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

Eradia 125 mg/ml oral suspension for dogs

Date: 15 February 2018

Last update: 10 March 2021

MODULE 1

PRODUCT SUMMARY

Dutch Registration number	REG NL 120912
EU Procedure number	NL/V/0232/001/DC
Name, strength and pharmaceutical form	Eradia 125 mg/ml oral suspension for dogs
Applicant	Virbac SA 1ère avenue 2065 LID Carros France
Active substance(s)	Metronidazole
ATC Vetcode	QP51AA01
Target species	dogs
Indication for use	Treatment of infections of the gastrointestinal tract caused by *Giardia* spp. and *Clostridium* spp. (i.e. *C. perfringens* or *C. difficile*). Treatment of infections of the urogenital tract, oral cavity, throat and skin caused by obligate anaerobic bacteria (e.g. *Clostridium* spp.) susceptible to metronidazole.

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	Hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of the original Decentralised procedure	31 January 2018
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LT, LU, LV, NO, PL, PT, RO, SE, SI, SK, UK.

I. SCIENTIFIC OVERVIEW

Eradia 125 mg/ml oral suspension for dogs 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.
Eradia 125 mg/ml oral suspension for dogs is safe for the user 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.

The safety and efficacy aspects of Eradia 125 mg/ml oral suspension for dogs are based on bioequivalence with the (European) Reference product Metrazol REG NL 5757.
Warnings statements and precautions are adopted from the reference product.
Additional statements have been added, based on increased knowledge and the current state of science. Adverse events, warnings and contraindications are indicated in the SPC.

II. QUALITY ASPECTS

A. QUALITATIVE AND QUANTITATIVE PARTICULARS

The proposed veterinary medicinal product is a non-aqueous suspension for oral administration to dogs. The product contains 125 mg/mL metronidazole as active substance and the following excipients: aluminium stearate, stearic acid, butylhydroxytoluene, poultry liver powder and triglycerides medium-chain.

The product is packed in a 30 mL or 100 mL multidose PET bottle closed with a plastic dispenser cap (a screw or snap cap). The outer carton box also contains a 3 mL graduated syringe.

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 two licensed manufacturing sites.

The manufacturing process is regarded as a non-standard process. Process validation results have been provided for six industrial scale batches, where three batches were of a maximum batch size.

The tests performed during production are described.

C. CONTROL OF STARTING MATERIALS

The active substance is metronidazole, an established active substance described in the European Pharmacopoeia (monograph 0675). For the active substance the CEP procedure is followed. 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 the drug substance specification have been provided.

The excipient poultry liver powder is of animal origin and is used in the manufacturing process of the veterinary medicinal product. BSE/TSE declarations have been provided. The product can be considered safe in regard to BSE/TSE and viral safety.

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 the corresponding acceptance criteria are considered to be acceptable.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data have been submitted for three batches of the maximum batch size, demonstrating compliance with the finished product specification.

F. STABILITY

Stability data on the active substance has been assessed by the EDQM in order to be granted a CEP. The assigned re-test period for the drug substance of 5 years with storage condition 'Store in double polyethylene bags placed in fibreboard drums' as mentioned on the CEP is applied by the finished product manufacturer as well.

Stability data on the finished product have been provided in accordance with applicable European guidelines. Based on the submitted real time stability data for the drug product a shelf-life of 36 months with storage conditions 'Store below 30 °C' can be granted.

Additional stability studies justify the claimed 3 months (30 mL bottle) and 6 months (100 mL bottle) in-use shelf-life of the product.

G. OTHER INFORMATION

None

III. SAFETY ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a hybrid application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological, pharmacological and clinical tests are not required.

Warnings and precautions as listed on the product literature are adequate to ensure safety of the product to users and the environment. Additional statements have been added, based on increased knowledge and the current state of science. Adverse events, warnings and contraindications are indicated in the SPC.

III.A SAFETY TESTING

USER SAFETY

Being a hybrid procedure the applicant refers to the reference product for information on this section.

Additionally, as the product is an oral suspension whereas the reference product is a tablet, the applicant has provided a user safety assessment in compliance with the relevant guideline. Based on the proposed packaging and risk management measures, there are no more residual risks for the user of the product. Combined with increased knowledge and the current state of science, warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

ENVIRONMENTAL RISK ASSESSMENT

The applicant provided a first phase environmental risk assessment according to the CVMP/VICH guidelines which showed that no further assessment is required.

The environmental risk assessment can stop in Phase I because this product is intended for use in dogs and a Phase II assessment is not deemed necessary.

The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a hybrid 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.

TOLERANCE IN THE TARGET SPECIES OF ANIMALS

Additionally to the above, based on increased knowledge and the current state of science, warning statements and precautions have been added to the product literature ensuring safety to the target animals. Adverse events, warnings and contraindications are indicated in the SPC.

RESISTANCE

As this is a hybrid application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological and pharmacological and clinical tests are not required. However, the SPC and Product Literature are updated according to the Revised Guideline on the SPC for Antimicrobial Products (EMEA/CVMP/SAGAM/383441/2005).

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 Heads of Veterinary Medicines 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.

Significant changes in administrative or quality data include any Type II change, which affects the initial report. The following Type IA or IB changes may also apply:

Variation

Type IA: B.III.1.a.3 New certificate from a new manufacturer (addition)	Approved 19 August 2018
Type IB: B.II.f.1. change in the shelf life or storage conditions of the finished product; b) Extension of the shelf life of finished product; 1. As packaged for sale The shelf life is increased from 24 months to 36 months, based on real time stability data.	Approved 2 August 2019