LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

# Public Assessment Report
# Scientific discussion

# Empagliflozin Reddy (empagliflozin)

# SE/H/2773/001-002/DC

**This module reflects the scientific discussion for the approval of Empagliflozin Reddy. The procedure was finalised at 2026-05-12. For information on changes after this date please refer to the module 'Steps taken after the finalisation of the initial procedure - Summary'.**

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

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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 Empagliflozin Reddy, 10 mg and 25 mg, Film-coated tablet.

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

# II. EXECUTIVE SUMMARY

## II.1 About the product

**Mechanism of action**

Empagliflozin is a reversible, highly potent ($IC_{50}$ of 1.3 nmol) and selective competitive inhibitor of sodium-glucose co-transporter 2 (SGLT2). Empagliflozin does not inhibit other glucose transporters important for glucose transport into peripheral tissues and is 5 000 times more selective for SGLT2 versus SGLT1, the major transporter responsible for glucose absorption in the gut. SGLT2 is highly expressed in the kidney, whereas expression in other tissues is absent or very low. It is responsible, as the predominant transporter, for the reabsorption of glucose from the glomerular filtrate back into the circulation. In patients with type 2 diabetes and hyperglycaemia a higher amount of glucose is filtered and reabsorbed.

**Pharmacological classification**

Pharmacotherapeutic group: Drugs used in diabetes, Sodium-glucose co-transporter 2 (SGLT2) inhibitors, ATC code: A10BK03

**Proposed indication**

Type 2 diabetes mellitus

Empagliflozin Reddy is indicated in adults and children aged 10 years and above for the treatment of insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise

- as monotherapy when metformin is considered inappropriate due to intolerance
- in addition to other medicinal products for the treatment of diabetes.

Heart failure

Empagliflozin Reddy is indicated in adults for the treatment of symptomatic chronic heart failure.

Chronic kidney disease

Empagliflozin Reddy is indicated in adults for the treatment of chronic kidney disease.

## II.2 General comments on the submitted dossier

The application for Empagliflozin Reddy, 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, IT, NL, NO, PL, RO as concerned member states (CMS). The application was withdrawn in CZ, SK on Day 160 of the procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data

protection period is Jardiance, 10 mg, film-coated tablet 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, 25 mg, film-coated tablet from Germany with Boehringer Ingelheim International GmbH 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.

For manufacturing sites outside the Community, the RMS has accepted copies of current GMP Certificates of satisfactory inspection summary reports, ‘close-out letters’ or ‘exchange of information’ issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community 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.

GCP aspects
A statement on the application of appropriate GCP standards in the submitted study has been provided. No issues regarding GCP have been identified. The clinical facility was inspected by MHRA (UK) in 2021, without any critical findings. The bioanalytical facility was inspected by MHRA (UK) in 2021 and by AEMPS (Spain) in 2023, without any critical findings. No inspection of the submitted bioequivalence study is needed.

## 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 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 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)**
The applicant has submitted an ERA document for the generic medicinal product Empagliflozin Reddy.

This Marketing Authorization is based on Article 10(1) of Directive 2001/83/EC (generic medicinal product). Empagliflozin Reddy 10 mg and 25 mg film-coated tablet is intended to be used therapeutically for the same indication, at the same dose levels and same route of administration as the reference medicinal product, 'Jardiance film-coated tablets' which is already marketed in European Union (EU).

Empagliflozin is a reversible, highly potent and selective competitive inhibitor of sodiumglucose co-transporter 2 (SGLT2). Empagliflozin does not inhibit other glucose transporters important for glucose transport into peripheral tissues and is 5000 times more selective for SGLT2 versus SGLT1, the major transporter responsible for glucose absorption in the gut. SGLT2 is highly expressed in the kidney, whereas expression in other tissues is absent or very low. It is responsible, as the predominant transporter, for the reabsorption of glucose from the glomerular filtrate back into the circulation. In patients with type 2 diabetes and hyperglycaemia a higher amount of glucose is filtered and reabsorbed.

The active substance empagliflozin is not an antibiotic, antiparasitic or endocrine active substance (EAS).

*Risk Assessment*
The Phase I risk assessment is performed based on a decision tree, as detailed in the current ERA guideline (EMEA/CHMP/SWP/4447/00 Rev. 1- Corr).

Empagliflozin is not a naturally occurring substance nor a non-natural peptide/protein.

The applicant identified an earlier ERA for the reference medicinal product Jardiance (Jardiance EPAR, EMEA/H/C/002677/II/0074) and claims that the scientific conclusions reached are applicable

to the current generic product. A letter of access to ERA studies was requested from the MAH of Jardiance, which was refused. However, repetition of ERA studies will generally not be required as the ERA for Jardiance was considered satisfactory by the CHMP. The most recent ERA for Jardiance was performed in 2023 and includes risk assessments for all environmental compartments that are mandatory under the new guideline i.e. surface water, sewage treatment plant functioning and sediment. This approach is agreed.

