COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Pantoprazol SUN 40 mg, powder for solution for injection (pantoprazole sodium sesquihydrate)

NL/H/5929/001/DC

Date: 5 September 2025

This module reflects the scientific discussion for the approval of Pantoprazol SUN 40 mg, powder for solution for injection. The procedure was finalised on 2 December 2024. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Pantoprazol SUN 40 mg, powder for solution for injection, from Sun Pharmaceutical Industries Europe B.V.

The product is indicated for use in adults for:

- Reflux oesophagitis.
- Gastric and duodenal ulcer.
- Zollinger Ellison Syndrome and other pathological hypersecretory conditions.

A comprehensive description of the up-to-date indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC, which concerns a generic application.

In this decentralised procedure, essential similarity is proven between the new product and the innovator product Pantozol i.v. powder for solution for injection 40 mg which has been registered by Takeda Nederland B.V. by means of a decentralised procedure in Germany (DE/H/0268/003). In the Netherlands, the product has been registered since 11 February 1998 (NL RVG 22084).

The concerned member states (CMS) involved in this procedure were Germany, Denmark, Finland, France, Italy, Norway and Sweden.

II. QUALITY ASPECTS

II.1 Introduction

Pantoprazol SUN is a powder for solution for injection. The powder is white to almost white.
Each vial contains as active substance 40 mg pantoprazole (as pantoprazole sodium sesquihydrate).

For the solution reconstituted with 10 ml of 0.9% NaCl solution the pH is approximately 10 and the osmolarity is approximately 300mOsm/Kg.
For the solution reconstituted with a further 100 ml of 0.9% NaCl solution or 5% glucose solution the pH is between 8.5 and 11.

The excipients are: disodiume edetate (E386) and sodium hydroxide (E524) (for pH adjustment).

The powder for solution for injection is packed in 10 ml clear glass (type I) vial with aluminium cap and chlorobutyl stopper.

II.2 Drug Substance

The active substance is pantoprazole sodium sesquihydrate, an established active substance described in the European Pharmacopoeia (Ph.Eur.). The active substance is a crystalline solid and is freely soluble in water. The crystalline form of the drug substance is not relevant for the drug product dosage form. The drug substance features one chiral centre and is produced in racemic form.

The CEP procedure is used for the active substance. Under the official Certification Procedures of the EDQM of the Council of Europe, manufacturers or suppliers of substances for pharmaceutical use can apply for a certificate of suitability concerning the control of the chemical purity and microbiological quality of their substance according to the corresponding specific monograph, or the evaluation of reduction of Transmissible Spongiform Encephalopathy (TSE) risk, according to the general monograph, or both. This procedure is meant to ensure that the quality of substances is guaranteed and that these substances comply with the Ph.Eur.

Manufacturing process
A CEP has been submitted; therefore no details on the manufacturing process have been included.

Quality control of drug substance
The active substance specification is in line with the CEP with additional requirements for residual solvents and one potentially genotoxic impurity. The specification is acceptable in view of various European guidelines. Batch analytical data demonstrating compliance with this specification have been provided for four full scale batches.

Stability of drug substance
The active substance is stable for 36 months/years when stored under the stated conditions. Assessment thereof was part of granting the CEP (and has been granted by the EDQM).

II.3 Medicinal Product

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

The development of the product has been described, the choice of excipients is justified and their functions explained. The manufacturing process development activities were adequately described and the choices for the various process parameters are supported by data. The choice for aseptic filtration and aseptic processing as sterilisation method is considered sufficiently justified in accordance to relevant guidelines.

Manufacturing process
The manufacturing process consists of dissolution of the active substance and excipients in water for injection, sterile filtration and fill and finish (lyophilisation). The manufacturing process has been completely validated according to relevant European guidelines. Process

validation data on the product have been presented for three full scale batches in accordance with the relevant European guidelines. The manufacturing process is non-standard.

Control of excipients
The excipients comply with Ph.Eur. requirements. These specifications are acceptable.

Microbiological attributes
Microbiological attributes are part of granting the CEP.

Quality control of drug product
The finished product specifications are adequate to control the relevant parameters for the dosage form. The specification includes tests for description, identification, pH, moisture, air-tightness, reconstitution time, clarity of the solution, colour of the solution, uniformity of dosage units (mass variation), assay, related substances, bacterial endotoxins, sterility, visible particles and subvisible particles. There are differences in the limits for release and shelf-life (e.g. wider limits for moisture, assay, and related substances at shelf-life). The limits are acceptable.

