HUNGARIAN NATIONAL CENTER FOR PUBLIC HEALTH AND PHARMACY

Public Assessment Report

Scientific discussion

Ampicillin Eberth 500 mg & 1 g & 2 g powder for solution for injection or infusion

(ampicillin sodium sterile)

HU/H/0774/001-003/DC

Date: 15.05.2026

This module reflects the scientific discussion for the approval of Ampicillin Eberth 500 mg & 1 g & 2 g powder for solution for injection or infusion. The procedure was finalised at 29-11-2022. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Ampicillin Eberth 500 mg & 1 g & 2 g powder for solution for injection or infusion from Dr. Friedrich Eberth Arzneimittel.

Indications:

In the treatment of the following infections in adults, adolescents and children:

- Acute exacerbation of chronic bronchitis
- Pyelonephritis
- Bacterial meningitis
- Community-acquired pneumonia when penicillin G has not given the desired effect or is unsuitable for other reasons
- Intra-abdominal infections
- Bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above

A comprehensive description of the indications and posology is given in the SmPC.

This decentralised procedure concerns a generic version (1 g and 2 g) and hybrid version (500 mg) of ampicillin claiming essential similarity with the innovator product Doktacillin Powder for solution for injection/infusion by Meda AB. The reference product was first authorised on 31.03.1964 in Sweden. The concerned member states (CMS) involved in this procedure were Austria and Germany. The marketing authorisation has been granted pursuant to Article 10(1) and 10(3) of Directive 2001/83/EC.

II. QUALITY ASPECTS

II.1 Introduction

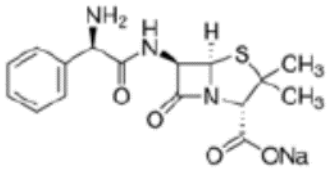
The chemical-pharmaceutical assessment report concerns the application for Marketing Authorisation via the Decentralised Procedure (DCP) for product Ampicillin Eberth 500 mg, 1 g and 2 g powder for solution for injection/infusion according to Article 10(1) of consolidated Directive 2001/83/EC (i.e. a generic application) and Article 10(3) of consolidated Directive 2001/83/EC (i.e. a hybrid application.
Reference product is Doktacillin 1 g respective 2 g pulver till injektions-/infusionsvätska, lösning (Meda AB).
The finished dosage form is powder for solution for injection. The powder is filled in a type III glass vial, closed with a chlorobutyl rubber stopper and flip-off aluminium cap.

II.2 Drug Substance

Data on the quality and manufacture of the active substance were provided in the applicant's submission using the Active Substance Master File (ASMF) procedure with additional data in the marketing authorization dossier. The Quality Overall Summary is adequate.

I.N.N.: Ampicillin sodium
Chemical name: Sodium (2S, 5R, 6R)-6-[[(2R)-2-amino-2-phenylacetyl] amino]-3, 3-dimethyl-7-oxo 4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate

Structure:



The active substance is white or almost white hygroscopic powder, freely soluble in water, sparingly soluble in acetone, practically insoluble in fatty oil and liquid paraffin.

The ASMF holder presented complete details of the manufacturing process. Description of the manufacturing process of the active pharmaceutical ingredient (API) is adequate.

Evidence of the structure has been confirmed by MS, Elemental analysis, IR, UV, NMR, XRPD. The impurity profile of the API contains detailed information about genotoxic impurities, residual solvents and catalysts.

The active substance specification is in compliance with the requirements of the current Ph. Eur. individual monograph for Ampicillin sodium (0578), the General Monographs: Substances for pharmaceutical use (2034) and 5.4 on Residual solvents. In addition, the microbiological and biological properties determined according to the Ph. Eur. requirements for drug substance used for manufacturing sterile drug product.
Testing of physical parameters is included in the drug substance specification as informative parameters.
Testing methods not described in detail in the Pharmacopoeia are adequately drawn up and sufficiently validated. Reference materials used by the active substance manufacturer and the drug product manufacturer for the control of the substance are adequately characterised.
The substance complies with the requirements of the EMA guideline on genotoxic impurities.

Batch analysis data justify the limits, indicate the good performance of testing methods and demonstrate the batch-to-batch consistency of the production.

There is no re-test period established but, the drug-product manufacturer confirms that every lot of API upon every receipt at its warehouse will be tested.

