LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Campenam, 500 mg pulver till infusionsvätska, lösning
(imipenemmonohydrat och cilastatinnatrium)

This module reflects the scientific discussion for the approval of Campenam. The procedure was finalised at 2013-04-25. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Campenam 500 mg pulver till infusionsvätska, lösning, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Campus Pharma AB applies through the Swedish National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Tienam 500 mg/500 mg, pulver till infusionsvätska, lösning authorised in Sweden since 1986, with Merck Sharp & Dohme BV as marketing authorisation holder.
The reference product used in the bioequivalence study is Tienam 500 mg/500 mg, pulver till infusionsvätska, lösning from Sweden with Merck Sharp & Dohme BV as marketing authorisation holder.
The active substance is not considered a new active substance.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Campenam is presented in the form of a powder for solution for infusion containing 530.6 mg of cilastatin sodium which corresponds to 500 mg of cilastatin and 530 mg of imipenem monohydrate which corresponds to 500 mg of imipenem. The excipient is sodium hydrogen carbonate. The powder is filled in glass bottles.

II.2 Drug Substance

Cilastatin sodium has a monograph in the Ph. Eur.

Cilastatin sodium is a white or light yellow amorphous, hygroscopic powder which is very soluble in water and slightly soluble in ethanol. The structure of cilastatin sodium has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism and chirality 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.

Imipenem monohydrate has a monograph in the Ph. Eur.

Imipenem monohydrate is a white or almost white or pale yellow powder which is slightly soluble in water and methanol. The structure of imipenem monohydrate has been adequately

proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism and chirality 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

Campenam, powder for solution for infusion is formulated using excipients described in the current Ph. Eur. All raw materials used in the product have 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, when stored below 25 °C.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of imipenem/cilastatine are well known. As imipenem/cilastatine is a widely used, well-known active substance, no further studies are required and the applicant provides none. Overview based on literature review is, thus, appropriate.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

Campenam is to be administered as an aqueous intravenous solution containing the same active substances in the same concentrations as the currently authorised product. No bioequivalence studies are required for this type of product according to Note for guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98) and the applicant has submitted none.

Following intravenous administration of 500 mg/500 mg, a mean maximum plasma level of imipenem of 39 µg/ml was observed. The plasma protein binding of imipenem is about 20%. Imipenem is mainly metabolised in the kidneys into the inactive open ring metabolite. Cilastatin is an inhibitor of this metabolism. The elimination half-life is about 1 h for imipenem as well as for cilastatin. Approximately 70% of the administered imipenem dose is excreted as unchanged drug in urine, and approximately 70– 80% of the cilastatin dose.

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.

The SmPC for Campenam is harmonised to the EU-SmPC for reference product Tienam, which underwent an article 30 harmonisation, finalised 2011.

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 product Imipenam/cilastatin 250 mg/ 250 mg and 500 mg/500 mg, powder for solution for injection and infusion which was assessed and accepted in PL 1577870829;UK/H/3257/02/DC.
The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and Campenam 500 mg pulver till infusionsvätska, lösning is recommended for approval.

VI. APPROVAL

Campenam 500 mg pulver till infusionsvätska, lösning was approved in the national procedure on 2013-04-25.

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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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