LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Amoxicillin CNP
(amoxicillin trihydrate)

SE/H/976/01-03/DC

This module reflects the scientific discussion for the approval of Amoxicillin CNP . 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

CNP Pharma GmbH has applied for a marketing authorisation for Amoxicillin CNP, tablets, 500, 750 and 1000 mg claiming essential similarity to Imacillin tablets, 500, 750 and 1000 mg 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 CNP is presented in the form of tablets containing amoxicillin trihydrate equivalent to 500 mg, 750 mg and 1000 mg of amoxicillin respectively. The excipients are microcrystalline cellulose, low-substituted hydroxypropylcellulose, saccharin, apricot flavour, magnesium stearate, colloidal anhydrous silica and vanillin. The tablets are packed in PVC/aluminium blister packages.

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 CNP tablets are formulated using excipients described in the current Ph Eur, except for low-substituted hydroxypropylcellulose which complies with the USP/NF monograph and the apricot 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, with the storage conditions “Do not store above 30°C. Store in the original package in order to protect from light.”.

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 two single-dose, two-way crossover studies conducted in 30 healthy volunteers, comparing Amoxi-saar 500 mg or 1000 mg, tablets with respective strength of the originator Imacillin under fasting conditions. 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% in both studies. From a pharmacokinetic point of view, absence of studies with the additional strength of 750 mg is acceptable.

Based on the submitted bioequivalence studies, Amoxicillin CNP is considered bioequivalent with Imacillin.

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
A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to Amoxicillin MIP

powder for oral suspension, SE/H/977/01/DC . The bridging report submitted by the applicant has been found acceptable.

The results of the conducted bioequivalence studies 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 Amoxicillin CNP, tablets, 500, 750 and 1000 mg is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Amoxicillin CNP, tablets, 500, 750 and 1000 mg 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