

Public Assessment Report

Scientific discussion

Zubatmin

**(nicotinamide, glucose monohydrate, ascorbic acid,
thiamine hydrochloride, riboflavin sodium
phosphate, pyridoxine hydrochloride)**

SE/H/2523/01/DC

This module reflects the scientific discussion for the approval of Zubatmin. The procedure was finalised at 2025-04-16. 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 Zubatmin, Concentrate for solution for infusion.

The active substance is nicotinamide, glucose monohydrate, ascorbic acid, thiamine hydrochloride, riboflavin sodium phosphate, pyridoxine hydrochloride. A comprehensive description of the indication and posology is given in the SmPC.

II. EXECUTIVE SUMMARY

II.1 About the product

Zubatmin is a product containing a combination of Vitamins B and C (Thiamine, Riboflavin, Pyridoxine, Ascorbic Acid, Nicotinamide and Glucose).

It is intended for intravenous administration for rapid therapy of severe depletion or malabsorption of the watersoluble vitamins B and C.

II.2 General comments on the submitted dossier

The application for Zubatmin, concentrate for solution for infusion, is a Hybrid Art. 10(3) application (due to “change in therapeutic indications” compared to the reference product) submitted according to Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK, FI, NO as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Pabrinex Intravenous High Potency, concentrate for solution for infusion authorised in Ireland since 1987, with Kyowa Kirin Holdings B.V. as marketing authorisation holder.

European Reference Product (ERP)

A European Reference Product is used in RMS and all CMS: Pabrinex Intravenous High Potency, concentrate for solution for infusion authorised in **Ireland** since 1987, with Kyowa Kirin Holdings B.V. as marketing authorisation holder.

II.3 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.

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 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 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 to support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III.2 Non-clinical aspects

Pharmacology/Pharmacokinetics/Toxicology

Pharmacodynamic, pharmacokinetic and toxicological properties of thiamine, riboflavin, pyridoxine, ascorbic acid, nicotinamide and glucose are well known. As thiamine, riboflavin, pyridoxine, ascorbic acid, nicotinamide and glucose are a widely used, well-known active substances, no further studies are required, nor does the applicant provide any. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)

Since Zubatmin is a “generic” product regarding the active substances and aimed to replace other products, it will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

Conclusions on studies:

The active substances are natural substances, the use of which will not alter the concentration or distribution of the substance in the environment. Therefore, thiamine, riboflavin, pyridoxine, ascorbic acid, nicotinamide, and glucose are not expected to pose a risk to the environment.

III.3 Clinical aspects

Pharmacokinetics

No bioequivalence study or pharmacokinetic studies have been submitted.

Biowaiver

The applied product is to be administered as an aqueous intravenous solution containing the same active substances as the currently authorised product. None of the excipients are known to interact with the drug substance. For this type of product, no bioequivalence studies are required according to the Guideline on the investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1).

Pharmacodynamics/Clinical efficacy/Clinical safety

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the originator product is demonstrated, or a biowaiver is accepted, additional data is not necessary for the same claims as the reference product.

Efficacy

The claimed indication was not completely in line with the reference product. To support the additional examples the applicant had provided literature data, but these indications were deleted during the procedure. Indications and doses for children were also deleted during the procedure.

Pharmacovigilance system

Proposed MAH: Macure Pharma ApS

The Applicant has submitted a signed Summary of the Applicant's/Proposed Future MAH'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 Zubatmin.

Part II Safety specification

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

Part III Pharmacovigilance Plan

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

Part V Risk minimisation measures

Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Part VI Summary of the RMP

The Summary of the RMP is endorsed.

Conclusion RMP assessment

An updated Risk Management Plan was submitted after the LoQ. This updated version 0.3 signed 12 March 2025 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)

Active substance is currently listed in the published EURD list

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 common renewal date will be 5 years after closure of the DCP.

IV. BENEFIT RISK ASSESSMENT

The quality of the hybrid product, Zubatmin, is found adequate. There are no objections to approval of Zubatmin, 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.

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

Post approval commitments

N/A

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

- **Additional risk minimisation measures (including educational material)**

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

The bridging was assessed and accepted at day 120.

VI. STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
-	-	-	-	-	-