LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

# Public Assessment Report
# Scientific discussion

# Piperacillin/Tazobaktam Aurobindo 2g/0.25g and 4g/0.5g powder for solution for injection/infusion (Piperacillin sodium, Tazobactam sodium)

## SE/H/844/01-02/DC

**This module reflects the scientific discussion for the approval of Piperacillin/Tazobaktam Aurobindo. The procedure was finalised at 2009-09-30. For information on changes after this date please refer to the module 'Update'.**

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# I. INTRODUCTION

Aurobindo Pharma Ltd, Malta has applied for a marketing authorisation for Piperacillin/Tazobaktam Aurobindo powder for solution for injection/infusion, 2g/0.25g and 4g/0.5g claiming essential similarity to Tazocin, powder for solution for injection/infusion marketed in Sweden by Wyeth AB. The product contains piperacillin sodium and tazobactam sodium as active substances. For approved indications see the Summary of Product Characteristics. No bio-equivalence study is performed due to the parenteral dosage form.

# II. QUALITY ASPECTS

## II.1 Introduction

Piperacillin/Tazobaktam Aurobindo is presented in the form of solution for injection/infusion containing piperacillin sodium wjich corresponds to 2 g piperacillin and tazobactam sodium which corresponds to 0.25 g tazobactam or piperacillin sodium which corresps to 4 g piperacillin and tazobactam sodium which corresponds to 0.5 g tazobactam. No excipients are used. The powder for injection/infusion is filled in clear glass vials stoppered with grey colour bromo butyl rubber stopper and sealed with violet colour PP/Al flip off seal.

## II.2 Drug Substance

Piperacillin sodium has a monograph in the Ph Eur.
Tazobactam sodium does not have a monograph in the Ph Eur.

Piperacillin monohydrate is a white or almost white powder which is freely soluble in methanol, slightly soluble in water and in ethyl acetate.. The structure of Piperacillin monohydrate has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on chirality is presented. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

Tazobactam is a white to pale yellow, non-hygroscopic, crystalline powder which is soluble in dimethylformamide, moderately soluble in water, in methanol, in acetone and in ethanol, slightly soluble in ethyl acetate, in ethyl ether and in chloroform, insoluble in hexane. The structure of tazobactam has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on 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 substances specifications include 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

Piperacillin/Tazobaktam Aurobindo solution for injection/infusion is formulated without the use of excipients. All raw materials used in the product are of vegetable origin/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, such as solubility and stability.

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

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

Piperacillin/Tazobaktam Aurobindo is a powder for solution for injection, which will be administered as a clear solution in the same concentration as the reference product. Therefore, no bioequivalence study has been submitted with the application. The product consists of a mixture of the active substances piperacillin sodium and tazobactam sodium. No excipients are present in the product.

According to the Note for Guidance on the Investigation of Bioavailability and Bioequivalence (CPMP/EWP/QWP/1401/98), the applicant is not required to submit a bioequivalence study if the product is to be administered as an aqueous intravenous solution containing the same active substance in the same concentration as the currently authorized product. The lack of bioequivalence studies is therefore acceptable.

### 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 testing of the package leaflet for Piperacillin/Tazobaktam Aurobindo 2 g/0.25 g and 4 g/0.5 g solution for injection/infusion has been performed and is acceptable.
User testing for the package leaflets for Piperacillin/Tazobactam Milpharm, Piperacillin/Tazobactam Winthrop, Piperato and Piperacillin/Tazobactam Actavis have not been performed but an acceptable bridging to the test for Piperacillin/Tazobaktam Aurobindo has been made. All package leaflets are identical in terms of information, design and layout with exception of product specific information.

The risk/benefit ratio is considered positive and Piperacillin/Tazobaktam Aurobindo 2 g/0.25 g and 4 g/0.5 g solution for injection/infusion is recommended for approval.

# VI. APPROVAL

The Decentralised procedure for Piperacillin/Tazobaktam Aurobindo 2 g/0.25 g and 4 g/0.5 g solution for injection/infusion was successfully finalised on 2009-09-30.

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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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