LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Dalbavancin Accord
(dalbavancin)

SE/H/2375/01/DC

This module reflects the scientific discussion for the approval of Dalbavancin Accord. The procedure was finalised on 2024-03-06. 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, a marketing authorisation has been granted for Dalbavancin Accord, 500 mg, Powder for concentrate for solution for infusion.

The active substance is dalbavancin. A comprehensive description of the indication and posology is given in the SmPC.

For recommendations to the marketing authorisation not falling under Article 21a/22a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a/22a/ 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

The application for Dalbavancin Accord, 500 mg, Powder for concentrate for solution for infusion, a generic application submitted according to Article 10(1) of Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and AT DE EL ES FR IT PL as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Xydalba 500 mg powder for concentrate for solution for infusion, authorised in EU since 2015, with AbbVie Deutschland GmbH & Co. KG as marketing authorisation holder.

Potential similarity with orphan medicinal products
According to the application form and a check of the Community Register of orphan medicinal products there is no medicinal product designated as an orphan medicinal product for a condition relating to the indication proposed in this application.

II. QUALITY ASPECTS

II.1 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.

II.2 Medicinal 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 support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

Pharmacology/Pharmacokinetics/Toxicology
Pharmacodynamic, pharmacokinetic and toxicological properties of dalbavancin are well known. As dalbavancin is a widely used, well-known active substance, no further studies are required and the applicant provides none. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
Since Dalbavancin Accord is a generic product, it will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

There are no objections to approval of Dalbavancin Accord from a non-clinical point of view.

IV. CLINICAL ASPECTS

Pharmacokinetics
No bioequivalence study has been submitted. The applicant claims that a bioequivalence study is not necessary according to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1) since the product is an aqueous parenteral solution.

Pharmacokinetic properties of the active substance
Systemic exposures to dalbavancin are dose proportional following single doses over a range of 140 to 1120 mg, indicating linear pharmacokinetics of dalbavancin. The mean terminal elimination half-life ($t_{1/2}$) was 372 (range 333 to 405) hours. The distributional half-life ($t_{1/2\beta}$), which constitutes most of the clinically-relevant concentration-time profile, ranged from 5 to 7 days and is consistent with once-weekly dosing.

Discussion and overall conclusion
The product applied for is to be administered as an aqueous intravenous solution containing the same active substance 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 (CHMP/QWP/EWP/1401/98 Rev. 1). Thus, the absence of bioequivalence studies is acceptable.

Pharmacodynamics/Clinical efficacy/Clinical safety
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted, which is acceptable.

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 Dalbavancin Accord.

Part II. Safety specification

Summary of safety concerns

Important identified risks	• Emergence of resistance • Pseudomembranous colitis • Hypersensitivity
Important potential risks	• Hepatic disorder • Otovestibular toxicity • Nephrotoxicity • Haematologic effects
Missing information	• Use in immunocompromised patients. • Use in patients with moderate and severe hepatic impairment. • Use in patients with a CrCl<30 ml/min receiving haemodialysis • Paediatric use • Use in pregnant and lactating women

The proposed summary of safety concerns is aligned with the RMP of the reference product Xydalba, which is endorsed.

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

Of note, according to the agreed RMP of the reference product *non-conditioned* targeted follow-up questionnaires are used (or have been used) for selected safety concerns. However, no follow-up questionnaire (or surveillance study) is mentioned in the RMP submitted in this application for Dalbavancin Accord, which is considered acceptable for a generic application.

Part V. Risk minimisation measures
The Applicant concludes that the safety information in the proposed product information is aligned to the reference medicinal product; no additional risk minimisation activities are proposed, which is endorsed.

Part VI. Summary of the RMP
The proposed RMP for Dalbavancin Accord is adequately summarised by the applicant.

Conclusion of the RMP assessment
The submitted Risk Management Plan, version 1.0, signed 2023.02.17, 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.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of a bridging report making reference to Xydalba 500 mg powder for concentrate for solution for infusion (content parent-PL; EMEA/H/C/002840) and to Zoledronic acid Accord 4 mg/5 ml concentrate for solution for infusion (layout parent-PL; EMEA/H/C/002667). The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Dalbavancin Accord, is found adequate. There are no objections to approval of Dalbavancin Accord, 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.

List of recommendations not falling under Article 21a/22a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a/22a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

The decentralised procedure for Dalbavancin Accord, 500 mg, Powder for concentrate for solution for infusion was positively finalised on 2024-03-06.

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Public Assessment Report – Update

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

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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