



Veterinary
Medicines
Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
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(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY
MEDICINAL PRODUCT

Fortekor Flavour 5 mg Tablets for Dogs
Fortekor Flavour 20 mg Tablets for Dogs

**PuAR correct as of 07/02/2018 when RMS was transferred
to IE. Please contact the RMS for future updates**

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0341/001/DC UK/V/0341/002/DC
Name, strength and pharmaceutical form	Fortekor Flavour 5 mg Tablets for Dogs Fortekor Flavour 20 mg Tablets for Dogs
Applicant	Novartis Animal Health UK Ltd
Active substance(s)	Benazepril Hydrochloride
ATC Vetcode	QC09AA07
Target species	Dogs
Indication for use	Treatment of congestive heart failure in dogs

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

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 completion of the original decentralised procedure	22 December 2009.
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Austria, Czech Republic, Hungary, Ireland, Poland, Romania, Slovakia, Slovenia.

I. SCIENTIFIC OVERVIEW

Fortekor Flavour 5 mg Tablets for Dogs and Fortekor Flavour 20 mg Tablets for Dogs are beige, ovaloid, divisible tablets intended to treat congestive heart failure in dogs. The tablets are given orally once daily, and are taken voluntarily, with or without food. The recommended dose for the products is 0.25-0.5 mg benazepril hydrochloride/kg bodyweight/day. The dose may be doubled, still administered once daily, if judged clinically necessary. For the 5 mg tablet, for dogs weighing 5 – 10 kg the standard dose is half a tablet, the double dose, one tablet. For dogs weighing 11 – 20 kg the standard dose is one tablet, the double dose is two tablets. For the 20 mg product, for dogs weighing 21 – 40 kg, the standard dose is half a tablet, the double dose one tablet. For dogs weighing 41 – 80 kg, the standard dose is 1 tablet, the double dose is two tablets.

These applications were for generic products, submitted in accordance with Article 13 (1) of Directive 2001/82/EC, as amended. The reference products were Benazepril Hydrochloride Novartis 5 mg and 20 mg Tablets for Dogs, authorised in the UK since 2006. The products should not be given to dogs with evidence of cardiac output failure due to aortic stenosis, and should not be used in cases of hypersensitivity to any of the ingredients. The product should also not be used in cases of hypotension, hypovolaemia, hyponatraemia or acute renal failure, or in pregnancy or lactation. 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. Composition

The products contain 5 mg or 20 mg benazepril hydrochloride and 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 absence of preservative is justified.

The container system consists of aluminium/aluminium blister packs containing 14, 28, 56 or 140 tablets. The particulars of the containers and controls performed are provided and conform to the regulation.

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. For validation studies on the finished product, two commercial batches gave satisfactory results for the 20 mg product. For the 5 mg product, three consecutive batches were analysed, all of which gave acceptable results. Until packaged, tablets are stored in metal containers lined with polyethylene bags.

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. Acceptable validation data were presented for all described methods of analysis. 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 except the flavouring, dibutyl stearate and silicon dioxide, anhydrous are described in the Ph. Eur. Dibutyl stearate and silicon dioxide, anhydrous are monographed in the United States National Formulary. An in-house test was developed for the flavouring.

D. 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. A Format 3 declaration states that no starting materials present a risk with regard to TSEs.

E. Control Tests on Intermediate Products

The results of tests performed for release on three batches each of the intermediate products are provided and comply with the specifications. Tests consist of analysis of appearance, colour, loss on drying, presence of impurities, particle size and dissolution. Two identity tests on benazepril hydrochloride are performed, in addition to a test on the content of benazepril hydrochloride. The specification was considered suitable for the analysis of the intermediate product.

F. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. Control tests on the finished products include tests for appearance, identity of the active substance, water content, mean mass, content of impurities and active substance, dissolution tests, uniformity of dose and microbiological analysis. 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.

G. Stability

Stability of the Active Substance

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 five year retest period was justified.

Stability of the Finished Product

Data were supplied for two batches of the 20 mg tablets, manufactured on a commercial scale, tested under VICH conditions for thirty-six months at 5°C, 25°C/60% RH and 30°C/60%RH and for six months at 40°C/75% RH, with tablets being contained in the blister packs proposed for marketing. The products met all requirements of the proposed shelf-life, as specified in the SPC.

H. Genetically Modified Organisms

Not Applicable.

J. Other Information

The shelf-life of the veterinary medicinal product as packaged for sale is three years. The shelf-life of halved tablets is two days. The product literature recommends placing remaining halved tablets back into the opened blister pack.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACOTOXICOLOGICAL)

As this is a generic application according to Article 13, and an exemption from bioequivalence studies under 4c) of EMEA/CVMP/016/00 has been permitted, results of bioequivalence studies are not required. The SPCs of these products are identical to the reference products.

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

Pharmacological Studies

As the applicant is the Marketing Authorisation Holder for the reference products, the formulation and manufacture of the generic and reference products are identical. There is therefore no requirement for data in this section.

Toxicological Studies

As the applicant is the Marketing Authorisation Holder for the reference products, the formulation and manufacture of the generic and reference products are identical. There is therefore no requirement for data in this section.

Other Studies

As the applicant is the Marketing Authorisation Holder for the reference products, the formulation and manufacture of the generic and reference products are identical. There is therefore no requirement for data in this section.

User Safety

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. These warnings are:-

- Wash hands after use.
- Pregnant women should take special care to avoid accidental exposure because ACE inhibitors have been found to affect the unborn child after oral exposure during pregnancy in humans.
- In case of accidental ingestion by children, seek medical advice immediately and show the doctor this warning.

Ecotoxicity

The applicant provided a Phase 1 environmental risk assessment in compliance with the relevant guideline, which showed that no further assessment was required. The assessment concluded that the product is intended for the treatment of dogs with congestive heart failure, that benazepril hydrochloride is converted *in vivo* to benazeprilat, a highly potent and selective inhibitor of angiotensin-converting enzyme. In addition, that the recommended dose may be doubled if clinically required, and that there is no limit on duration of treatment.

The products are not to be used in food-producing animals, and as sick animals are likely to be kept indoors, any waste material will be collected by the dog owner and disposed of with other waste. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed. There was no requirement for the evaluation of environmental risk to proceed beyond Phase 1, the use of the products will not pose a risk to the environment when used as recommended.

Withdrawal Periods

As these products are to be used in non-food producing species, there is no requirement for data in this section.

IV CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and an exemption from bioequivalence studies under 4c) of EMEA/CVMP/016/00 has been permitted, 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

As this is a generic application according to Article 13, and an exemption from bioequivalence studies under exemption 4c) of EMEA/CVMP/016/00 has been permitted, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13, and an exemption from bioequivalence studies under 4c) of EMEA/CVMP/016/00 has been permitted, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.B Clinical Studies

Laboratory Trials

As this is a generic application according to Article 13, and an exemption from bioequivalence studies under 4c) of EMEA/CVMP/016/00 has been permitted, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

Field Trials

As this is a generic application according to Article 13, and an exemption from bioequivalence studies under 4c) of EMEA/CVMP/016/00 has been permitted, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

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 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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