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IRISH MEDICINES BOARD

PUBLIC ASSESSMENT REPORT FOR A MEDICINAL PRODUCT FOR HUMAN USE

Scientific discussion

Zinatan 250 mg & 500 mg film-coated tablets
CEFUROXIME
PA0126/191/001-002

The Public Assessment Report reflects the scientific conclusion reached by the Irish Medicines Board (IMB) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the IMB for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. 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 IMB leading to the approval of the medicinal product for marketing in Ireland.

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the IMB has granted a marketing authorisation for Zinatan 250 mg and 500 mg film-coated tablets from Clonmel Healthcare Ltd on 19th July 2013 indicated for the treatment of the infections listed below in adults and children from the age of 3 months
(see sections 4.4 and 5.1).

- Acute streptococcal tonsillitis and pharyngitis.
- Acute bacterial sinusitis.
- Acute otitis media.
- Acute exacerbations of chronic bronchitis.
- Cystitis.
- Pyelonephritis.
- Uncomplicated skin and soft tissue infections.
- Treatment of early Lyme disease.

This application for a marketing authorisation was submitted in accordance with Article 10(1) of Directive 2001/83/EC and is referred to as a 'generic' application. Zinatan 250 mg and 500 mg film-coated tablets have the same qualitative and quantitative composition in terms of the active substance, and the same pharmaceutical form, as Zinnat 250 mg and 500 mg film-coated tablets.

The Summary of Product Characteristics for (SPC) for this medicinal product is available on the IMB's website at www.imb.ie

Name of the product	Zinatan 250 mg & 500 mg film-coated tablets
Name of the active substance (INN)	CEFUROXIME, as CEFUROXIME AXETIL
Pharmacotherapeutic classification (ATC code)	J01D
Pharmaceutical form and strength(s)	250 mg & 500 mg
Marketing Authorisation Number(s) in Ireland (PA)	PA0126/191/001-002
Marketing Authorisation Holder	Clonmel Healthcare Limited

II QUALITY ASPECTS

II.1. Introduction

This application is for Zinatan 250 mg and 500 mg film-coated tablets.

II.2 Drug substance

The active substance is cefuroxime, an established active substance described in the European Pharmacopoeia and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

The 250 mg tablets are presented as light blue coloured, film-coated, capsule-shaped tablet embossed with ‘250’ on one side and ‘P125’ on the other side.

The 500 mg tablets are presented as light blue coloured, film-coated, capsule-shaped tablet embossed with ‘500’ on one side and ‘P126’ on the other side.

The tablets contain either 250 mg or 500 mg of cefuroxime, as cefuroxime axetil.

The tablet cores of both strengths also contain the following ingredients: pregelatinised starch, croscarmellose sodium, sodium laurilsulfate, microcrystalline cellulose, colloidal anhydrous silica and hydrogenated vegetable oil.

The film-coats of both strengths contain hypromellose 6cP (E464), titanium dioxide (E171), propylene glycol (E1520), brilliant blue FCF aluminium lake (E133) and indigo carmine (indigotine) aluminium lake (E132).

P.2 Pharmaceutical Development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process has been validated according to relevant European/ICH guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipiemts)

All ingredients comply with Ph. Eur. monographs, where such exist, or are adequately controlled by the manufacturer’s specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for coated tablets, and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The product is supplied in PVC/Aclar/aluminium blisters. Pack sizes of 2, 5, 7, 10, 14, 20, 28, 30, 50, 56, 60, 90, 100 or 250 tablets may be available.

Evidence has been provided that the blisters comply with EU legislation for packaging materials intended for use with foodstuffs.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines demonstrating the stability of the product for 3 years.

Zinatan 250 mg and 500 mg film-coated tablets do not require any special storage conditions.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of Zinatan 250 mg and 500 mg film-coated tablets.

III NON-CLINICAL ASPECTS

This active substance is a generic formulation of Zinnat film coated tablets, which are on the European market. No new preclinical data have been submitted. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application.

IV CLINICAL ASPECTS

IV.1 Introduction

Cefuroxime is a well known active substance with established efficacy and tolerability.

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Zinnat marketed by GSK.

For this generic application, the applicant has submitted two bioequivalence studies in which the pharmacokinetic profile of the test product Zinatan is compared with the pharmacokinetic profile of the reference product Zinnat.

A single-dose, randomised, two-period, two-treatment, two-sequence, crossover bioequivalence study was carried out. Zinatan 500mg tablets, were compared to the reference product Zinnat 500mg tablet. Based on the pharmacokinetic parameters of active substance, the reference tablet Zinnat marketed by GSK and test tablet Zinatan are bioequivalent with extent to the rate and extent of absorption and fulfil the bioequivalence requirements outlined in the relevant CHMP Note for Guidance.

The pharmacokinetics of the active substance are linear in the range 250mg to 500mg. The results of the bioequivalence study performed with the 500mg tablets therefore apply to the other strengths.

The IMB has been assured that GCP standards were followed in an appropriate manner in the studies conducted.

The applicant submitted a set of documents describing the Pharmacovigilance System, including information on the availability of an EU Qualified Person for Pharmacovigilance (EU-QPPV) and the means for notification of adverse reaction reports in the EU or from a Third Country.

IV.6 Discussion on the clinical aspects

The applicant submitted an abridged application and provided a study comparing the blood levels of this product and those of the reference product. This study confirms that the two can be considered equivalent and so it is not necessary to repeat all of the studies required for the original product.

V OVERALL CONCLUSIONS

Benefit/Risk Assessment and Recommendation

Zinatan 250mg and 500mg tablets are a generic form of Zinnat. Zinnat is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

Bioequivalence has been shown to be in compliance with the CHMP guidance documents. The SmPC is consistent with that of the reference product.

The applicant has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The IMB, on the basis of the data submitted considered that Zinatan demonstrated bioequivalence with the reference product, as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.