Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Boflox Flavour 20 mg Tablets for Dogs and Cats
Boflox Flavour 80 mg Tablets for Dogs

Date Created: 12/05/2017

PuAR correct as of 07/06/2018 when RMS was transferred to ES.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0596/001/DC UK/V/0596/002/DC
Name, strength and pharmaceutical form	Boflox Flavour 20 mg Tablets for Dogs and Cats Boflox Flavour 80 mg Tablets for Dogs
Applicant	Livisto Int'l S.L. Avda. Universitat Autònoma 29 08290 Cerdanyola del Vallès Barcelona Spain
Active substance(s)	Marbofloxacin
ATC Vetcode	QJ01MA93
Target species	Dogs (20 mg and 80 mg strengths) and cats (20 mg strength only)
Indication for use	Treatment of infections caused by strains of microorganisms susceptible to marbofloxacin. In dogs: • skin and soft tissue infections (skinfold pyoderma, impetigo, folliculitis, furunculosis, cellulitis) • urinary tract infections (UTI) associated or not with prostatitis or epididymitis • respiratory tract infections. In cats: • skin and soft tissue infections (wounds, abscesses, phlegmons) • upper respiratory tract infections.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

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 conclusion of the decentralised procedure	23/11/2016
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	AT, CZ, EE, DE, EL, HU, IE, IT, LV, LT, PL, RO, SK, SI, ES

I. SCIENTIFIC OVERVIEW

This was an application for generic products, in accordance with Article 13(1) of Directive 2001/82/EC. The reference products are Marbocyl P 20 mg tablets and Marbocyl P 80 mg tablets, authorised in the UK since 2003. The applicant provided *in vivo* bioequivalence studies comparing the 20 mg test product and the reference product Marbocyl P 20 mg tablets. The applicant has justified a waiver from submitting a bioequivalence study for the 80 mg strength by providing a dissolution study which demonstrated very rapid dissolution for both strengths of the test product and reference products, and therefore bioequivalence can be accepted.

The products are indicated for the treatment of infections caused by strains of microorganisms susceptible to marbofloxacin. In dogs, this includes skin and soft tissue infections (skin pyoderma, impetigo, folliculitis, furunculosis, cellulitis); irinary tract infections (UTI) associated or not with prostatitis or epididymitis, and respiratory tract infections. In cats, the product is indicated for skin and soft tissue infections (wounds, abscesses, phlegmons), and upper respiratory tract infections. The recommended dose rate is 2 mg/kg/d (1 tablet for 10 kg per day) in a single daily administration. In dogs, the treatment duration can vary between 5 days and 40 days depending on the condition being treated and the course of the disease. In cats, the product should be used for 3 to 5 days for skin and soft tissue infections, and 5 days for upper respiratory infections.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto the market. It has been shown that the product can be safely used in the target species, any 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 [2] 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. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

Each tablet of Boflox Flavour 20 mg contains 20 mg of marbofloxacin. Each tablet of Boflox Flavour contains 80 mg marbofloxacin. The products contain lactose monohydrate, cellulose (powdered), povidone, crospovidone, silica (colloidal anhydrous), calcium behenate, yeast and beef flavour as excipients.

The container/closure system consists of Alu /PA-Alu-PVC blister packs enclosed in cartons. The 20 mg strength is presented in blister packs of 10 tablets, in boxes containing 10 tablets, 20 tablets, 50 tablets, 100 tablets, 150 tablets, and 200 tablets. The 80 mg strength is presented in blister packs of 6 tablets, in boxes containing 6 tablets, 12 tablets, 36 tablets, 72 tablets, 120 tablets, and 240 tablets. 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.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from licensed manufacturing sites. The manufacturing method consists of a standard process for tablets.

Process validation data on the product have been presented in accordance with the relevant European guidelines

II.C. Control of Starting Materials

The active substance is marbofloxacin an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

for active substances and in accordance with an Active Substance Master File (ASMF).

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 excipients lactose monohydrate, crospovidone, cellulose, colloidal anhydrous silica and povidone are described in the European Pharmacopoeia. Calcium behenate is controlled in accordance with the monograph in the Deutsches Arzeibuch (DAB). Yeast and beef flavour are controlled in accordance with the manufacturers specifications.

II.C.4. Substances of Biological Origin

The only substance of biological origin present in the product is lactose monohydrate which is declared to be sourced from healthy animals in the same condition as that collected for human consumption, Compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.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. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification. Control tests on the finished product include those for appearance, tablet dimensions and weight, uniformity of dosage units, resistance to crushing, dissolution, identity and assay of the active substance, total impurities and microbial count.

II.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 three production scale batches of the finished product have been provided in accordance with applicable European guidelines,

demonstrating the stability of the product throughout its shelf life of 3 years when stored under the approved conditions.

The claim of a 4 day stability after tablet division is based on the demonstration of stability form an in-use stability study which showed that there was no significant change in parameters tested when tablet portions are stored in the blister pocket.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life of tablet halves: 4 days

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

These applications are for generic products in accordance with Article 13(1) of Directive 2001/82/EC as amended. As bioequivalence to the reference product has been demonstrated, pharmacological and toxicological data are not required.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that the hazard, exposure and risk to the user will comparable to that of the reference products. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

- People with known hypersensitivity to (fluoro)quinolones should avoid contact with the veterinary medicinal product.
- In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.
- Wash hands after use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:
The Phase I assessment ends at Question 3 of the VICH decision tree. The product will only be used in non-food animals and as a result environmental exposure will be low. A Phase II ERA was not required.

Exposure of the environment from the product is not considered significant. The products are not expected to pose a risk to the environment when used as recommended in the SPC.

IV CLINICAL DOCUMENTATION

Two *in-vivo* bioequivalence studies and two *in-vitro* dissolution studies were conducted in line with the relevant guidelines, the results of which demonstrate bioequivalence to the reference products. Therefore, the applicant was not required to present the results of safety tests or pre-clinical and clinical trials.

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 of the product(s) is favourable.

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 Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)