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

Enrotab 15 mg tablets for cats and dogs
Enrotab 50 mg tablets for dogs
Enrotab 150 mg tablets for dogs

NL/V/0136/001-003/DC

Created: June 2022

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0136/001-003/DC
Name, strength and pharmaceutical form	Enrotab 15 mg, 50 mg and 150 mg tablets
Applicant	CP-Pharma Handelsges. mbH Ostlandring 13 31303 Burgdorf Germany
Active substance(s)	Enrofloxacin
ATC Vetcode	QJ01MA90
Target species	Dogs, cats.
Indication for use	In cats (15 mg tablets only): Treatment of upper respiratory tract infections. In dogs (15, 50 and 150 mg tablets): - Treatment of lower urinary tract infections (associated or not with prostatitis) and upper urinary tract infections caused by *Escherichia coli* or *Proteus mirabilis*. - Treatment of superficial and deep pyoderma.

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	Generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	2 June 2010
Concerned Member States for original procedure	AT, BE, CZ, DE, DK, ES, FI, FR, HU, IE, IT, NO, PL, PT, SE, SK, UK(NI). (Marketing authorisations withdrawn in AT, BE, CZ, DE, DK, FI, FR, IE, IT, NO, PL, PT, SE, SK, UK(NI); current CMS's are ES, HU).

I. SCIENTIFIC OVERVIEW

Enrotab is a generic veterinary medicinal product. The reference products are Baytril Flavour 15 mg (REG NL 7865) , 50 mg (REG NL 7866) and 150 mg (REG NL 7867).

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 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 enrofloxacin at respectively 15, 50 and 150 milligram per tablet and excipients lactose monohydrate, powdered cellulose, maize starch, povidon K25, croscarmellose sodium, crospovidone, colloidal anhydrous silica and magnesium stearate. The choice of the formulation is justified.

The tablets are packed in blister strips composed of Alu-PVC/PE/PVDC or of Alu-PCV/PVDC.

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 an established 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.

The ASMF procedure is applied for the active substance supplier.

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.

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.

The claim of a 24-hour stability after broaching is based on the demonstration of stability for a batch broached and stored unprotected as half tablets for 24 hours at 25 °C/60% RH.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

None.

III. SAFETY ASSESSMENT (PHARMACO-TOXICOLOGICAL)

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

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the product may cause a hypersensitivity reaction. People with a known hypersensitivity should not handle the product. Furthermore, persons administering the product are warned to wash their hands after handling the product, to rinse their eyes if contact with eyes occurs and to seek medical advice in case of accidental ingestion.
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 veterinary medicinal product is intended for use in non-food producing species.

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 are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

The applicant has conducted *in vivo* bioequivalence studies in dogs and cats.

In dogs, Baytril 150 mg was used as the control product and plasma levels of enrofloxacin, its metabolite ciprofloxacin and the sum of both substances were compared after single oral administration in a randomised cross-over design including 24 dogs. Dogs were treated with the reference product and Enrotab, with a wash out period of 7 days in between. Ratios for C_{max} and AUC were within the predetermined 90% confidence interval limits of 80-125%. It is concluded that both products are bioequivalent when administered to the dog by the oral route.

In cats, Baytril 50 mg was used as the control product and plasma concentrations of enrofloxacin, its metabolite ciprofloxacin and the sum of both substances were compared after single oral administration in a randomised cross-over design including 12 cats. Cats were treated with the reference product and Enrotab, with a wash out period of 7 days in between. Plasma levels of enrofloxacin and ciprofloxacin were somewhat higher for the test product compared to the reference product and maximum levels were reached somewhat faster with the test product. It is concluded that, considering the results of the bioequivalence study in the cat, efficacy for Enrotab and the reference product will be 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 for this product are equivalent to those of the reference product.

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.

Summary of change **(Application number)**	**Section updated**	**Approval date**
Change in the address of the MAH NL/V/xxxx/IA/002/G (NL/V/0136/001-003/IA/001/G)	Module 1	30 March 2011
Change of MAH in the Netherlands (Le Vet B.V. to CP- Pharma Handelsgesellschaft mbH) National procedure	Module 1	12 November 2014
Introduction of a new DPPS which has been assessed for another product of the same MAH. NL/V/0136/001-003/IB/002	N/A	27 February 2015
Renewal NL/V/0136/001-003/R/001	N/A	26 July 2015
New CEP from a new manufacturer for an active substance Replacement of a manufacturer responsible for batch release, not including batch control/testing Change in the specification parameters of the finished product. Update of the dossier to comply with the provisions of an updated general monograph of the Ph. Eur for the finished product NL/V/0136/001-002/IA/003/G	N/A	27 November 2015

New CEP from a new manufacturer for an active substance Replacement of a manufacturer responsible for batch release, not including batch control/testing Change in the specification parameters of the finished product. Update of the dossier to comply with the provisions of an updated general monograph of the Ph. Eur for the finished product Change in the shape or dimensions of the pharmaceutical form NL/V/0136/003/IB/004/G	N/A	27 November 2015
Submission of an updated Ph. Eur. certificate of suitability from an already approved manufacturer NL/V/0136/001-003/IA/005	N/A	15 November 2017
Submission of an updated Ph. Eur. certificate of suitability from an already approved manufacturer NL/V/0136/001-003/IA/006	N/A	17 September 2019