According to the EPAR of Jardiance, the default Fpen was used in the reference ERA, meaning that the outcome of the risk assessment will not change and the risk assessment of Empagliflozin Reddy stops in phase I.

*PBT/vPvB assessment*
The applicant has determined Log Kow for empagliflozin experimentally by shake flask method in line with OECD 107 and submitted the study report. Based on this, the Log Kow was 1.5 which is below the action limit of 4.5 and further PBT screening is not required. Empagliflozin does not have the potential to bioaccumulate in aquatic species.

**Conclusions**
The ERA stops in Phase I. A Phase II environmental assessment is not required as according to the Phase I decision tree, question 2a/b/c/d, possible environmental risks for empagliflozin have already been sufficiently assessed in the authorization procedure for the medicinal product *Jardiance*.

Empagliflozin is not expected to pose a risk to the environment.

There are no objections to approval of Empagliflozin Reddy from a non-clinical point of view.

## III.3 Clinical aspects

**Pharmacokinetics**
To support the marketing authorisation application the applicant has conducted one bioequivalence study comparing Empagliflozin Reddy (Empagliflozin) with the reference product Jardiance.

Pharmacokinetic properties of the active substance
*Absorption:* Following an oral dose of empagliflozin maximal plasma concentrations occur at approximately 1.5 hours. Administration of empagliflozin 25 mg after intake of a high-fat and high calorie meal resulted in slightly lower exposure; AUC decreased by approximately 16% and $C_{max}$ by approximately 37% compared to fasted condition. 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 apparent terminal elimination half-life of empagliflozin was estimated to be 12.4 hours.

Study C1B04009
*Methods*
This was a single-dose, two-way crossover study conducted in 36 healthy volunteers, comparing Empagliflozin, 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 a LC-MS/MS method. Analysis of variance (ANOVA) was performed on the ln-transformed data for $AUC_{0-t}$ and $C_{max}$.

*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=35.**

| Treatment | $AUC_{0-t}$ ng*h/ml | $C_{max}$ ng/ml | $t_{max}$ h |
|---|---|---|---|
| **Test** | **3067.763 ± 652.072** | **322.914 ± 52.738** | **4.000 (1.500-6.500)** |
| **Reference** | **2996.017 ± 637.467** | **316.594 ± 63.037** | **4.000 (2.000-12.000)** |
| ***Ratio (90% CI)** | **102.50 (100.34-104.70)** | **102.69 (97.05-108.67)** | **-** |
| **$AUC_{0-t}$** area under the plasma concentration-time curve from time zero to t hours<br>**$C_{max}$** maximum plasma concentration<br>**$t_{max}$** 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) and ICH M13A Guideline on bioequivalence for immediate-release solid oral dosage forms (EMA/CHMP/ICH/953493/2022). The bioanalytical method was adequately validated.

Based on the submitted bioequivalence study, Empagliflozin Reddy is considered bioequivalent with Jardiance.

Absence of studies with the additional strength of 10 mg is acceptable, as all conditions for biowaiver for additional strength(s), as described in the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1) are fulfilled and since the pharmacokinetics of empagliflozin is linear between 10 mg and 25 mg.

**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.

**Pharmacovigilance system**
Proposed MAH : Reddy Holding GmbH

The Applicant has submitted a signed Summary of the Applicant's/Proposed Future MAH's Pharmacovigilance System together with an annex listing all relevant subsidiaries. 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 Empagliflozin Reddy.

Part II Safety specification
The MAH has submitted the version 0.3 RMP dated 18 March 2026 and proposed the following summary safety concerns:

Table SVIII.1: Summary of safety concerns

| **Summary of safety concerns** | |
|---|---|
| Important identified risks | • None |
| Important potential risks | • None |
| Missing information | • None |

Part III Pharmacovigilance Plan
Routine pharmacovigilance is suggested and additionally the applicant has proposed questionnaires concerning pancreatitis, which is in line with given conditions and acknowledged. 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
The submitted Risk Management Plan, version 0.3 signed 18 March 2026 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 generic product, Empagliflozin Reddy, is found adequate. There are no objections to approval of Empagliflozin Reddy, 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.

# 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

N/A.

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

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

A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of three bridging reports making reference to Sitagliptin/Metformin (AT/H/1183/001-002/DC), Sitagliptin (DE/H/6648/001-003/DC) and Jardiance (EU/1/14/930/001-018).

The bridging reports submitted by the applicant has been found acceptable.

# 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 |
|---|---|---|---|---|---|
| - | - | - | - | - | - |