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June 2026

Public Assessment Report

Scientific discussion

TERSEN 500 mg powder for solution for injection/infusion
TERSEN 1 g powder for solution for injection/infusion
TERSEN 2 g powder for solution for injection/infusion
(ceftizoxime sodium)

SK/H/0324/001-003/DC

Date of this report:	August 2026

This module reflects the scientific discussion for the approval of TERSEN. The procedure was finalised at 11 September 2025. 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, the Member States have agreed to grant a marketing authorisation for TERSEN, powder for solution for injection/infusion, 500 mg, 1 g, 2 g. The product is indicated for severe infections caused by bacteria sensitive to ceftizoxime such as:
- Lower respiratory tract infections
- Intra-abdominal infections, including bile ducts
- Gynaecological infections
- Urinary tract infections
- Septicaemia
- Skin and soft tissue infections
- Bone and joint infections
- Meningitis

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

II EXECUTIVE SUMMARY

TERSEN 500 mg powder for solution for injection/infusion
TERSEN 2 g powder for solution for injection/infusion

II.1 Rationale for the product

N/A

II.2 About the product

Mechanism of action
The bactericidal effects of ceftizoxime are, similarly to other cephalosporin antibiotics, caused by the inhibition of the synthesis of the cell wall of sensitive bacteria.

Mechanism of resistance
Ceftizoxime is stable against staphylococcal penicillinase and has a high degree of stability against a range of beta-lactamases produced by gram-negative bacteria.

Aerobic Gram-negative bacteria are very sensitive: *Escherichia coli*, *Klebsiella* sp., *Enterobacter* sp., *Citrobacter* sp., *Proteus* sp., *Providencia* sp., *Serratia marcescens*, *Acinetobacter* sp., *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Borrelia burgdorferi*, *Streptococcus pneumoniae*, group A, B, C, G streptococci and other streptococci.

It is effective against staphylococci (including penicillinase-producing strains) and anaerobic bacteria *Bacteroides fragilis*.

Strains of gram-negative bacilli with constitutive production of chromosomal cephalosporinase, most strains of *Pseudomonas*, enterococci, *Listeria monocytogenes* and staphylococci resistant to oxacillin (methicillin) are resistant.

Pharmacological classification
Pharmacotherapeutic group: Antibacterials for systemic use; Third-generation cephalosporins
ATC code: J01DD07

Approved indications

Severe infections caused by bacteria sensitive to ceftizoxime such as:

- Lower respiratory tract infections
- Intra-abdominal infections, including bile ducts
- Gynaecological infections
- Urinary tract infections
- Septicaemia
- Skin and soft tissue infections
- Bone and joint infections
- Meningitis

Consideration should be given to official guidelines on the appropriate use of antibacterial agents.

Posology

Adults and children over 12 years old
Usually, 1-2 g every 8-12 hours to be given intramuscularly or intravenously.

The dosage must be adjusted according to the severity of the disease, the patient's condition and the sensitivity of the microorganisms:
- Urinary system infections: 500 mg - 1 g IV every 12 hours
- Septicaemia and severe life-threatening infections: 6-12 g/day IV divided into three doses.

The maximum daily dose should not exceed 12 g.

Paediatric population
Children from 6 months
- 50 mg/kg every 6-8 hours IV.

The maximum daily dose should not exceed 200 mg/kg/day.

Method of administration
For intravenous or intramuscular use after reconstitution and dilution.
When given by intravenous injection, administer the solution within 3-5 minutes.

For special populations (e.g. patients with impaired renal function) please refer to the SmPC.

II.3 General comments on the submitted dossier

TERSEN 500 mg powder for solution for injection/infusion
TERSEN 2 g powder for solution for injection/infusion
This concerns an application for marketing authorisation for TERSEN 500 mg powder for solution for injection/infusion and TERSEN 2 g powder for solution for injection/infusion according to Article 10(3) of Directive 2001/83/EC, a hybrid application.

European Reference Product (ERP)
A European Reference Product is used in CMS CY: CEFIZOX 1000 I.V. (1000 mg powder for solution for injection) held by MAH Hikma Farmacêutica (Portugal) S.A., registered in SK.