Good Manufacturing Practice (GMP) compliance of the API manufacture is demonstrated by the applicant.

II.3 Medicinal Product

Pharmaceutical development aimed to manufacture a stable powder for solution/infusion as a generic formulation of Reference Product Doktacillin 1 g respektive 2 g pulver till injektions-/infusionsvätska, lösning (Meda AB). The same quantity of drug substance in one vial and the same route of administration is used.

Compliance of the product with the general monograph of the European Pharmacopoeia on the Products with the risk of TSE has been demonstrated by the applicant.

A description and flow chart of the manufacturing method has been provided. Appropriate in-process controls are included in the manufacturing process. Satisfactory batch formula were also presented. GMP compliance of the manufacturing site has been demonstrated.

The finished product specification is satisfactory. Acceptance criteria have been justified with respect to conventional pharmaceutical requirements as prescribed in the relevant dosage form monograph of the Ph. Eur. and the ICH Q6A guideline. Appropriate control strategy was selected. The test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and complied with the specification. The testing results of the batches demonstrate that the drug product can be manufactured in a consistently good quality.

The provided data and documents of the container closure system confirm the suitability of the immediate packaging materials.

Finished product stability studies have been conducted in accordance with the current guidelines. Based on the results, a shelf-life of 30 months is approved with the following storage condition: 'These medicinal products do not require any special storage conditions.'

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The Summary of Product Characteristics, patient Information Leaflet and label texts are pharmaceutically acceptable.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Conclusion: Ampicillin Eberth 500 mg, 1 g and 2 g powder for solution for injection/infusion has been shown to meet the current regulatory requirements with regards to its quality and content of the active substance as well as dosage-form characteristics until the end of the approved shelf-life consistently. The manufacture and the quality standards applied adequately support the safe use and efficacy of the product.

III. NON-CLINICAL ASPECTS

III.1 Introduction

Pharmacodynamic, pharmacokinetic and toxicological properties of ampicillin are well known. As ampicillin is a widely used, well-known active substance, the applicant has not provided additional studies, and further studies are not required. Overview based on literature review is, thus, appropriate.

III.2 Ecotoxicity/environmental risk assessment (ERA)

Since Ampicillin Eberth is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.3 Discussion on the non-clinical aspects

This product is a generic formulation of Doktacillin, which is available on the European market. Reference is made to the preclinical data obtained with the innovator product. A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which is based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional nonclinical pharmacology, pharmacokinetics and toxicology data. Therefore, the member states agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Introduction

Ampicillin is a well-known active substance with established efficacy and tolerability.
A clinical overview has been provided, which is based on scientific literature. The overview justifies why there is no need to generate additional clinical data. Therefore, the member states agreed that no further clinical studies are required.

IV.2 Pharmacokinetics

Biowaiver
No clinical studies, including bioequivalence studies have been performed with the product applied for. Ampicillin Eberth is a powder for solution for injection/infusion and contains the same active substance as the ERP Doktacillin powder for solution for injection/infusion. The applied strengths of 1g and 2 g for the generic product correspond to available strengths of the ERP (i.e. 1 g and 2 g, respectively), and therefore the efficacy and safety profile is considered the same. The same conclusion stands for the proposed strength of 500 mg, which differs only from the ERP in terms of strength and has previously been available for the reference product.

With reference to the EMA bioequivalence (BE) guideline (CPMP/EWP/QWP/1401/98 Rev. 1/ Corr **), bioequivalence studies are not required if the test product is to be administered as an aqueous intravenous solution containing the same active substance as the reference product and when excipients are not expected to have an impact on drug disposition. This is applicable for the current product and a biowaiver is acceptable for all applied strengths.

IV.3 Pharmacodynamics

Ampicillin is a beta-lactam antibiotic that has been used extensively to treat bacterial infections since 1961. Ampicillin is active against gram positive and some gram-negative bacteria. The following bacteria have been shown in in vitro studies to be susceptible to ampicillin: Gram-Positive Organisms: Hemolytic and nonhemolytic streptococci, D. pneumoniae, nonpenicillinase-producing staphylococci, Clostridia spp., B. anthracis, Listeria monocytogenes, and most strains of enterococci. Gram-Negative Organisms: H. influenzae, N. gonorrhoeae, N. meningitidis, Proteus mirabilis, and many strains of Salmonella, Shigella, and E. coli.

