IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Bexepril 2.5 mg Film-coated tablet for dogs

PRODUCT SUMMARY

EU Procedure number	IE/V/0226/001/DC
Name, strength and pharmaceutical form	Bexepril 2.5 mg Film-coated tablet for dogs
Active substance(s)	Benazepril hydrochloride
Marketing Authorisation Holder	Chanelle Pharmaceuticals Manufacturing Ltd. Loughrea Co. Galway Ireland
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of Authorisation	22nd December 2009
Target species	Dogs
Indication for use	Dogs - for the treatment of heart failure
ATCvet doce	QC09AA07
Concerned Member States	BE, DE, DK, ES, FI, FR, IT, NL, SE, UK

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.

The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

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 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 2.5 mg benazepril hydrochloride and excipients (lactose monohydrate, maize starch, microcrystalline cellulose, colloidal anhydrous silica, crospovidone, talc and magnesium stearate).Opadry II white is used as a film-coating material.
The container/closure system consists of a blister made up of PVC/PE/PVDC laminate with a 20 µm aluminium lidding foil.
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.

C.Control of Starting Materials

The active substance is benazepril hydrochloride, 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.
Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

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 when stored under the approved conditions.
The claim of a 24-hour in-use shelf life for half tablets is supported by studies carried out on each tablet strength.

G.Other Information

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

The application is presented in accordance with Article 13.1 of Council Directive 2001/82/EC, as amended (a generic application).Given the legal basis of the application, the applicant is not required to submit results of pharmacological, toxicological and clinical trials.

In support of this application, the applicant has presented that findings of an *in-vivo* bioequivalence study in the dog comparing plasma concentrations of benazeprilat following administration of the test product (Benazepril 20 mg Tablets) to those following administration of the reference product (Fortekor 20 mg tablets for dogs). In addition, the applicant has presented *in-vitro* data showing that the dissolution profiles of Benazepril 2.5 mg Tablets, Benazepril 5 mg Tablets and Benazepril 20 mg Tablets are similar and that dissolution profiles of the test products (Benazepril 2.5 mg Tablets, Benazepril 5 mg Tablets and Benazepril 20 mg Tablets) are similar to those of the respective reference products (Fortekor 2.5 mg Tablets, Fortekor 5 mg Tablets and Fortekor 20 mg Tablets).

Based on the *in vivo* data provided, the Applicant concludes that the test and reference items are bioequivalent when administered to dogs. Based on the *in vitro* data provided, it appears that rapid dissolution of the test and reference items is achieved in a variety of test media such that, for the different tablet strengths, similar *in vivo* availability can be expected.

On the basis of the user safety assessment provided, it can be concluded that the test item will present no greater risk to the user than that posed by the reference product. User safety statements proposed by the Applicant are in line with those of the reference product and similar products authorised recently through European procedures.

A Phase I environmental safety assessment has been provided. It can be concluded that use of the product does not pose a risk to the environment.

The various safety warnings included on the proposed SPC are in line with those on the authorised SPC's of the reference products in the RMS and can be accepted.

III.B Residues Documentation

Not applicable.

IV. CLINICAL ASSESSMENT

The application is presented in accordance with Article 13.1 of Council Directive 2001/82/EC, as amended (a generic application).Given the legal basis of the application, the applicant is not required to submit results of pharmacological, toxicological and clinical trials.

In support of this application, the applicant has presented that findings of an in-vivo bioequivalence study in the dog comparing plasma concentrations of benazeprilat following administration of the test product (Benazepril 20 mg Tablets) to those following administration of the reference product (Fortekor 20 mg tablets for dogs). In addition, the applicant has presented in-vitro data showing that the dissolution profiles of Benazepril 2.5 mg Tablets, Benazepril 5 mg Tablets and Benazepril 20 mg Tablets are similar and that dissolution profiles of the test products (Benazepril 2.5 mg Tablets, Benazepril 5 mg Tablets and Benazepril 20 mg Tablets) are similar to those of the respective reference products (Fortekor 2.5 mg Tablets, Fortekor 5 mg Tablets and Fortekor 20 mg Tablets).

Based on the *in vivo* data provided, the Applicant concludes that the test and reference items are bioequivalent when administered to dogs. Based on the *in vitro* data provided, it appears that rapid dissolution of the test and reference items is achieved in a variety of test media such that, for the different tablet strengths, similar *in vivo* availability can be expected.

The applicant has not presented tolerance data for the test product. The following justification is given: this product is for oral administration; the safety profile of the active substance is well known and can be accepted as well tolerated when administered at the recommended treatment dose; the test product is comparable to the reference product in terms of qualitative and quantitative composition of active substance; the excipients present in the test product are widely used in pharmaceutical manufacturing and are regarded as safe; the test product was well tolerated when administered to dogs at the recommended dose rate during the bioequivalence study. The absence of tolerance data for the test product has been adequately justified.

The proposed indications and posology reflect the indications and posology of the reference products in the RMS.

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.

VI. 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 HPRA website.

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.

Changes:
None.