TERSEN 1 g powder for solution for injection/infusion
This concerns an application for marketing authorisation for TERSEN 1 g powder for solution for injection/infusion according to Article 10(1) of Directive 2001/83/EC, a generic application.

European Reference Product (ERP)
A European Reference Product is used in CMS CY: CEFIZOX 1000 I.V. (1000 mg powder for solution for injection) held by MAH Hikma Farmacêutica (Portugal) S.A., registered in SK.

II.4 General comments on compliance with GMP, GLP, GCP and agreed ethical principles

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

For manufacturing sites outside the Community, the RMS has accepted copies of current GMP Certificates of satisfactory inspection summary reports, 'close-out letters' or 'exchange of information' issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community sites.

GMP active substance
Regarding the statement on GMP for the active substance a statement/declaration is provided from the manufacturer(s) responsible for manufacture of the finished product and batch release situated in the EU.

III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 Quality aspects

Drug substance
The chemical-pharmaceutical documentation and Quality Overall Summary in relation to TERSEN are of sufficient quality in view of the present European regulatory requirements.

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.

Drug Product
The development of the product has adequately been performed and described.
The manufacturing process has been sufficiently described and critical steps identified.
The control tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.
The limits for impurities and degradation products have been justified. The issue of nitrosamines is comprehensively and adequately addressed. The analytical methods applied are suitably described and validated.
Batch analysis has been performed on four batches of each strength. The batch analysis results show that the finished products meet the specifications proposed.
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.
The conditions used in the stability studies are according to the ICH stability guidelines.

III.2 Non clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of ceftizoxime sodium are well-

known. As ceftizoxime sodium is a widely used, well-known active substance, the applicant has not provided additional non-clinical studies, and further studies are not required. The non-clinical overview provided based on literature review is thus appropriate.

Thus, marketing authorisation was recommended from a non-clinical point of view.

Environmental Risk Assessment (ERA)
Since TERSEN is intended for generic substitution, this should not lead to an increased exposure to the environment. A complete environmental risk assessment was therefore not deemed necessary.

III.3 Clinical aspects

Pharmacokinetics

No bioequivalence study was submitted to support the application. The applicant justifies waiving of clinical studies by referring to the guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/Corr**), appendix II - parenteral solutions on the following grounds: *the proposed product contains the same active substance (ceftizoxime as sodium), is in general of the same pharmaceutical form (solution for injection/infusion (after reconstitution)) and is to be administered via the same route of administration (intravenously/intramuscularly) as the reference product*.
These conditions were fulfilled in the present application.

Pharmacodynamics/Clinical efficacy/Clinical safety
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the reference product is demonstrated, additional data is not necessary.

Summary Pharmacovigilance system

The Applicant has submitted a signed Summary of the Applicant's Pharmacovigilance System. 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 RMS considers the Summary 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 TERSEN.

Safety specification

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 0.1 signed 27 February 2024, 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 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.

Periodic Safety Update Report (PSUR)

With regard to PSUR submission, the MAH should take the following into account:
- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.
- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.
- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

Common renewal date
The applicant proposed a common renewal date 5 years after approval date. The proposed renewal date is acceptable.

IV BENEFIT RISK ASSESSMENT

This application concerns a hybrid and a generic medicinal product referencing CEFIZOX 1000 I.V. (1000 mg powder for solution for injection).
No clinically relevant differences in efficacy or safety are anticipated in the proposed indication.
Overall, the benefit–risk balance is favourable.

V RECOMMENDATIONS AND CONDITIONS FOR MARKETING AUTHORISATION AND PRODUCT INFORMATION

V.1 List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC

Description	Due date
N/A	N/A

V.2 List of conditions pursuant to Article 21a or specific obligations pursuant to Article 22 of Directive 2001/83/EC

N/A

V.3 Summary of Product Characteristics (SmPC)

The approved SmPC is available in the MRI Product Index.

V.4 Package Leaflet (PL)

V.4.1 Package Leaflet

The approved PL is available in the MRI Product Index.

V.4.2 Assessment of User Testing

Assessment of the User Testing is attached in the 'QRD Guidance and Checklist for the Review of User Testing Results'.

V.5 Labelling

The approved Labelling is available in the MRI Product Index.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
-	-	-	-	-	-