Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

MiPet Benazapet 20 mg Tablets for Dogs

Date Created: December 2015

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	MiPet Benazapet 20 mg Tablets for Dogs
Applicant	Elanco Europe Ltd. Lilly House Priestley Road Basingstoke Hampshire RG 24 9NL
Active substance	Benazepril hydrochloride
ATC Vetcode	QC09AA07
Target species	Dogs
Indication for use	Treatment of congestive heart failure.

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.

I. SCIENTIFIC OVERVIEW

This was an application for a generic product, submitted under Article 13 (1) of Directive 2001/82/EC as amended. The reference product is Benazepril Hydrochloride Novartis 20 mg Tablets for Dogs (originally Fortekor Flavour 20 mg Tablets for Dogs), marketed in the UK since 2006, which expired in January 2011. The product is also identical to the generic Fortekor Flavour 20 mg Tablets for Dogs. All products are owned by the applicant. The proposed formulation fulfilled the criteria for bioequivalence exemption 7.1d of guideline EMA/CVMP/016/00-Rev.2. The applicant states that the reference product is part of the Global Marketing Authorisation of Fortekor 20 mg Film Coated Tablets for Dogs The product is intended for use in dogs for the treatment of congestive heart failure, and is given voluntarily to most dogs at a dose rate of 0.25 mg benazepril hydrochloride/kg bodyweight/day.

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, 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.

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

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains 20 mg benazepril hydrochloride and the excipients cellulose microcrystalline, crospovidone, povidone, basic butylated methacrylate copolymer, silicon dioxide anhydrous, sodium laurilsulfate, dibutyl sebacate, silica colloidal anhydrous, stearic acid, yeast powder and artificial powdered beef flavour.

The container/closure system consists of a cardboard box containing 2 blisters of 14 tablets, 28 tablets in total. The particulars of the containers and controls performed are provided and conform to the regulation. The choice of 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 a licensed manufacturing site. The manufacturing method consists of a layering of the active substance onto microcrystalline pellets and coating with a polymer film. The pellets are mixed with the excipients and then compressed into 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 benazepril hydrochloride, 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 comply with monographs within the Ph. Eur, apart from dibutyl sebacate, which complies with the United States Pharmacopoeial monograph. The flavouring materials comply with in-house specifications.

II.C.4. Substances of Biological Origin

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

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

Pellets are prepared separately and stored, therefore detailed release and shelf-life specifications were developed. These checks include those for appearance, identification, loss on drying, related impurities, particle size and dissolution.

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 identification, loss on drying, related impurities, particle size and dissolution, uniformity of content and mass, 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. The active substance was shown to be highly stable, except in aqueous conditions, with degradation increasing with rises in temperature and pH. Data were provided for 3 batches stored in polyethylene bags, placed within steel drum and kept at 25°C/60% RH for 5 years. No significant change was noted, therefore a retest period of 5 years was agreed.

G. Other Information

Shelf life of veterinary medicinal product as packaged for sale: 3 years

Shelf life of tablet halves: 2 days

This veterinary medicinal product does not require any special storage conditions.

Return half tablet to blister pocket and store in original carton, use at next administration.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13 (1) and bioequivalence with a reference product was stated and accepted, results of pharmacological or 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 Documentation

User Safety

No data were required for this section. Warnings and precautions as listed on the product literature, which reflect those of the parent product are adequate to ensure safety to users of the product:

- Wash hands after use.
- In case of accidental oral ingestion, seek medical advice immediately and show the label or the package leaflet to the physician.
- Pregnant women should take special care to avoid accidental oral exposure because angiotensin converting enzyme (ACE) inhibitors have been found to affect the unborn child during pregnancy in humans.

Environmental Safety

A Phase I environmental safety assessment was provided. The product is given to a small number of animals, mainly kept indoors, and most of the residue remaining in faeces will be collected by the owner for disposal. A Phase II assessment was therefore not required. The SPC sates the following:

- Any unused veterinary medicinal product or waste material derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

IV CLINICAL DOCUMENTATION

As this is a generic application according to Article 13 (1), and bioequivalence with a reference product has been assumed because the applicant has stated that the formulation for the proposed product and the reference product is identical, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product. The proposed formulation fulfilled the criteria for bioequivalence exemption 7.1d of guideline EMA/CVMP/016/00-Rev.2.

IV.I. Pre-Clinical Studies

Pharmacology

No data were submitted. The applicant stated that the proposed and reference formulations are identical, and claimed an exemption from the requirement for bioequivalence studies in accordance with Section 4(c) the Guideline for the Conduct of Bioequivalence Studies for Veterinary Medicinal Products,

EMEA/CVMP/016/00-corr-Final, (superseded by EMA/CVMP/016/00-Rev.2, the equivalent exemption is Section 7.1 d).

Tolerance in the Target Species

As bioequivalence with the reference product could be assumed based on the applicant's statement, no data were required for this section.

IV.II. Clinical Documentation

As bioequivalence with the reference product could be assumed based on the applicant's statement, no data were required for this section.

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

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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.

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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.

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