LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Piperacillin/Tazobactam STADA

(piperacillin, tazobactam, tazobactam sodium, piperacillin sodium)

SE/H/2107/01-02/DC

This module reflects the scientific discussion for the approval of Piperacillin/Tazobactam STADA. The procedure was finalised on 2021-11-16. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Piperacillin/Tazobactam STADA, 4 g/0,5 g, 2 g/0,25 g, Powder for solution for infusion.

The active substance is piperacillin and tazobactam. A comprehensive description of the indication and posology is given in the SmPC.

For recommendations to the marketing authorisation not falling under Article 21a/22a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a/22a/ 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

The application for Piperacillin/Tazobactam STADA, 2 g/0,25 g and 4 g/0,5 g, powder for solution for infusion, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, ADOH B.V., applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DE, ES, FR, IT, UK(NI) as concerned member states (CMS).

CMS DE was withdrawn by the Applicant in the day 106 response.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is TAZOCILLINE, 2 g/0.25 g, 4 g/0.5 g, powder for solution for infusion, authorised in France since 1992, with Pfizer Holding France as marketing authorisation holder.

European Reference Product (ERP)
A European Reference Product is used in CMS DE (withdrawn by the Applicant in the day 106 response): Tazocin, 2 g/0.25 g, powder for solution for infusion authorised in SE 1993 and deregistered 2015, with Pfizer AB as marketing authorisation holder.
The justification to use this product is based on RMS's own files.
The ERP information received from RMS was circulated during validation period.

Potential similarity with orphan medicinal products
According to the application form and a check of the Community Register of orphan medicinal products there is no medicinal product designated as an orphan medicinal product for a condition relating to the indication proposed in this application.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

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

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

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 have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

Pharmacodynamic, pharmacokinetic and toxicological properties of piperacillin and tazobactam are well known. As piperacillin and tazobactam are widely used, well-known active substances, no further studies are required, and the applicant provides none. A non-clinical overview based on literature review has been provided which is appropriate.

Environmental Risk Assessment (ERA)
Piperacillin/Tazobactam STADA is a generic medical product and is as such not anticipated to generate increased exposure to the environment compared to existing equivalent products. It can be noted that an estimation of a prevalence refined Fpen for 5 days treatment (based on healthcare-associated infections (HAI) data in Europe) gave a value of 0.00000108 and predicted environmental concentrations for surface water (PECsw) of 0.0065ug/L (piperacillin) and 0.00081ug/L (tazobactam), not triggering a phase II assessment. The Log Kow values were also log Kow <4.5 and did not necessitate a PBT assessment. A more detailed/extensive environmental risk assessment is therefore not deemed necessary.

There are no objections to approval of Piperacillin/Tazobactam STADA from a non-clinical point of view.

IV. CLINICAL ASPECTS

Pharmacokinetics
The applicant has not submitted any bioequivalence studies. Absence of bioequivalence studies is acceptable. Since the product applied for is to be administered as an aqueous intravenous solution containing the same active substances as the currently authorised product, no bioequivalence study is required according to the Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1). There are no objections to approval of Piperacillin-Tazobactam STADA 4 g/ 0.5 g and 2 g/ 0.25 g, powder for solution for infusion from a pharmacokinetic point of view.

Pharmacodynamics/Clinical efficacy/Clinical safety
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted, which is acceptable.

Risk Management Plan
The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Piperacillin/Tazobactam STADA.

Safety specification
The MAH has submitted the version 0.4 RMP dated 20 September 2021 and proposed the following summary safety concerns:

Table SVIII.1 Summary of safety concerns

Important identified risks	None
Important potential risks	None
Missing information	None

Pharmacovigilance Plan
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Summary of the RMP
The submitted Risk Management Plan, version 0.4 signed 20 September 2021 is considered acceptable. The RMP has been updated in line with the revised RMP for the reference product Piperacillin/Tazobaktam Aurobindo, 4 g/0,5 g, 2 g/0,25 g, Powder for solution for infusion – SE/H/844/01-02/IB/35.

An updated RMP should be submitted:
- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. 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.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Piperacillin/Tazobactam STADA, is found adequate. There are no objections to approval of Piperacillin/Tazobactam STADA, from a non-clinical and clinical point of view. The product information is acceptable. The benefit/risk is considered positive, and the application is therefore recommended for approval.

List of recommendations not falling under Article 21a/22a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a/22a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

The decentralised procedure for Piperacillin/Tazobactam STADA, 4 g/0,5 g and 2 g/0,25 g, Powder for solution for infusion was positively finalised on 2021-11-16.

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SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report – Update

Procedure number*	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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