LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Amoxicillin MIP
(amoxicillin trihydrate)

SE/H/977/01/DC

This module reflects the scientific discussion for the approval of Amoxicillin-MIP. The procedure was finalised at 2012-01-18. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se

I. INTRODUCTION

MIP Pharma GmbH has applied for a marketing authorisation for Amoxicillin MIP, powder for oral suspension 50 mg/ml claiming essential similarity to Imacillin granules for oral suspension 50 mg/ml marketed in Sweden by Meda AB. The product contains amoxicillin trihydrate as active substance. For approved indications see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Amoxicillin MIP is presented in the form of a powder for oral suspension. Each ml of the suspension contains amoxicillin trihydrate equivalent to 50 mg of amoxicillin. The excipients are sucrose, sodium citrate, colloidal anhydrous silica, polysorbate 60 and raspberry flavour. The medicinal product is packed in brown glass bottles with polypropylene caps.

II.2 Drug Substance

The drug substance amoxicillin trihydrate is described in a Ph Eur monograph.

The drug substance is a white or almost white, crystalline powder. It is slightly soluble in water, very slightly soluble in ethanol and insoluble in fatty oils. It dissolves in dilute acids and dilute solutions of alkali hydroxides. The structure has been adequately proven and its physico-chemical properties sufficiently described. 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 have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Amoxicillin MIP powder for oral suspension is formulated using excipients described in the current Ph Eur, except for the raspberry flavour which is tested according to an acceptable in-house specification. No excipients of human or animal origin are used in the manufacture of the finished product.

The product development and the manufacturing process have been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control and ensure 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, without any storage conditions, as well as the claimed shelf life of the reconstituted suspension when stored in a refrigerator at 2-8°C.

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

Bioequivalence was evaluated in one single-dose, two-way crossover study conducted in 30 healthy volunteers, comparing Baktocillin, 50 mg/ml, powder for oral suspension with Imacillin, 50 mg/ml, granules for oral suspension under fasting conditions. A dose of 500 mg (10 ml) of the reconstituted suspension was administered. Blood samples were collected pre-dose and up to 14 hours post-dose. The study design is considered acceptable. Plasma concentrations of amoxicillin were determined with an adequately validated LC/MS/MS method. For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

Based on the submitted bioequivalence study, Amoxicillin MIP, 50 mg/ml, powder for oral suspension is considered bioequivalent with Imacillin, 50 mg/ml, granules for oral suspension.

IV.2 Discussion on the clinical aspects

Amoxicillin is an oral antibiotic that has been widely used for many years and the clinical experience is therefore extensive.
Since the product has been shown to be essentially similar and refer to a product approved based on a full application with regard to clinical efficacy and 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 English.
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 risk/benefit ratio is considered positive and Amoxicillin MIP, powder for oral suspension 50 mg/ml is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Amoxicillin MIP, powder for oral suspension 50 mg/ml was successfully finalised on 2012-01-18.

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

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)

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se