IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Meropenem 1g Powder for solution for injection/infusion
Meropenem Trihydrate
PA1122/015/002

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 Meropenem 500 mg & 1 g powder for solution for injection or infusion, from Noridem Enterprises Limited, for the treatment of the following infections in adults and children over 3 months of age:
- Pneumonia, including community acquired pneumonia and nosocomial pneumonia.
- Broncho-pulmonary infections in cystic fibrosis
- Complicated urinary tract infections
- Complicated intra-abdominal infections
- Intra- and post-partum infections
- Complicated skin and soft tissue infections
- Acute bacterial meningitis

Meropenem Noridem may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection.

Treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

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

This is an application submitted in accordance with article 10(1) of Directive 2001/83/EC claiming essential similarity to the Meronem 500 mg, and 1g, Powder for solution for injection or infusion marketed by AstraZeneca.

The reference member state (RMS) of the initial procedure was the United Kingdom and the concerned member states (CMSs) involved in this procedure were Austria, Germany, Greece, Spain, Poland and Ireland. The role of RMS was transferred to Ireland on 23rd July 2019.

In this Repeat Use Procedure (IE/H/0707/001-002/E/001), authorisation is extended to CMSs Italy, Portugal and Romania on 10th November 2025.

No scientific advice was requested by of offered to the applicant.

The product is intended for supply as a prescription-only medicinal product.

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	Meropenem 1 mg powder for solution for injection or infusion
Name(s) of the active substance(s) (INN)	Meropenem trihydrate
Pharmacotherapeutic classification (ATC code)	J01DH02
Pharmaceutical form and strength(s)	1 mg powder for solution for injection or infusion
Marketing Authorisation Number(s) in Ireland (PA)	PA1122/015/002
Marketing Authorisation Holder	Noridem Enterprises Limited
MRP/DCP No.	IE/H/0707/002/E/001
Reference Member State	IE
Concerned Member State	IT PT RO

II. QUALITY ASPECTS

II.1. Introduction

This application is for Meropenem 500 mg & 1 g powder for solution for injection or infusion.

II.2 Drug substance

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

The EDQM CEP procedure is followed for the drug substance.

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

Meropenem 0.5 g and 1 g Powder for Solution for Injection or Infusion is white to light yellow powder is presented in Type III glass vial with stopper with aluminum seal.

Each vial contains either 500 mg anhydrous meropenem (as meropenem trihydrate) or 1 g anhydrous meropenem (as meropenem trihydrate).

Prior to administration, the vial contents are dissolved in sterile water for injections. For infusion, this solution may be diluted further with appropriate infusion solutions only as specified in section 6.6 of the SmPC.

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.

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P.2 Pharmaceutical Development

The product is an established pharmaceutical form. The aim was to develop a stable, robust, generic injectable dosage form of Meropenem 0.5g and 1g Powder for Solution for Injection or Infusion, which is pharmaceutically equivalent to the reference product Meronem IV/ Merrem IV of M/s Astra Zeneca Inc; marketed in various EU countries.

The pharmaceutical development is adequately described in accordance with the relevant European guidelines. Compatibility between the active substance and the excipient sodium carbonate is demonstrated. The packaging materials have shown to be suitable by acceptable stability studies.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP). The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing site. Manufacture is two step involving preparation of the sterile active substance and sodium carbonate blend and filling of sterile powder into the market containers. Batch formulae have been provided for the manufacture of the product. In-process controls are appropriate considering the nature of the product and the method of manufacture. The manufacturing process has been validated according to relevant European and the process is considered to be sufficiently validated.

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

The excipient sodium carbonate anhydrous is a well known pharmaceutical excipient and it complies with its Ph. Eur. monograph and with additional requirements to monitor the quality of this excipient. None of the raw materials used in the manufacturing process of sodium carbonate, anhydrous (sterile) are of animal origin. Sodium carbonate anhydrous (sterile) is manufactured by aseptic filtration. Satisfactory description of the process is provided, together with the flow diagram.

P.5 Control of Finished Product

The finished product specification is adequate to control the relevant parameters for the dosage form and they are and in line with ICH Q6A and Ph Eur requirements for parenteral preparations.

Limits in the specification have been adequately justified and are considered appropriate for adequate quality control of the product. The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data from the proposed production site 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. requirements and EU legislation.

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 Meropenem 0.5g and 1g Powder for solution for injection or infusion.

III. NON-CLINICAL ASPECTS

III.1 Introduction

The pharmacodynamic, pharmacokinetic and toxicological properties of Meropenem trihydrate are well known. As Meropenem trihydrate is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required.

A non-clinical overview based on bibliographic references is provided. GLP standards cannot be established for these literature reference, however, 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 Meropenem Noridem 500 mg and 1 g Powder for solution for injection or infusion is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects

This application for Meropenem Noridem 500 mg and 1 g Powder for solution for injection or infusion is intended for generic substitution. As Meropenem trihydrate is a widely used, well-known active substance, the applicant has not provided additional non-clinical studies and further repetitive tests on animals are not required. The MAA is acceptable from a non-clinical perspective.

IV. CLINICAL ASPECTS

IV.1 Introduction

Meropenem 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.

As the product is administered through injection of infusion, no pharmacokinetic study is required to support this application and none has been provided.

Pharmacodynamic, pharmacokinetic and efficacy/safety data of the active substance are well known. This is a generic application and no new indications have been applied for.

The applicant has not submitted new clinical information and an overview based on a literature review is therefore appropriate and acceptable to the RMS, in accordance to directive 83/2001 as amended.

The pharmacokinetics of the active substance are known to be linear are linear in the indicated dose range.

IV.2 Pharmacokinetics

As above.

IV.3 Pharmacodynamics

As above.

IV.4 Clinical Efficacy

As above.

IV.5 Clinical Safety

No new safety concerns have arisen following the assessment of this application.

Pharmacovigilance System
The marketing authorisation holder (MAH) submitted a summary of the Pharmacovigilance System, including confirmation of the availability of an EU Qualified Person for Pharmacovigilance (EU-QPPV) and the means for notification of adverse reaction reports in the EU or from a Third Country.

Risk Management Plan

The Applicant 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 Meropenem 0.5g and 1 g powder for solution for injection or infusion.

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

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

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

The clinical aspects of this application are acceptable. As this is an abridged application under the appropriate legislation, fewer data are needed to establish a positive benefit-risk profile, and as such the information provided by the applicant are acceptable.

V. OVERALL CONCLUSIONS

Meropenem Noridem is a generic form of Meronem. Meronem is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

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 Meropenem Noridem demonstrated a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

VI. REVISION DATE

June 2021