IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Cephacare Flavour 1000 mg Tablets for Dogs

PRODUCT SUMMARY

EU Procedure Number	IE/V/0454/004 (formerly UK/V/0251/004)
Name, Strength, Pharmaceutical Form	Cephacare Flavour 1000 mg Tablets for Dogs
Active Substances(s)	Cefalaxin monohydrate
Applicant	Ecuphar NV Legeweg 157-I 8020 Oostkamp Belgium
Legal Basis of Application	Generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Target Species	Dogs
Indication For Use	Treatment of infections of the respiratory tract, gastro-intestinal tract, urogenital tract, the skin and localised infections in soft tissue caused by bacteria sensitive to cefalexin.
ATC Code	QJ01DB01
Date of conclusion of the decentralised procedure	21 December 2016 (UK) 01 March 2017 (IE)
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	Austria, Belgium, France, Germany, Ireland (now RMS), Luxembourg, Portugal, Spain UK added via RMS change

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

This application was for a line extension to add Cephacare Flavour 1000 mg tablets to the existing marketing authorisation for Cephacare Flavour 50, 250 and 500 mg tablets for cats and dogs. These tablets were authorised in December 2008. The original applications were submitted in accordance with Article 13(1) of EC Directive 2001/82/EC (as amended) citing Ceporex Vet 50, 250 and 500 mg tablets as the reference product.
The product is indicated for use in dogs for the treatment of infections of the respiratory tract, gastro-intestinal tract, urogenital tract, the skin and localised infections in soft tissue caused by bacteria sensitive to cefalexin.
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.
[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

II. QUALITY ASPECTS

II.A. Composition

The product contains 1000 mg cefalaxin as cefalaxin monohydrate and the excipients lactose monohydrate, potato starch, magnesium stearate and beef flavour.
The container/closure system consists of in PVC/PE/PVDC/Aluminum foil blister packs each containing 10 tablets, in cardboard boxes containing 100 or 250 tablets. The particulars of the containers and controls performed are provided and conform to the regulation.
The choice of the formulation is 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 simple mixing and compressing process.
The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

II.C. Control of Starting Materials

The active substance is Cefalexin, an established 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.
The active substance is supplied in accordance with a European Pharmacopoeia Certificate of Suitability.
Excipients, apart from the Beef Flavour, are the subject of monographs in the European Pharmacopoeia. Compliance with the requirements of the pharmacopoeia was therefore applied as the specification for each of these ingredients. The Beef Flavour complies fully with Directive 88/388/EC concerning labelling of foods flavours and meets an in-house specification.

II.C.4. Substances of Biological Origin

Scientific data 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

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 sites have been provided demonstrating compliance with the specification. Control tests on the finished product include those for appearance, mass, uniformity, friability, crushing strength, identification, disintegration time, dissolution, microbial quality and water content.

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 has 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

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This application is a line extension of Cephacare Flavour 50, 250 and 500 mg tablets for cats and dogs by the addition of a higher strength tablet, Cephacare Flavour 1000 mg tablets for dogs. The original applications were submitted in accordance with Article 13(1) of Directive 2001/82/EC (as amended). No pharmacology or toxicology data were required.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that there is a risk of sensitisation. 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:

- Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillin may lead to cross-reactions to cephalosporin and vice versa. Allergic reactions to these substances may occasionally be serious. Do not handle this product if you know you are sensitised or if you have been advised not to be in contact with such substances.

- Handle this product with great care to avoid exposure, taking all recommended precautions. If you develop symptoms following exposure such as skin rush, you should seek medical advice immediately and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty breathing are more serious symptoms and require urgent medical attention.

- To avoid accidental ingestion, particularly by a child, unused part-tablets should be returned to the open blister space and inserted back into the outer packaging. 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

An environmental risk assessment (ERA) has been provided according to Phase I guideline (CVMP/VICH/592/98-FINAL) and the supporting CVMP technical guidance note (EMEA/CVMP/ERA/418282/2005-Rev.1). The assessment terminated at question 3 of the VICH Phase I decision tree as the product is only intended for non-food animals and therefore no Phase II assessment is required.

No environmental warnings are proposed and the standard disposal advice is stated in section 6.6 of the SPC, 'Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.'

IV. CLINICAL ASSESSMENT

This application is a line extension of Cephacare Flavour 50, 250 and 500 mg tablets for cats and dogs by the addition of a higher strength tablet, Cephacare Flavour 1000 mg tablets for dogs. The original applications were submitted in accordance with Article 13(1) of Directive 2001/82 (as amended).

In the original application, *in vivo* bioequivalence between Cephacare Flavour 250 mg tablets and Ceporex Vet 250 mg tablets was demonstrated in the dog. The applicant further conducted *in vitro* dissolution studies to link the 500 mg and 50 mg Cephacare Flavour tablet sizes to the 250 mg tablet size.

The applicant has justified conducting a dissolution study to link the 1000 mg size Cephacare Flavour tablet to the other tablet strengths within the product range. The applicant provided adequate *in vitro* dissolution studies in compliance with the bioequivalence guideline EMA/CVMP/016/00-Rev 2 to demonstrate bioequivalence with the previously authorised products in the range.

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.

VI. POST-AUTHORISATION ASSESSMENTS

Quality Changes

Summary of change (Application number)	**Approval date**
Extension to finished product shelf-life from 12 months to 36 months (IE/V/0454/II/002/G) (Note: reference to the finished product shelf-life has been removed from the PuAR; this	01/02/2019

information can be seen on the authorised SPC).	