IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Vitamins B and C concentrate for solution for infusion
Thiamine hydrochloride
Riboflavin Sodium Phosphate Hydrate
Pyridoxine hydrochloride
Ascorbic acid
Nicotinamide
Glucose monohydrate
PA1122/037/001

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.

CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Vitamins B and C Concentrate for Solution for Infusion, from Noridem Enterprises Ltd on 22nd November 2024 for :

Rapid therapy of severe depletion or malabsorption of the water-soluble vitamins B and C:

- particularly in alcoholism where a severe depletion of thiamine can lead to Wernicke's encephalopathy.

Wernickes encephalopathy may also occur as a consequence of other medical conditions.

This application for a marketing authorisation was submitted in accordance with Article 10(1) of Directive 2001/83.

With Ireland as the Reference Member State (RMS) in this Decentralised Procedure, Noridem Enterprises Limited is applying for the Marketing Authorisations for Vitamin B and C Concentrate for Solution for Infusion in CMSs Greece and Norway.

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	Vitamins B and C Concentrate for Solution for Infusion
Names of the active substances (INN)	Thiamine hydrochloride, Riboflavin sodium phosphate hydrate, Pyridoxine hydrochloride , Ascorbic acid, Nicotinamide, Glucose monohydrate
Pharmacotherapeutic classification (ATC code)	A11EB
Pharmaceutical form and strength(s)	concentrate for solution for infusion
Marketing Authorisation Number(s) in Ireland (PA)	PA1122/037/001
Marketing Authorisation Holder	Noridem Enterprises Ltd
MRP/DCP No.	IE/H/1266/001/DC
Reference Member State	IE
Concerned Member State	EL, NO

II. QUALITY ASPECTS

II.1. Introduction

This application is for Vitamins B and C Concentrate for Solution for Infusion.

II.2 Drug substance

The active substances are established active substances described in the European Pharmacopoeia, and are manufactured in accordance with the principles of Good Manufacturing Practice (GMP).

The active substance specifications are considered adequate to control the quality and meet current pharmacopoeial requirements. Batch analytical data demonstrating compliance with the specifications have been provided.

II.3 Medicinal product

P.1 Composition

The product consists for two ampoules. Ampoule 1 (5 ml) contains Thiamine Hydrochloride 250 mg, Riboflavin (as sodium phosphate hydrate) 4 mg, Pyridoxine Hydrochloride 50 mg. Ampoule 2 (5 ml) contains Ascorbic Acid 500 mg, Nicotinamide 160 mg, Glucose (as monohydrate) 1000 mg.
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 will be validated according to relevant European/ICH guidelines at each commercial batch size.

P.4 Control of Other Substances

All ingredients comply with the 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 applicable requirements for this dosage form, 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 sites 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 Vitamins B and C Concentrate for Solution for Infusion.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Pabrinex on the European market. No new preclinical data have been submitted. As such, no pre-clinical assessment has been made on the application. 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 *Vitamins B and C Concentrate for Solution for Infusion* is intended for generic substitution, an increased exposure to the environment is not anticipated. Additional environmental risk assessment studies are therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of Vitamins B and C Concentrate for Solution for Infusion containing thiamine, riboflavin, pyridoxine, nicotinamide and ascorbic acid are well known. The reference product Pabrinex® has been on the market since 1987 and is a widely used, well-known medicinal product. The applicant has not provided additional nonclinical studies and further studies are not required. Nonclinical sections of the SmPC are in line with the reference product SmPC which is acceptable.

IV. CLINICAL ASPECTS

IV.1 Introduction

The active substances thiamine hydrochloride, riboflavin sodium phosphate hydrate, pyridoxine hydrochloride, ascorbic acid, nicotinamide, glucose monohydrate are well known active substances 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 Pabrinex Intravenous High Potency Concentrate for Solution for Infusion marketed by Kyowa Kirin Holdings B.V. (PA2288/001/001).

For this generic application, the proposed product is considered similar to the reference medicinal product Pabrinex Intravenous High Potency concentrate for solution for infusion, which contains the same active substances in the same pharmaceutical form and strength.
The Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev.1/Corr) states that bioequivalence studies are generally not required if the test product is to be administered as an aqueous solution containing the same active substance as the currently approved product. Therefore, no bioequivalence studies have been provided.

IV.2 Pharmacokinetics

Vitamins B and C Concentrate for Solution for Infusion is administered intravenously and therefore has 100% bioavailability. B complex vitamins and vitamin C are water-soluble. They are excreted in the urine.

IV.3 Pharmacodynamics

B vitamins play essential roles in catabolic and anabolic metabolism. They act as coenzymes in several enzymatic processes that support every aspect of cellular physiological functioning, including major functions within the brain and nervous system. Any B vitamin deficiency can negatively affect mitochondrial metabolism of amino acids, glucose, and fatty acids through the citric acid cycle and electron transport chain.

Vitamin C is known to be an electron donor for eight human enzymes. Vitamin C plays an important role in eliminating oxidative stress which, in combination with its water solubility, makes it the main antioxidant of extracellular fluid. At a molecular level, vitamin C is needed in the Krebs cycle for the formation of ATP. At a cellular level, vitamin C is involved in the synthesis of collagen and tissue healing.

Glucose is included in the formulation as a 'secondary' active ingredient to treat non-specific low blood sugar or water loss without electrolyte loss that may occur in malnourished patients. Its role is supportive.

IV.4 Clinical Efficacy

The clinical efficacy of this intravenous vitamin B and vitamin C combination product for the proposed indications has been well established.

IV.5 Clinical Safety

A Risk Management Plan, version 0.1, signed 21 August 2024, has been submitted, 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 *Vitamins B and CConcentrate for Solution for Infusion*. It is concluded that routine pharmacovigilance and risk minimisation measures are sufficient.

Periodic Safety Update Reports (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.
- For medicinal products that do not fall within the categories waived of the obligation to submit routine PSURs by the revised pharmacovigilance legislation, the MAH should follow the DLP according to the EURD list.

No new clinical safety data was submitted with this application. The safety profile of this product is stated in the SmPC.

IV.6 Discussion on the clinical aspects

This is a generic product of an already approved product. The use of Article 10(1) of Directive 2001/83 for the authorisation of this product has been justified. The justification of not submitting a bioequivalence study for a comparison of the test and reference products is in line with the current guidelines on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev.1/Corr).

V. OVERALL CONCLUSIONS

Vitamins B and C Concentrate for Solution for Infusion is a generic form of Pabrinex Intravenous High Potency Concentrate for Solution for Infusion marketed by Kyowa Kirin Holdings B.V. (PA2288/001/001) which is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

Consideration of bioequivalence is 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 Vitamins B and C Concentrate for Solution for Infusion can be considered as bioequivalent with the reference product as well as having a satisfactory risk/benefit profile, and therefore granted a marketing authorisation.

VI. REVISION DATE

13.10.2029

VII. UPDATES

This section reflects the significant changes following finalisation of the initial procedure.

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
New DCP as RMS	IE/H/1226/001/DC	SmPC, IPAR and PIL		