IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Teicoplanin Seacross 200 mg powder for solution for injection/infusion or oral solution
Teicoplanin
PA22766/011/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Teicoplanin Seacross 200 mg powder for solution for injection/infusion or oral solutions and Teicoplanin Seacross 400 mg powder for solution for injection/infusion or oral solutions, from Seacross Pharma (Europe) Limited on 10th January 2025 for the treatment of several infections (complicated skin and soft tissue infections, bone and joint infections, hospital acquired pneumonia, community acquired pneumonia, complicated urinary tract infections, infective endocarditis, peritonitis associated with continuous ambulatory peritoneal dialysis (CAPD), bacteraemia that occurs in association with any of these indications) and as an alternative oral treatment for Clostridioides difficile infection-associated diarrhoea and colitis.

This application for a marketing authorisation was submitted via a decentralised procedure in accordance with Article 10(3) of Directive 2001/83/EC and is referred to as a 'hybrid' application.

Ireland was the Reference Member State (RMS) and the Concerned Member States (CMS) were Germany, France, Italy, the Netherlands and Portugal.

These are prescription-only medicinal products.

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA's website at www.hpra.ie

Name of the product	Teicoplanin Seacross 200 mg powder for solution for injection/infusion or oral solutions and Teicoplanin Seacross 400 mg powder for solution for injection/infusion or oral solutions
Name(s) of the active substance(s) (INN)	Teicoplanin
Pharmacotherapeutic classification (ATC code)	J01XA02
Pharmaceutical form and strength(s)	200mg & 400mg Powder for solution for injection/infusion or oral solution
Marketing Authorisation Number(s) in Ireland (PA)	PA22766/011/001-002
Marketing Authorisation Holder	Seacross Pharma (Europe) Limited
MRP/DCP No.	IE/H/1270/001-002/DC
Reference Member State	IE
Concerned Member State	DE, FR, IT, NL, PL

II. QUALITY ASPECTS

II.1. Introduction

This application is for Teicoplanin Seacross 200 mg powder for solution for injection/infusion or oral solutions and Teicoplanin Seacross 400 mg powder for solution for injection/infusion or oral solutions.

II.2 Drug substance

The active substance teicoplanin, an established active substance described in the European Pharmacopoeia, and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

The finished drug products are lyophilised powders containing 200 mg and 400 mg of teicoplanin.

The excipients in the medicinal product are listed in section 6.1 of the SmPC.
A visual description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process has been validated according to relevant European/ICH guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients/*Ancillary Substances*)

All ingredients comply with Ph. Eur. or are adequately controlled by the manufacturer's specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for parenteral preparations, and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site(s) have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the packaging complies with Ph. Eur./EU legislation for use with foodstuffs requirements.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of the finished products.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Targocid 200 mg and 400 mg powder and solvent for solution for injection/infusion or oral solution on the European market. No new preclinical data have been submitted. This is acceptable for this type of application.

III.2 Pharmacology

N/A

III.3 Pharmacokinetics

N/A

III.4 Toxicology

N/A

III.5 Ecotoxicity/environmental risk assessment

Since Teicoplanin Seacross 200 mg and 400 mg powder for solution for injection/infusion or oral solution is a generic product, it will not lead to an increased exposure to the environment. Further environmental risk assessment is therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of teicoplanin are well known. As teicoplanin is a widely used, well-known active substance, the applicant has not provided additional studies, and further studies are not required. A nonclinical overview based on literature review was provided and is acceptable for this type of application.
Nonclinical sections of the SmPC are in line with the originator which is acceptable.

IV. CLINICAL ASPECTS

IV.1 Introduction

Teicoplanin is a well known active substance with established efficacy and tolerability.

The content of the SmPC approved during the decentralised procedure is in accordance with that accepted for the reference product Targocid marketed by MAH.

For this hybrid application, a biowaiver has been requested and accepted in line with Appendix II of guideline on the investigation of bioequivalence (Doc.Ref.:CPMP/EWP/QWP/1401/98 Rev.1/Corr **).

The submitted clinical efficacy and safety overviews are based on the reference product data and on recent clinical data available in literature which further corroborate the positive risk-benefit balance of varenicline intended for oral use.

IV.2 Pharmacokinetics

Absorption
Teicoplanin is administered by parenteral route (intravenously or intramuscularly). After intramuscular administration, the bioavailability of teicoplanin (as compared to intravenous administration) is almost complete (90%). After six daily intramuscular administrations of 200 mg the mean (SD) maximum teicoplanin concentration (Cmax) amounts to 12.1 (0.9) mg/L and occurs at 2 hours after administration.
After a loading dose of 6 mg/kg administered intravenously every 12 hours for 3 to 5 administrations, Cmax values range from 60 to 70 mg/L and Ctrough are usually above 10 mg/L. After an intravenous loading dose of 12 mg/kg administered every 12 hours for 3 administrations, mean values of Cmax and Ctrough are estimated to be around 100 mg/L and 20 mg/L, respectively. After a maintenance dose of 6 mg/kg administered once daily Cmax and Ctrough values are approximately 70 mg/L and 15 mg/L, respectively. After a maintenance dose of 12 mg/kg once daily Ctrough values range from 18 to 30 mg/L.
When administered by oral route teicoplanin is not absorbed from the gastrointestinal tract. When administered by oral route at 250 or 500 mg single dose to healthy subjects, teicoplanin is not detected in serum or urine but only recovered in feces (about 45% of the administered dose) as unchanged medicinal product.

