IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Daptomycin Noridem 500 mg Powder for solution for injection/infusion
Daptomycin
PA1122/021/002

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 Daptomycin Noridem 350mg & 500 mg Powder for solution for injection/infusion, from Noridem Enterprises Ltd on 25th August 2020 for the treatment of:

- *Adult and paediatric (1 to 17 years of age) patients with complicated skin and soft-tissue infections (cSSTI).*
- *Adult patients with right-sided infective endocarditis (RIE) due to Staphylococcus aureus. It is recommended that the decision to use daptomycin should take into account the antibacterial susceptibility of the organism and should be based on expert advice. See sections 4.4 and 5.1.*
- *Adult and paediatric (1 to 17 years of age) patients with Staphylococcus aureus bacteraemia (SAB). In adults, use in bacteraemia should be associated with RIE or with cSSTI, while in paediatric patients, use in bacteraemia should be associated with cSSTI.*

Daptomycin is active against Gram positive bacteria only (see section 5.1). In mixed infections where Gram negative and/or certain types of anaerobic bacteria are suspected, Daptomycin should be co-administered with appropriate antibacterial agent(s).

Consideration should be given to official guidance on the appropriate use of antibacterial agent(s).

This decentralised application was submitted as an Article 10 (1) of Directive 2001/83 as amended.

In this Assessment Report, the name Daptomycin Noridem 350 mg and 500 mg Powder for solution for injection/infusion is used.

The originator product is Cubicin (350 mg and 500 mg, Powder for solution for injection or infusion) by Merck Sharp & Dohme, Ltd., registered since 19-01-2006 (EMEA/H/C/000637).
With Ireland as the Reference Member State in this Decentralized Procedure, Noriderm Enterprise Ltd applied for the Marketing Authorisations for Daptomycin Noridem in CMS: FR, CY, UK, IT, DE & EL.

Daptomycin Noridem 350mg & 500 mg Powder for solution for injection/infusion is subject to prescription only.

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	Daptomycin Noridem 350 mg & 500 mg Powder for solution for injection/infusion
Name(s) of the active substance(s) (INN)	Daptomycin
Pharmacotherapeutic classification (ATC code)	J01XX09 Daptomycin
Pharmaceutical form and strength(s)	350mg & 500 mg Powder for solution for injection/infusion
Marketing Authorisation Number(s) in Ireland (PA)	PA1122/021/001-002
Marketing Authorisation Holder	Noridem Enterprises Ltd
MRP/DCP No.	IE/H/0586/001-002/DC
Reference Member State	IE
Concerned Member State	CY DE EL FR IT UK

II. QUALITY ASPECTS

II.1. Introduction

This application is for Daptomycin Noridem 350 mg Powder for solution for injection/infusion and Daptomycin Noridem 500 mg Powder for solution for injection/infusion.

II.2 Drug substance

The active substance is Daptomycin, an established active substance and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP).

The active substance specification is considered adequate to control the quality of the active substance. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

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)

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 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. 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 Daptomycin Noridem 350 mg & 500 mg Powder for solution for injection/infusion.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Cubicin on the European market. No new preclinical data have been submitted.

The pharmacodynamic, pharmacokinetic and toxicological properties of daptomycin are well known. As daptomycin is a widely used, well-known active substance, the applicant has not provided additional studies. An overview based on literature review is acceptable for this type of application.

III.2 Ecotoxicity/environmental risk assessment

Since Daptomycin Noridem 350 mg and 500 mg Powder for solution for injection/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.3 Discussion on the non-clinical aspects

The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology provided is adequate. As daptomycin is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. Non-clinical findings are adequately represented in the appropriate sections of the SmPC.

IV. CLINICAL ASPECTS

IV.1 Introduction

Daptomycin 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 Cubicin (350 mg and 500 mg, powder for solution for injection or infusion) by Merck Sharp & Dohme, Ltd., registered since 19-01-2006 (EMEA/H/C/000637).

According to the appropriate guideline (CHMP/EWP/QWP/1401/98 Rev. 1/Corr **, January 2010), bioequivalence studies are not required if the test product is to be administered as an aqueous intravenous (i.v.) solution containing the same active substance as the currently approved reference product. Therefore, no bioequivalence study was required for this application for Daptomycin Noridem 350 mg and 500 mg Powder for solution for injection/infusion and no such study was submitted.

IV.2 Pharmacokinetics

No new pharmacokinetics studies were presented and no such studies are required for this application**.** The applicant has provided a clinical overview outlining the pharmacokinetics of Daptomycin based on literature; this is considered acceptable.

IV.3 Pharmacodynamics

No new pharmacodynamic studies were presented and no such studies are required for this application**.** The applicant has provided a clinical overview outlining the pharmacodynamics of Daptomycin based on literature; this is considered acceptable.

IV.4 Clinical Efficacy

The efficacy of Daptomycin has been demonstrated in several well-controlled studies. A summary of these studies can be found in the EPAR of the reference product Cubicin (350 mg and 500 mg, powder for solution for injection or infusion)

IV.5 Clinical Safety

The safety of Daptomycin has been demonstrated in several well-controlled studies. A summary of these studies can be found in the EPAR of the reference product Cubicin (350 mg and 500 mg, Powder for solution for injection/infusion)

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 Daptomycin 350mg &500mg powder for solution for infusion/injection.

Summary table of safety concerns as approved in RMP

Important identified risks	• None;
Important potential risks	• None;
Missing information	• None;

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

Risk minimisation measures
Routine risk minimisation are suggested. No additional risk minimisation activities are proposed by the applicant, which is endorsed.

IV.6 Discussion on the clinical aspects
Daptomycin Noridem 350 mg and 500 mg powder for solution for injection or infusion is a generic of the centrally authorised product Cubicin (350 mg and 500 mg, Powder for solution for injection/infusion) by Merck Sharp & Dohme, Ltd., registered since 19-01-2006 (EMEA/H/C/000637).

A bioequivalence study was not required for this application for Daptomycin Noridem 350 mg and 500 mg powder for solution for injection or infusion and no such study was submitted.

From a clinical perspective, this application did not contain new data on the pharmacokinetics and pharmacodynamics nor new data on the efficacy and safety of the active substance; the applicant's clinical overview on these clinical aspects based on information from published literature was considered sufficient.

A benefit/risk ratio comparable to the reference product can be concluded.

V. OVERALL CONCLUSIONS

Assessor's overall conclusions on the Risk Management Plan
The current approved RMP in place for Daptomycin is RMP version 0.4 with 21 May 2020 as date of final sign off is considered acceptable.

Periodic Safety Update Report (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.

OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

Daptomycin Noridem 350 mg and 500 mg powder for solution for injection or infusion is a generic form of the centrally authorised product Cubicin (350 mg and 500 mg, powder for solution for injection/infusion) by Merck Sharp & Dohme, Ltd., registered since 19-01-2006 (EMEA/H/C/000637).

Cubicin (350 mg and 500 mg, Powder for solution for injection/infusion) is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

A bioequivalence study was not submitted for this application for Daptomycin Noridem 350 mg and 500 mg powder for solution for injection or infusion as according to the regulatory requirements a bioequivalence study is not required for parenteral aqueous solutions.

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 Daptomycin Noridem 350 mg and 500 mg powder for solution for injection or infusion demonstrated bioequivalence with the reference product as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

VI. REVISION DATE

04.06.2025