LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Empagliflozin Devatis
(empagliflozin)

SE/H/2553/01-02/DC

This module reflects the scientific discussion for the approval of Empagliflozin Devatis. The procedure was finalised on 2025-06-18. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.lakemedelsverket.se E-mail: registrator@lakemedelsverket.se

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Empagliflozin Devatis, 10 mg, 25 mg, Film-coated tablet.

The active substance is empagliflozin. 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 Empagliflozin Devatis, 10 mg, 25 mg, Film-coated tablet, is a Generic Art. 10(1) application submitted according to Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and AT, DE, DK, FI, NL and NO as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Jardiance, Film-coated tablet, 25 mg, authorised in the Union since 2014, with Boehringer Ingelheim International GmbH as marketing authorisation holder.

The reference product used in the bioequivalence study is Jardiance, Film-coated tablet, 25 mg from Germany with Boehringer Ingelheim International GmbH as marketing authorisation holder.

Potential similarity with orphan medicinal products
N/A.

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 empagliflozin are well known. As empagliflozin is a widely used, well-known active substance, no further studies are required, nor does the applicant provide any. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
Since Empagliflozin Devatis 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 Empagliflozin Devatis from a non-clinical point of view.

IV. CLINICAL ASPECTS

Pharmacokinetics
To support the marketing authorisation application the applicant has conducted one single-dose bioequivalence study under fasting conditions, comparing Empagliflozin Devatis, 25 mg, film-coated tablet, with the reference product Jardiance, 25 mg, film-coated tablet.

Pharmacokinetic properties of the active substance
Absorption: Empagliflozin has an oral bioavailability of 78 %. Following an oral dose of empagliflozin maximal plasma concentrations occur at approximately 1.5 hours.

Concomitant food intake decreases the C_{max} and AUC by 37 and 16 %. The observed effect of food on empagliflozin pharmacokinetics was not considered clinically relevant and empagliflozin may be administered with or without food.

Linearity: Systemic exposure of empagliflozin increased in a dose-proportional manner. The single-dose and steady-state pharmacokinetic parameters of empagliflozin were similar suggesting linear pharmacokinetics with respect to time.

Elimination: The terminal half-life is 12.4 hours.

Study C1B02637 – 25 MG, FASTING
Methods
This was a single-dose, two-way crossover study conducted in 24 healthy volunteers, comparing Empagliflozin Devatis, 25 mg, film-coated tablet, with Jardiance, 25 mg, film-coated tablet under fasting conditions. Blood samples for concentration analysis were collected pre-dose and up to 48 hours post-dose. Plasma concentrations of empagliflozin were determined with an LC-MS/MS method. Analysis of variance (ANOVA) was performed on the ln-transformed data for AUC_{0-t} and C_{max}. The study was conducted between 2023-08-28 and 2023-09-26.

Results

The results from the pharmacokinetic and statistical analysis are presented in Table 1 below.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} median, range) for empagliflozin, n=22.

Treatment	AUC_{0-t} ng*h/ml	C_{max} ng/ml	t_{max} h
Test	**3140.027 ±488.961**	**349.318 ±78.314**	**3.50 (1.00 - 5.50)**
Reference	**2934.786 ±470.620**	**318.255 ±58.171**	**4.500 (2.00 - 7.00)**
***Ratio (90% CI)**	**107.13 (102.76 - 111.68)**	**109.37 (100.58 - 118.93)**	**-**
AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours C_{max} maximum plasma concentration t_{max} time for maximum plasma concentration			

**calculated based on ln-transformed data*

For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

A biowaiver was sought for the additional strength of 10 mg.

Discussion and overall conclusion

The bioequivalence study and its statistical evaluation were in accordance with accepted standards for bioequivalence testing, as stated in the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr). The bioanalytical methods were adequately validated.

From a pharmacokinetic point of view, absence of studies with the additional strength of 10 mg is acceptable, as all conditions for biowaiver for additional strength, as described in the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr) are fulfilled and since the pharmacokinetics of empagliflozin is linear.

Based on the submitted bioequivalence study, Empagliflozin Devatis, 25 mg, film-coated tablet is considered bioequivalent with Jardiance, 25 mg, film-coated tablet.

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, additional data is not necessary.

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 Empagliflozin Devatis.

Part II Safety specification

The MAH has submitted the version 0.1 RMP date of final sign off 2024-02-23 and proposed the following summary safety concerns:

Summary of safety concerns	
Important identified risks	• None
Important potential risks	• Urinary tract carcinogenicity • Pancreatitis
Missing information	• None

Assessor's comment: Having considered the data in the safety specification the assessor agrees that the safety concerns listed by the MAH are appropriate. The safety concerns are aligned with the most recent version of the originator's RMP Jardiance.

Part III Pharmacovigilance Plan
Routine pharmacovigilance is suggested and in accordance with the originator the applicant has proposed non-conditioned follow-up questionnaires concerning pancreatitis, which is acknowledged.

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
The submitted Risk Management Plan, version 0.1 signed 2024-02-23 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 Jardiance 10 mg & 25 mg film-coated tablets, EU/1/14/930/001-018 and Lenalidomide Devatis 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg & 25 mg hard capsules, NL/H/4989/001-007/DC.

Layout
The applicant has proposed a bridging to a user test carried out on the product Lenalidomide Devatis 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg & 25 mg hard capsules, NL/H/4989/001-007/DC.

Content
The applicant has proposed a bridging to a user test carried out on the product Jardiance 10 mg & 25 mg film-coated tablets, EU/1/14/930/001-018. A comparison between the parent PL and the daughter PL together with a critical discussion hereof has been provided.

The proposed bridging regarding layout and content is considered acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Empagliflozin Devatis, is found adequate. There are no objections to approval of Empagliflozin Devatis, from a non-clinical and clinical point of view. Bioequivalence between the test and reference product has been adequately demonstrated. 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 Empagliflozin Devatis, 10 mg, 25 mg, Film-coated tablet was positively finalised on 2025-06-18.

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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)

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.lakemedelsverket.se E-mail: registrator@lakemedelsverket.se