**FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS**

**DECENTRALISED PROCEDURE**

# PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

## Dozuril 50 mg/ml oral suspension for pigs

**Date: 18/10/2013**

*French agency for food, environnemental and occupational health safety– French Agency for Veterinary Medicinal Products*
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# MODULE 1

**PRODUCT SUMMARY**

| | |
|---|---|
| EU Procedure number | FR/V/0257/001/DC |
| Name, strength and pharmaceutical form | Dozuril 50 mg/ml oral suspension for pigs |
| Applicant | Dopharma Research B.V.<br>Zalmweg 24<br>4941 VX Raamsdonksveer<br>The Netherlands |
| Active substance(s) | Toltrazuril |
| ATC Vetcode | QP51AJ01 |
| Target species | Pig (Piglet, 3-5 days old). |
| 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 website http://www.anmv.anses.fr/

# 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 | 25/09/2013 |
| Concerned Member States for original procedure | AT, BE, DE, DK, EE, HU, LT, LV, NL, PL, RO |

## 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 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 50 mg toltrazuril as active substance and excipients sodium benzoate, sodium propionate, anhydrous citric acic, bentonite, docusate sodium, xanthane gum, simethicone emulsion, propyleneglycol and purified water.

The suspension is packed in HDPE bottles of 250 and 1000 ml. The particulars of the containers and controls performed are provided and conform to the regulation.

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.

### *D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies*

There are no substance within the scope of the TSE Guideline present or used in the manufacture of this product.

### *E. Control on intermediate products*

Not applicable.

### *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.

An in-use shelf-life as details on the SPC has been supported by appropriate data.

### *H. Genetically Modified Organisms*

Not applicable.

### *J. Other Information*

Not applicable.

## III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

### *III.A Safety Testing*

### *Pharmacological Studies*

The applicant has conducted an *in vivo* bioequivalence study in weaned piglets. The results of this study indicate that the test product is bioequivalent to the reference product BAYCOX 5% oral suspension.

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.

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*

The applicant has provided a user safety assessment in compliance with the relevant guideline.

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

### *Ecotoxicity*

The applicant has provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.

## *III.B Residues documentation*

### *Residue Studies*

No residue depletion studies were conducted since the tested product is bioequivalent to the reference product and the product is administered via oral route.

### *MRLs*

**a. active substances**

The active substance, toltrazuril, is included in table 1 of the MRL regulation 37/2010, as follows:

| Marker residue | Animal Species | MRL | Target Tissues | Other Provisions | Therapeutic Classification | Regulation |
|---|---|---|---|---|---|---|
| Toltrazuril sulfone | All mammalian food producing species | 100 µg/kg<br>150 µg/kg<br>500 µg/kg<br>250 µg/kg | Muscle<br>Fat<br>Liver<br>Kidney | For porcine species the fat MRL relates to “skin and fat in natural proportions”.<br>Not for use in animals from which milk or eggs are produced for human consumption. | Antiparasitic agents/ Agents acting against protozoa | 37/2010 of 22.12.2009 |
| | Poultry | 100 µg/kg<br>200 µg/kg<br>600 µg/kg<br>400 µg/kg | Muscle<br>Skin + fat<br>Liver<br>Kidney | | | |

**b. excipients**

The MRL status of excipients of the tested product is indicated in the following table:

| Excipient | MRL status |
|---|---|
| Propylene glycol (E1520) | Table 1, no MRL required, all food producing species |
| Citric acid, anhydrous | Table 1, no MRL required, all food producing species |
| Sodium propionate (E281) | Table 1, no MRL required, all food producing species |
| Sodium benzoate (E211) | Table 1, no MRL required, all food producing species |
| Sodium docusate | Table 1, no MRL required, all food producing species |
| Bentonite | Table 1, no MRL required, all food producing species |
| Xanthan gum (E451) | Table 1, no MRL required, all food producing species |
| Simethicone emulsion | Out of scope list |
| Purified water | Out of scope list |

***Withdrawal Periods***

The tested product was applied identical withdrawal periods than the reference product that is:
Meat and offal: 77 days.

## IV. CLINICAL ASSESSMENT (EFFICACY)

### *IV.A Pre-Clinical Studies*

### *Tolerance in the Target Species of Animals*

The applicant has not provided a tolerance study which is acceptable because the tested product and the reference product are bioequivalent and their formulations are similar.

### *IV.B Clinical Studies*

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 of the tested product are based on the reference product documentation.

## 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.