



**College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board**

**Graadt van Roggenweg 500  
3531 AH Utrecht  
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**

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|-----------------|--------------------------------------|
| Coccinox        | NL/V/0272/001/DC                     |
| Avimedical B.V. | DCP                                  |
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## MODULE 1

### PRODUCT SUMMARY

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

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## **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>).

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## 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

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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.

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### **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.

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### **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 Coccinnox 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.

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### ***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 Coccinnox 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.

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## 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<br>Extension of the shelf life of the finished product as packaged for sale<br>Extension of the shelf life of the finished product after dilution<br>(NL/V/0272/II/001/G) | SPC,<br>package<br>leaflet,<br>Module 1,<br>Module 3 | 7 November 2021 |