Bundesamt für Verbraucherschutz und Lebensmittelsicherheit

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
10117 Berlin
(Germany)

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Enroxal (DE)

Enroxal 100 mg/ml oral solution for chickens and turkeys (PL, NL, IT)

Enrofloxacin Krka 100 mg/ml oral solution for chickens and turkeys (IE)

Enroxil 100 mg/ml oral solution for chickens and turkeys (BG)

Floxatryl 100 mg/ml oral solution for chickens and turkeys (CY)

Date: 01 August 2019

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0336/001/MR
Name, strength and pharmaceutical form	Enroxal, 100 mg/ml, oral solution
Applicant	KRKA d.d. NOVO mesto Smarjeska cesta 6 8501 NOVO MESTO SLOVENIA
Active substance(s)	Enrofloxacin
ATC Vetcode	QJ01MA90
Target species	Chickens, turkeys
Indication for use	Treatment of infections caused by the following bacteria susceptible to enrofloxacin: Chickens *Mycoplasma gallisepticum,* *Mycoplasma synoviae,* *Avibacterium paragallinarum,* *Pasteurella multocida.* Turkey *Mycoplasma gallisepticum,* *Mycoplasma synoviae,* *Pasteurella multocida.*

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicinal Agencies website (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 Mutual recognition procedure	20 February 2013
Date product first authorised in the Reference Member State (MRP only)	07 September 2012
Concerned Member States for original procedure	BE, BG, CY, IE (former RMS), IT, NL, PL

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 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 benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Qualitative and Quantitative Particulars

The product contains 100 mg/ml enrofloxacin and the following excipients: Potassium hydroxide, hypromellose, benzyl alcohol and purified water.

The product is presented in amber Type III glass vials of 100 ml and in high density polyethylene bottles of 1L and 5L.The glass vials are closed with a HD polyethylene cap containing a LD polyethylene sealing liner. The polyethylene bottles are closed with high density polyethylene screw closures. The 100 ml and 1L presentations are supplied with dosing cups of 25 ml and 50 ml respectively.

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 in accordance with the relevant European guidelines.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

C. Control of Starting Materials

The active substance is enrofloxacin, an established active substance 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.

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

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.

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 and in-use shelf life when stored under the approved conditions.

G. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

As this is a generic application according to Article 13(1), and bioequivalence with a reference product (Baytril 10% Oral Solution, VPA 10021/022/001) has been demonstrated, results of pharmacological and toxicological tests are not required.

User Safety

As the test product is bioequivalent to Baytril 10% Oral Solution, it is accepted that the user safety profile will be similar to that of the reference product.

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

Environmental Risk Assessment

An environmental risk assessment in accordance with relevant guidance was presented in support of this application: The assessment concluded that no risks to

the environment are anticipated when the product is used in accordance with label recommendations.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted because this application has been submitted in accordance with article 13(1) of Directive 2001/82/EC, as amended and the applicant has claimed and justified an exemption from the requirement to demonstrate bioequivalence of their product with the reference product.

MRLs

Enrofloxacin is listed in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 (O.J. 20.1.2010, L 15/30).The marker substance is the sum of enrofloxacin and ciprofloxacin.

MRLs are listed below:

	Poultry
Muscle	100 µg/kg
Liver	200 µg/kg
Kidney	300 µg/kg
Fat / skin	100 µg/kg

Withdrawal Periods

Based on the information provided above, the withdrawal period accepted for the reference product can be applied to Enrofloxacin HCS 100 mg/ml oral solution for chickens and turkeys. The product is not authorised for use in laying birds producing eggs for human consumption.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and acceptable justification for the omission of bioavailability studies to demonstrate bioequivalence with a reference product has been provided, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

No target animal safety studies were conducted.

Given that:

- The product is an oral dose form,
- Bioequivalence with the reference product Baytril 10% oral solution is accepted
- The toxicological profile of the active substance is well known
- The excipients are recognised as being safe

the absence of tolerance studies specific to the test product can be accepted.

Resistance

Statements relating to appropriate use of fluoroquinolones, in accordance with the requirements of EMEA/CVMP/416168/06 (Reflection Paper on the use of fluoroquinolones in food producing animals - Precautions for use in the SPC regarding prudent use guidance), are included on the SPC.

IV.B Clinical Studies

The indications and posology proposed for the test product reflect the approved indications and posology for the reference product, Baytril 10% Oral Solution. As the test product is bioequivalent to Baytril 10% Oral Solution, it is accepted that the efficacy profile will be similar to that 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 Medicinal 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.

•	01 August 2019	Change of RMS from IE to DE
•	15 March 2019	Change in the pharmacovigilance system
•	29 May 2018	Change in indication for use
•	23 February 2015	Change in the address of the active substance manufacturer
•	25 March 2014	Extension of the withdrawal period from 3 days to 7 days for chickens and 13 days for turkeys
•	06 November 2013	Introduction of a new active substance manufacturer
•	11 September 2013	Change in the batch release site
•	27 June 2013	Change in the Marketing Authorisation Holder from HCS bvba to TAD Pharma GmbH
•	27 May 2013	Change in the name of the medicinal product in DE, IE, IT, NL, PL