LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Flucloxacillin Orion
(Flucloxacillin sodium)

SE/H/981/01-02/DC

This module reflects the scientific discussion for the approval of Flucloxacillin Orion. The procedure was finalised at 2011-02-04. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Orion Corporation has applied for a marketing authorisation for Flucloxacillin Orion, film-coated tablets, 500 mg and 750 mg claiming essential similarity to Heracillin, film-coated tablet, 500 mg marketed the EU by Meda AB. The product contains flucloxacillin sodium as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Heracillin, film-coated tablet marketed by Meda AB in Sweden.

II. QUALITY ASPECTS

II.1 Introduction

Flucloxacillin Orion is presented in the form of film-coated tablets containing flucloxacillin sodium corresponding to 500 mg and 750 mg of the flucloxacillin. The excipients are magnesium stearate, povidone, croscarmellose sodium, microcrystalline cellulose, titanium dioxide (colour E171), hypromellose, macrogol and liquid paraffin light. The tablets are packed in HDPE container closed with white opaque polypropylene closure. Each HDPE container contains sachet(s) as desiccant.

II.2 Drug Substance

Flucloxacillin sodium has a monograph in the Ph Eur.

Flucloxacillin sodium is a white or almost white, hygroscopic, crystalline powder which is freely soluble in water and in methanol, soluble in ethanol (96 per cent). The structure of flucloxacillin sodium has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism is presented. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The active substance specification includes relevant tests and the limits for impurities/degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies under ICH conditions have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Flucloxacillin Orion film-coated tablet is formulated using excipients described in the current Ph Eur. All raw materials used in the product has demonstrated compliance with Commission Directive 2003/63/EC and the NfG on Minimising the risk of transmitting Animal Spongiform Encephalopathy Agents via human and veterinary medicinal products (EMEA/410/01).

The product development has taken into consideration the physico-chemical characteristics of the active substance.

The manufacturing process has been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control and ensure both batch to batch reproducibility and compliance with the product specification.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies under ICH conditions have been performed and data presented support the shelf life claimed in the SPC, with no special storage precautions.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to preclinical data, no further such data have been submitted or are considered necessary.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

To support the application, the applicant has submitted one single-dose bioequivalence study in the fasting state with the strength 750 mg. The study was a randomised, two-treatment, two-period, two-sequence single-dose crossover study conducted in 36 (35 completed) healthy male and female volunteers under fasting conditions. Plasma concentrations of flucloxacillin were determined with a validated HPLC/UV method. The 90% confidence intervals for the test/reference ratio of the population geometric means for AUC_{0-t} and C_{max} for flucloxacillin were within the conventional acceptance range of 80-125%. Thus, bioequivalence has been demonstrated.

The pharmacokinetics of flucloxacillin is linear within the therapeutic dose range.

IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to clinical efficacy/safety data, no further such data have been submitted or are considered necessary.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

User consultation

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was Finnish.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

The results of the conducted bioequivalence study can be extrapolated to other strengths since the criteria for biowaiver for additional strengths are fulfilled according to the Note for Guidance on the Investigation of Bioavailability and Bioequivalence.

The risk/benefit ratio is considered positive and Flucloxacillin Orion, film-coated tablets, 500 mg and 750 mg is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Flucloxacillin Orion, film-coated tablets, 500 mg and 750 mg was successfully finalised on 2011-02-04.

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Public Assessment Report – Update

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)

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