Veterinary Medicines Directorate

**United Kingdom**
**Veterinary Medicines Directorate**
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**NATIONAL PROCEDURE**

# PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

## BenazeVet 5 mg Tablets for Cats and Dogs

**Date Created:** June 2022

# MODULE 1

## PRODUCT SUMMARY

| | |
|---|---|
| Name, strength and pharmaceutical form | BenazeVet 5 mg Tablets for Cats and Dogs, Tablet |
| Applicant | Elanco Europe Ltd, Form 2, Bartley Way, Bartley Wood Business Park, Hook, RG27 9XA, United Kingdom |
| Active substance | Benazepril Hydrochloride |
| ATC Vetcode | QC09AA07 |
| Target species | Dogs<br>Cats |
| Indication for use | Dogs: Treatment of congestive heart failure.<br>Cats: Treatment of proteinuria associated with chronic kidney disease. |

# 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 | MA application for a generic 'hybrid' product in accordance with Article 13(3) of Directive 2001/82/EC, as amended by 2004/28/EC |
| Date of conclusion of the procedure | 29/03/2022 |

## I. SCIENTIFIC OVERVIEW

The application is for an MA submitted in accordance with Article 13(3) of Directive 2001/82/EC, as amended by 2004/28/EC. This was determined a generic 'hybrid' application because of the addition of a new target species (cats) and associated indication compared to the reference product.

BenazeVet 5 mg Tablets for Cats and Dogs contain 5 mg of the active substance benazepril hydrochloride, per tablet. The proposed indications are for the treatment of congestive heart failure in dogs and the treatment of proteinuria associated with chronic kidney disease in cats. For dogs, *'the product should be administered orally at a minimum dose of 0.25 mg (range 0.25 - 0.5 mg) benazepril hydrochloride per kg body weight once daily. The dose may be doubled, still administered once daily, to a minimum dose of 0.5 mg/kg (range 0.5 - 1.0 mg), if judged clinically necessary and advised by the veterinary surgeon'*. For cats, '*the product should be administered orally at a minimum dose of 0.5 mg (range 0.5 - 1.0 mg) benazepril hydrochloride per kg body weight once daily'*.

The proposed reference product is Benazepril Hydrochloride Novartis 5 mg Tablets (originally Fortekor Flavour 5 mg Tablets for Dogs) authorised in January 2006 and expired in January 2011. The initial marketing authorisation for the reference product was obtained by Novartis Animal Health UK Ltd, which is now part of Elanco.

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 benazepril hydrochloride and the excipients Cellulose microcrystalline, Crospovidone, Povidone, Basic butylated methacrylate copolymer, Silicon dioxide anhydrous, Sodium laurilsulphate, Dibutyl sebacate, Silica colloidal anhydrous, Stearic acid, Yeast powder and Artificial powdered beef flavour.

The tablets are packaged in aluminium/aluminium blisters containing 14 tablets per strip. A single pack size of 28 tablets is proposed. 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.

The proposed product, BenazeVet 5 mg Tablets for Cats and Dogs is identical to the reference product Benazepril Hydrochloride Novartis 5 mg Tablets for Dogs (originally called Fortekor Flavour 5 mg Tablets for Dogs) which is now expired. The proposed new product is also identical to the currently authorised generic product Fortekor Flavour 5 mg Tablets for Cats and Dogs. Consequently, the quality section of the dossier is the same as that submitted for the Fortekor Flavour 5 mg Tablets for Cats and Dogs (Vm 00879/4045) and Benazepril Hydrochloride Novartis 5 mg Tablets for Dogs.

## *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 two stages, initial production of Benazepril Pellets 10% and then mixing of the pellets with yeast, artificial beef flavour and remaining excipients before being compressed into tablets.

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

## *II.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.

A copy of the CEP is provided in the dossier, specifying additional tests/limits for the residual solvents; ethanol and ethyl acetate. A retest period of 4 years is specified on the CEP and the certificate of suitability states that the CEP holder has declared the absence of the use of materials of human or animal origin in the manufacture of the active substance.

All excipients with the exception of the flavouring materials are pharmacopoeial and comply with the requirements of the current monographs. The Ph. Eur. has been applied where relevant, however the excipient dibutyl sebacate is in compliance with the USP monograph. This is considered acceptable since it is not the subject of a Ph. Eur. monograph.

### *II.C.4. Substances of Biological Origin*

Scientific data and/or certificates of suitability issued by the EDQM have been provided and 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*

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

### *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 are those for: Appearance, Mean mass, Dissolution of benazepril hydrochloride after 30 minutes, Identification, Water content, Total Aerobic Microbial Count, Total Yeasts and Moulds Count, Specified species of microorganisms, Uniformity of dosage, Impurities and Assay.

### *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 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.

### *G. Other Information*

Shelf-life of the 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.
Each time an unused half tablet is stored, it should be returned to the open blister space, inserted back into the cardboard box and kept in a safe place out of the sight and reach of children.

## III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

### *III.A Safety Documentation*

#### *Pharmacological and Toxicological Studies*

Due to the legal base of the application, the applicant is not required to provide toxicological or pharmacological data. The proposed product has the same qualitative and quantitative composition as the reference product in terms of the active substance, is for use in the same target species, for the same indications and at the same posology. The proposed product is identical to another generic product, Fortekor Flavour 5 mg Tablets for Dogs and Cats (formerly Benazepril Hydrochloride Novartis 5 mg tablets for Dogs), which has the same reference product, and which was authorised in the UK on 28/04/2010.

#### *User Safety*

In place of a user risk assessment (URA), a statement was supplied that says that due to the legal status of the application, the safety to the user of the product will be the same as the reference product.

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:

- The product may cause hypotension after ingestion. To avoid accidental ingestion, particularly by a child, unused part-tablets should be returned to the open blister space and inserted back into the carton. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
- Angiotensin converting enzyme (ACE) inhibitors have been found to affect the unborn child during pregnancy in humans. Pregnant women

should therefore take special care to avoid accidental ingestion, including hand to mouth contact.
- Wash hands after use.

### *Environmental Safety*

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

**Phase I:**
The product is for companion animals only, so Phase I of the environmental risk assessment ends at Question 3. The disposal advice is correct according to current guidance.

No unacceptable risk to the environment is expected if the product is used as recommended.

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.

## IV. CLINICAL DOCUMENTATION

### *IV.I. Pre-Clinical Studies*

### *Pharmacology*

This is a generic application submitted in accordance with Article 13(3) of Directive 2001/82/EC as amended and bioequivalence with the reference product Benazepril Hydrochloride Novartis 5 mg Tablets for Dogs can be assumed, the results of toxicological, pharmacological or clinical tests are not required.

## 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 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.

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