits, based on well-established use and abundant literature on toltrazuril and because these species are considered minor species. Bibliographical evidence was provided to support the safety in pigeons and pet rabbits.

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

Resistance

The information provided suggests that at time of application, no data on resistance in pigeons nor rabbits have been published and for poultry bibliographical data is provided which shows drug resistance against toltrazuril did not occur in at least five successive drug exposures in field studies for *Eimeria*.
Adequate warnings and precautions appear in the product literature.

IV.B Clinical Studies

As this is a generic application according to Article 13, no data was provided for chickens and turkeys. For pigeons and pet rabbits, the applicant provided peer-reviewed published literature on the reference product and other formulations. An efficacious posology is adequately described in the product literature.

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

Summary of change	Section updated	Approval date
Addition of two non-food producing species: pigeons and rabbits held as “hobby” animals Extension of the shelf life of the finished product as packaged for sale Extension of the shelf life of the finished product after dilution (NL/V/0272/II/001/G)	SPC, package leaflet, Module 1, Module 3	7 November 2021