The analytical methods have been adequately described and validated. An adequate nitrosamines risk evaluation report has been provided. No risk for presence of nitrosamines in the drug product was identified.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data from three full scaled batches from the proposed production site have been provided, demonstrating compliance with the specification.

Stability of drug product
Stability data on the product has been provided on three full scaled batches stored at 25ºC, 60% RH (24 months) and 30ºC, 75% RH (12 months) and 40ºC, 75% RH (6 months), both in normal and inverted positions. The conditions used in the stability studies are according to the ICH stability guideline (increased humidity is used at the intermediate condition). The batches were stored in the market packaging (vial and outer carton). No changes were observed at any of the conditions.

Photostability studies were performed in accordance with ICH recommendations and showed that the product is photolabile but stable when exposed to light when stored in the proposed packaging (including outer carton).

On basis of the data submitted, a shelf life for the unopened vial is 2 years. The labelled storage conditions are: '*This medicinal product does not require any special temperature storage conditions. Keep the vial in the outer carton in order to protect from light*'.

After reconstitution, or reconstitution and dilution, chemical and physical in use stability has been demonstrated for 12 hours at 25^{o}C protected from light.

From a microbiological point of view, the product should be used immediately.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Pantoprazol SUN has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.

No post-approval commitments were made.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

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

III.2 Discussion on the non-clinical aspects

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

IV. CLINICAL ASPECTS

IV.1 Introduction

Pantoprazole is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The member states agreed that no further clinical studies are required (see section IV.2).

IV.2 Pharmacokinetics

Pantoprazol SUN 40 mg, powder for solution for injection is a parenteral formulation and therefore fulfils the exemption mentioned in the Note for Guidance on bioequivalence "5.1.6 parenteral solutions", which states that a bioequivalence study is not required if the product is administered as an aqueous intravenous solution containing the same active substance in the same concentration as the currently authorized reference medicinal product (NfG CPMP/EWP/QWP 1401/98). The quantitative composition of Pantoprazol SUN is entirely the same as the originator. Therefore, it may be considered as therapeutic equivalent, with the same efficacy/safety profile as known for the active substance of the reference medicinal product. The current product can be used instead of its reference product.

IV.3 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 Pantoprazol SUN. At the time of approval, the most recent version of the RMP was version 2.1 dated 24 October 2023.

Table 1. Summary table of safety concerns as approved in RMP

Important identified risks	None
Important potential risks	None
Missing information	None

The member states agreed that routine pharmacovigilance activities and routine risk minimisation measures are sufficient for the risks and areas of missing information.

IV.4 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Pantozol. No new clinical studies were conducted. Risk management is adequately addressed. This generic medicinal product can be used instead of the reference product.

V. USER CONSULTATION

A user consultation with target patient groups on the package leaflet (PL) has been performed on the basis of a bridging report making reference to Pantoprazole SUN Pharma 40 mg powder for solution for injection, NL/H/3573/001/DC for design/lay-out. This leaflet has undergone readability test successfully and an EPAR as proof has been provided. For content including key messages reference is made to Pantozol i.v., powder for solution for injection, 40 mg, DE/H/0268/003 (Protium). The MAH did not provide an user consultation of the PL of the reference product but stated that the key messages of both PL's were identical. Normally, proof should be provided by the MAH that the parent leaflet has undergone readability test

successfully. However, due to an article 30 referral procedure the content of the parent leaflet of Pantoprazole SUN Pharma 40 mg powder for solution for injection is the same as the leaflet for Pantoprazol SUN. Therefore, the RMS concluded that the readability of the content of the leaflet is also sufficiently covered and no full user testing is considered necessary. The MAH is requested for future applications to perform a comparison for the content with a parent leaflet for which an EPAR can be provided as proof of successful readability testing.

The bridging report submitted by the MAH has been found acceptable; bridging is justified for both content and layout of the leaflet.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Pantoprazol SUN 40 mg, powder for solution for injection has a proven chemical-pharmaceutical quality and is a generic form of Pantozol i.v. powder for solution for injection 40 mg. Pantozal is a well-known medicinal product with an established favourable efficacy and safety profile.

Since both the reference and current product are intended for parenteral use, no bioequivalence study is deemed necessary. A biowaiver has been granted.

The Board followed the advice of the assessors.

There was no discussion in the CMD(h). Agreement between member states was reached during a written procedure. The member states, on the basis of the data submitted, considered that essential similarity has been demonstrated for Pantoprazol SUN with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 2 December 2024.

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
-	-	-	-	-	-