LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Tobramycin EQL Pharma
(tobramycin sulfate)

Asp-no: 2022-1319, 2022-1320

This module reflects the scientific discussion for the approval of Tobramycin EQL Pharma. The procedure was finalised on 2024-05-22. 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 Tobramycin EQL Pharma, 40 mg/ml, 80 mg/ml, Solution for injection.

The active substance is tobramycin sulfate. 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 Tobramycin EQL Pharma, 40 mg/ml and 80 mg/ml, solution for injection, is a generic application submitted according to Article 10(1) of Directive 2001/83/EC. The applicant applies for a marketing authorisation in Sweden through a National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Nebcina, 40 mg/ml, solution for injection, authorised in SE since 1977, with Meda AB as marketing authorisation holder.

Potential similarity with orphan medicinal products
N/A.

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

Pharmacology/Pharmacokinetics/Toxicology
Pharmacodynamic, pharmacokinetic and toxicological properties of tobramycin are well known. As tobramycin 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.

Environmental Risk Assessment (ERA)
Since Tobramycin EQL Pharma is a generic product, it will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

IV. CLINICAL ASPECTS

Pharmacokinetics
To support the marketing authorisation application the applicant has not conducted any bioequivalence studies. The applicant claims that a bioequivalence study is not necessary according to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1) since the product is an aqueous parenteral solution with a qualitative composition that is comparable to the that of the reference product and with no excipients interacting with the drug substance.

Pharmacokinetic properties of the active substance
Following intramuscular injection, maximum plasma concentration is reached after 30-60 minutes. The half-life in serum is approximately 2 hours.

Discussion and overall conclusion
The applied product is to be administered either as an intravenous solution or as an intramuscular solution containing the same active substance in the same concentration as the currently authorised product. None of the excipients are known to interact with the drug substance. The applied product contains the same excipients as the reference product (sodium metabisulfite, disodium edetate and water for injections) and in addition sodium hydroxide and sulphuric acid for pH adjustment. Thus, the product contains comparable excipients in similar amounts, and it is not expected that this difference in excipients should have an impact on the viscosity. For this type of product, no bioequivalence studies are required according to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1.

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 Tobramycin EQL Pharma.

Safety specification
The MAH has submitted the version 0.1 RMP dated 2022-11-27 and proposed the following summary safety concerns:

Table SVIII.1: Summary of safety concerns

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

Assessor's comments: The Applicant has proposed no safety concerns which is accepted. The active substance tobramycin have an established safety and tolerability profile. Given the fact the tobramycin products are well characterized, have been on the market since 1977, it is acceptable to have no remaining important risks.

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 0.1 signed 2022-11-27 is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the Swedish MPA;
- 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 PL was Swedish.
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, Tobramycin EQL Pharma, is found adequate. There are no objections to approval of Tobramycin EQL Pharma, from a non-clinical and clinical point of view. The absence of bioequivalence studies is acceptable. 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

Tobramycin EQL Pharma, 40 mg/ml, 80 mg/ml, Solution for injection was approved in the national procedure on 2024-05-22.

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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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