Mode of action.
Ampicillin is a penicillin with a broad antibacterial spectrum. Ampicillin inhibits bacterial cell wall synthesis via blockade of the penicillin-binding proteins such as the transpeptidases. It inhibits the third and final stage of bacterial cell wall synthesis in binary fission, which ultimately leads to cell lysis. The effect is bactericidal.

No new data have been submitted. No data are required for an abridged application provided bioequivalence has been satisfactorily demonstrated.

IV.4 Clinical efficacy

No new efficacy study has been performed by the applicant.

IV.5 Clinical safety

No new safety data have been submitted by the applicant.

IV.6 Risk Management Plan

Ampicillin Eberth 500 mg Powder for Solution for Injection/ Infusion Solution;
Ampicillin Eberth 1 g Powder for Solution for Injection/ Infusion Solution;
Ampicillin Ebert 2 g Powder for Solution for Injection/ Infusion Solution.
Applicant: Dr. Friedrich Eberth Arzneimittel GmbH
HU/H/0774/001-003/DC

1) Summary of Pharmacovigilance System

The applicant has submitted a signed Summary of the Dr. Friedrich Eberth Arzneimittel GmbH's Pharmacovigilance System dated on 15.10.2014.

Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation and as detailed in the GVP module, the Assessor considers the Summary acceptable.

2) Risk Management Plan (version number: 0.5, dated on 10.11.2022)

- **Summary of safety concerns**

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

As the active substance of this product (ampicillin) has been used for decades and their safety concerns are well-known there were no safety concerns applicable for this EU RMP based on the requirement to present only the important identified or potential risks and missing information linked to further pharmacovigilance activities or additional risk minimization measures in the EU.

- **Pharmacovigilance Plan**

Routine pharmacovigilance activities are considered sufficient to manage all the safety concerns connected to Dr. Friedrich Eberth Arzneimittel GmbH's product containing ampicillin sodium.
No additional activities are proposed.

- **Risk Minimisation Measures**

Routine risk minimisation measures (i.e. wording in SmPC, PL and classification as a prescription only medicine) are considered sufficient to manage all the safety concerns connected to Dr. Friedrich Eberth Arzneimittel GmbH's product containing ampicillin sodium.
No additional activities are proposed. For any further information on risk minimisation, please refer to the product information.

3) PSUR

The requirements for submission of periodic safety update reports for these medicinal products are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European

IV.7 Discussion on the clinical aspects

The application concerns a generic product (1 g and 2 g) and hybrid version (500 mg) of ampicillin.
Ampicillin Eberth 500 mg & 1 g & 2 g powder for solution for injection or infusion is essentially similar to the reference product Doktacillin Powder for solution for injection/infusion (1964-03-31), Sweden, Meda AB, no bioequivalence study is deemed necessary.
No new efficacy or safety data have been submitted, and none are required.
There were no objections against granting the marketing authorization from a clinical point of view.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Ampicillin is a well-known medicinal product with an established favourable efficacy and safety profile.
Bioequivalence has been shown in compliance with the requirements of European guidance documents.

Modul 6
Steps taken after the initial procedure with an influence on the Public Assessment Report

Procedure number	Type of modification [1]	Date of start of the procedure	Date of end of procedure	Approval/non approval
HU/H/0774/001-003/IB/001	B.II.f).1.b).1. As packaged for sale (supported by real time data)	2023.04.03	2023.05.03	Approved
HU/H/0774/001-003/IB/002	B.II.d).1.h). Update of the dossier to comply with the provisions of an updated general monograph of the Ph. Eur for the finished product*	2023.06.27	2023.07.27	Approved
HU/H/0774/001-003/II/003	B.II.b).4.d). The change relates to all other pharmaceutical forms manufactured by complex manufacturing processes	2023.06.27	2024.03.17	Approved
HU/H/0774/001-003/IA/004	B.II.d).1.z). Other variation	2024.05.02	2024.06.01	Approved
HU/H/0774/001-003/IB/005	B.III.1.a).3. New certificate from a new manufacturer (replacement or addition)	2025.07.17	2025.08.06	Approved
HU/H/0774/001-003/IB/006	B.II.d).2.d). Other changes to a test procedure (including replacement or addition)	2025.11.11	2025.12.11	Approved