Distribution
The binding to human serum proteins ranges from 87.6 to 90.8% without any variation in function of the teicoplanin concentrations. Teicoplanin is mainly bound to human serum albumin. Teicoplanin is not distributed in red cells.
The volume of distribution at steady-state (Vss) varies from 0.7 to 1.4 mL/kg. The highest values of Vss are observed in the recent studies where the sampling period was superior to 8 days.

Teicoplanin distributed mainly in lung, myocardium and bone tissues with tissue/serum ratios superior to 1. In blister fluids, synovial fluid and peritoneal fluid the tissue/serum ratios ranged from 0.5 to 1. Elimination of teicoplanin from peritoneal fluid occurs at the same rate as from serum. In pleural fluid and subcutaneous fat tissue the tissue/serum ratios are comprised between 0.2 and 0.5. Teicoplanin does not readily penetrate into the cerebrospinal fluid (CSF).

Biotransformation
Unchanged form of teicoplanin is the main compound identified in plasma and urine, indicating minimal metabolism. Two metabolites are formed probably by hydroxylation and represents 2 to 3% of the administered dose.

Elimination
Unchanged teicoplanin is mainly excreted by urinary route (80% within 16 days) while 2.7% of the administered dose is recovered in feces (via bile excretion) within 8 days following administration.
Elimination half-life of teicoplanin varies from 100 to 170 hours in the most recent studies where blood sampling duration is about 8 to 35 days.
Teicoplanin has a low total clearance in the range of 10 to 14 mL/h/kg and a renal clearance in the range of 8 to 12 mL/h/kg indicating that teicoplanin is mainly excreted by renal mechanisms.

Linearity
Teicoplanin exhibited linear pharmacokinetics at dose range of 2 to 25 mg/kg.

Special populations
Renal impairment:
As teicoplanin is eliminated by renal route, teicoplanin elimination decreases according to the degree of renal impairment. The total and renal clearances of teicoplanin depends on the creatinine clearance.

Elderly patients:
In the elderly population the teicoplanin pharmacokinetics is not modified unless in case of renal impairment.

Paediatric population
A higher total clearance (15.8 mL/h/kg for neonates, 14.8 mL/h/kg for a mean age 8 years) and a shorter elimination half-life (40 hours neonates; 58 hours for 8 years) are observed compared to adult patients.

IV.3 Pharmacodynamics

Teicoplanin inhibits the growth of susceptible organisms by interfering with cell-wall biosynthesis at a site different from that affected by beta-lactams. Peptidoglycan synthesis is blocked by specific binding to D-alanyl-D-alanine residues.

IV.4 Clinical Efficacy

No additional efficacy clinical studies to demonstrate efficacy have been included in the application. This is appropriate for this type of application.

IV.5 Clinical Safety

No additional safety clinical studies to demonstrate safety have been included in the application.

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 Teicoplanin.

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

Risk minimisation Plan
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the MAH which is endorsed.

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.

IV.6 Discussion on the clinical aspects

This is a hybrid application, the application dossier has been submitted in accordance with the Directive 2001/83/EC, as amended as a hybrid 10(3) application.

The reference product is well established in the EU being authorised since 1990. Teicoplanin has demonstrated efficacy and has a well-established documented safety profile.

A biowaiver has been requested and accepted in line with Appendix II of guideline on the investigation of bioequivalence (Doc.Ref.:CPMP/EWP/QWP/1401/98 Rev.1/Corr **).

The product information is in line with that of the reference product.

V. OVERALL CONCLUSIONS

Teicoplanin Seacross 200 mg powder for solution for injection/infusion or oral solutions and Teicoplanin Seacross 400 mg powder for solution for injection/infusion or oral solutions is a generic form of Targocid. Targocid is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

An acceptable biowaiver has been requested in compliance with the CHMP guidance documents. The SmPC is consistent with that of the reference product.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The HPRA, on the basis of the data submitted considered that Teicoplanin Seacross 200 mg powder for solution for injection/infusion or oral solutions and Teicoplanin Seacross 400 mg powder for solution for injection/infusion or oral solutions demonstrated bioequivalence with the reference product as well as a satisfactory risk/benefit profile and therefore granted marketing authorisations.

VI. REVISION DATE

10.12.2029