Public Assessment Report
Scientific discussion

Calcifediol Faes 0.266 mg Soft Capsules

(Calcifediol)

ES/H/0412/001/DC

Applicant: FAES FARMA, S.A.

Registration number in Spain:

This module reflects the scientific discussion for the approval of **Califediol Faes 0.266 mg soft capsules.** The procedure was finalised on February 2017. For information on changes after this date please refer to the module óUpdateô.

INTRODUCTION

This decentralised procedure concerns a generic application claiming essential similarity with the innovator product Hidroferol 0.266 mg oral solution (Faes Farma, S.A.) registered in Spain since January 21st, 1977. This MAH developed soft gelatin capsules (Hidroferol 0.266 mg soft capsules) as a line extension in order to facilitate the drug administration since the oral solution is dosed in ampoules that are difficult to open by elderly patients.

The legal basis of the application is Article 10(1) of Directive 2001/83/EC.

The Concerned Member States involved in this procedure are BE, DE, FR, IT, PL and PT.

The efficacy and safety of calcifediol has been demonstrated in several studies conducted with the reference product as well as with its use experience after placed in the market. Calcifediol Faes 0.266 mg soft capsules is submitted under an abridged application and no studies regarding pharmacology, pharmacokinetic, safety and efficacy has been carried out besides the bioequivalence studies against the reference product.

Calcifediol is indicated in adults for:

Treatment of vitamin D deficiency, in those cases where the initial administration of high doses is required or administration spaced in time is preferred, as in the following situations:

- As adjuvant for the treatment of osteoporosis
- In patients with malabsorption syndrome
- Renal ostheodystrophy
- Bone diseases induced by treatment with corticosteroid drugs.

RECOMMENDATION

Based on the review of the data on quality, safety and efficacy, the Member States have granted a marketing authorisation for **Calcifediol Faes 0.266 mg soft capsules** for Faes Farma, S.A.

I. SCIENTIFIC OVERVIEW AND DISCUSSION

II-1 Quality aspects

ACTIVE SUBSTANCE

Calcifediol is a known active substance described in Ph.Eur. A Ph. Eur. Certificate of Suitability has been submitted to support the quality of the active ingredient.

The CEP does not include re-test period but stability data have been included in the dossier to support the proposed the re-test period.

Due to the origin and type of tissues of raw material and the manufacturing process applied, the CEP indicates than the active substance meets the criteria described in the current version of the monograph Products with risk of transmitting agents of animal spongiform encephalopathies no. 1483 of the European Pharmacopoeia, current edition including supplements.

FINISHED PRODUCT

Description of the product

Calcifediol Faes 0.266 mg soft capsules medicinal product is an orange, oval soft gelatine capsule containing a clear, low viscous and free from particles liquid.

The qualitative composition of the capsule content and the capsule shell are as follows:

Capsule content:

Calcifediol

Ehtanol, anhidrous

Medium-chain triglycerides

Capsule shell:

Gelatine

Glycerol

Sorbitol

Titanium, dioxide (E-171)

Sunset yellow S (E-110)

The capsules are packages into either PVC-PCDC/Al or Al/Al blisters

Pharmaceutical development

The pharmaceutical development has been adequately described.

The proportion of each solvent in cosolvent mixture has been discussed. The composition of capsule shell has been justified.

Test for disintegration and dissolution of soft capsules has been performed.

The fostostability of calcifediol concern has been discussed along the production process.

Manufacture of the product and process controls

The manufacturing process is sufficiently described and the process controls are appropriate, considering the nature of the product and the manufacturing method.

The commercial batch size is defined.

The dossier includes sufficient validation data to guarantee that the manufacturing process is controlled and to ensure batch to batch reproducibility and compliance with product specifications.

Excipients

The information provided is adequate. The specifications for the different excipients are justified by their official adoption in the relevant Ph. Eur. monograph or by an in-house monograph (for the non-compendial excipient). All the gelatin sources used for capsules have CEP on TSE risk evaluation.

Product specification

The specifications proposed for the soft capsule is adequate. The limits proposed for the different parameters have been adequately justified.

The analytical methods have been properly described and validated.

Container closure system

Two type of blisters are used for soft capsule: the Al/Al blister is made with a coldformer foil composed by polyamide (OPA) layer, aluminium layer and the contact PVC layer. The PVC-PVDC/Al blister is made with aluminium foil and film of two layers, one of PVC and PVDC the other

The components of the container closure system comply with the specifications established in the applicable Ph. Eur. Monographs and/or EU directives on foodstuff contact.

Stability of the product

The stability studies have been performed following the ICH guidelines. The stability data support the proposed shelf-life and storage conditions.

II-2 Non-clinical aspects

A non-clinical overview on the pharmacology, pharmacokinetics and toxicology of the active substance has been provided, which is based on up-to-date and adequate scientific literature.

The submitted application concerns film coated tablets with the active substances in the same form as the reference product.

The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate and the Member States agreed that no further non-clinical studies are required.

Environmental Risk Assessment (ERA)

Since Calcifediol Faes 0.266 mg soft capsules is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

II.3 Clinical aspects

Introduction

Calcifediol is a well-known drug with established efficacy and safety.

No new clinical efficacy or safety studies were conducted, which is acceptable for this abridged application. A clinical overview has been provided, which is based on scientific literature. The Member States agreed that no further clinical studies are required.

Since the dossier is identical to the dossier approved for the reference product Hidroferol 0.266 mg soft capsules and have an identical Module 3, the active pharmaceutical ingredient used, the manufacturing process and manufacturing site for the finished dosage form being the same.

A bioavailability study is therefore not required to demonstrate bioequivalence, and none is provided in this application.

Biowaiver

Not applicable

Bioequivalence

Not Applicable

Risk Management Plan

A risk management plan in accordance with the requirements of Directive 2001/83/EC as amended has been submitted.

No additional risk minimization activities were required beyond those included in the product information.

Discussion on the clinical aspects

Efficacy and safety of the active substance calcifediol is well documented for the reference medicinal product. The design of the submitted bioequivalence study is adequate and the results allow us to conclude bioequivalence with the reference.

III OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

No bioequivalence study is necessary since Calcifediol Faes 0.266 mg soft capsules are identical to the originator Hidroferol 0.266 mg soft capsules.

Agreement between Member States was reached during the procedure. The decentralised procedure was finalised with a positive outcome in February 2017.