Bundesamt für
Verbraucherschutz und
Lebensmittelsicherheit

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

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Zobuxa 100 mg Tablets for Dogs

Date: 24th April 2018

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0197/003/DC
Name, strength and pharmaceutical form	Zobuxa 100 mg Tablets for Dogs
Applicant	Elanco Europe Ltd Lilly House, Priestley Road RG24 9NL Basingstoke, Hampshire UNITED KINGDOM
Active substance(s)	Enrofloxacin
ATC Vetcode	QJ01MA90
Target species	Dogs
Indication for use	Treatment of bacterial infections of the alimentary, respiratory and urogenital tracts, skin, wound infections and otitis externa.

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 (3) of Directive 2001/82/EC as amended.
Date of completion of the original Decentralised procedure	27th July 2011
Date product first authorised in the Reference Member State (MRP only)	
Concerned Member States for original procedure	Austria, Belgium, Czech Republic, Denmark, Finland, France, Hungary, Italy, The Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom (former RMS)

I. SCIENTIFIC OVERVIEW

This was an application via the decentralised procedure for a 'hybrid' product, submitted in accordance with Article 13 (3) of Directive 2001/82/EC, as amended by 2004/28/EC. Bioequivalence was claimed with the reference product, Baytril Flavour Tablets 15 mg. Reference products used in bioequivalence studies were and Baytril Flavour 15 mg Tablette für Katzen und Hunde, and Baytril Flavour 50 mg Tablette für Katzen und Hunde in dogs and cats respectively. The product contains 100 mg of enrofloxacin, and the indication is for the treatment of bacterial infections of the alimentary, respiratory and urogenital tracts, skin, wound infections and otitis externa. The dose is 5 mg enrofloxacin/kg/bodyweight once daily (1 tablet per 20 kg bodyweight), for 5-10 consecutive days.

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

[1] SPC – Summary of Product Characteristics.

II. QUALITY ASPECTS

A. Composition

The product contains enrofloxacin and excipients lactose monohydrate, microcrystalline cellulose, povidone (K-30), croscarmellose sodium, silica, (colloidal anhydrous), magnesium stearate and artificial beef flavour.

The container system is an aluminium foil blister contained in a box with 10 or 100 tablets, 10 tablets per blister. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the absence of preservative are justified. 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. The ingredients are granulated and dried, prior to sieving through an oscillating screen. The mixture is then formed into tablets.

C. Control of Starting Materials

The active substance is enrofloxacin, an established active substance described in the European Pharmacopoeia, (Ph. Eur). 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. All excipients (apart from the beef flavouring which is tested in accordance with the applicant's specifications), are cited in the Ph. Eur.

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

Declarations were provided in compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products.

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. Tests are for appearance, dimensions, dissolution, identification, enrofloxacin assay, uniformity of dosage, purity and microbiological purity.

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. A retest period of three years was deemed satisfactory for the active substance.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the blister: 2 days.

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.

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

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 is safe when used as directed, in line with precautions cited on the reference product. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

- Wash hands after handling the product.
- People with known hypersensitivity to fluoroquinolones should avoid contact with the product.
- In case of contact with eyes, wash immediately with plenty of clean water.
- In case of accidental injection, seek medical advice immediately and show the package leaflet to the
- Do not smoke, eat or drink while handling 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 assessment concluded that as the product is to be used in dogs, exposure to the environment will be minimal, and the product is not expected to pose a risk when used as directed.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

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

Pharmacokinetics

A bioequivalence study was submitted. The GLP[2]-compliant study was a two-way, cross-over, single dose, two treatment trial comparing Baytril Flavour 50 mg Tabletten and a generic formulation of enrofloxacin tablets in dogs. A suitable

[2] GLP – Good Laboratory Practise.

number of animals were given one dose of either the test product or reference product, and samples taken at suitable time points. After a 7 day washout period, the animals received the reciprocal product, and final analysis showed that bioequivalence between the test product and reference product was achieved. A pilot study supported the findings of the pivotal study. Dissolution studies confirmed that the product was suitably dissolved.

Tolerance in the Target Species of Animals

No data were required in this section of the application, as this was a generic application and tolerance data are equivalent to those of the reference product. The SPC and product literature were updated accordingly to match current requirements.

Resistance

No data were required in this section of the application, as this was a generic application and resistance data are equivalent to those of the reference product. The SPC and product literature were updated accordingly to match current requirements.

IV.B Clinical Studies

No clinical data were required, as this was a generic application.

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 benefit/risk 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.

•	24 April 2018	Change in RMS from UK to DE.
•	16 April 2018	Change to in-process test applied during the manufacture of the finished product.
•	12 October 2017	Update to the SPC, labelling or package leaflet to implement the outcome of a PSUR
•	12 May 2017	Deletion of manufacturing site for a site where batch control takes place Submission of an updated Ph. Eur. certificate of suitability for an active substance from an already approved manufacturer
•	07 March 2017	Introduction of a new pharmacovigilance system.
•	12 January 2017	Change in the name of a manufacturer of the finished product.
•	21 December 2016	Renewal - UK as RMS
•	21 June 2016	Change in the name and address of the Marketing Authorisation Holder from Novartis Animal Health S.p.A to Elanco Italia S.p.A. in Italy only, and from Novartis Sanidad Animal, S.L. to Elanco Spain, S.L.U. in Spain only.
•	13 January 2016	Change of Marketing Authorisation Holder from Novartis Animal Health UK Ltd to Elanco Europe Ltd. Change in distributor details.
•	27 March 2014	Change to the QPPV contact details and updates to the DDPS that do not affect the pharmacovigilance system.
•	16 January 2014	Change to the address of the MAH.
•	04 July 2013	Change to the address of the MAH.
•	28 March 2013	Change to the address of the MAH.
•	03 August 2012	Change to DDPS.
•	07 June 2012	Submission of updated certificate of suitability.
•	30 March 2012	To change the flavouring component of the product.
•	01 March 2012	To change the shelf life as packaged for sale from 2 years to 3 years.