LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Sitagliptin Devatis
(sitagliptin phosphate monohydrate)

SE/H/2601/01-03/DC

This module reflects the scientific discussion for the approval of Sitagliptin Devatis. The procedure was finalised on 2025-09-10. 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 Sitagliptin Devatis, 25 mg, 50 mg, 100 mg, Film-coated tablet.

The active substance is sitagliptin phosphate monohydrate. 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 Sitagliptin Devatis, 25 mg, 50 mg, 100 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 DE, DK, FI, NL, NO as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Januvia, 25 mg, film-coated tablet authorised in Union since 2007, with Merck Sharp & Dohme B.V. 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 sitagliptin are well known. As sitagliptin 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 Sitagliptin 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 Sitagliptin Devatis from a non-clinical point of view.

IV. CLINICAL ASPECTS

Pharmacokinetics
Absorption: Sitagliptin has an oral bioavailability of approximately 87 %.

The pharmacokinetics of sitagliptin is not affected by food, and therefore there are no restrictions with respect to food in the SmPC of the originator.

Linearity: Plasma AUC of sitagliptin increased in a dose-proportional manner. Dose-proportionality was not established for C_{max}, which increased in a greater than dose-proportional manner.

Elimination: The terminal half-life is 12.4 hours.

BCS-based biowaiver
The application is based on a BCS (Biopharmaceutical Classification System)-based biowaiver and no bioequivalence study has been submitted. The applicant claims that sitagliptin is a BCS class I substance.

According to the ICH M9 guideline on biopharmaceutics classification system-based biowaivers (EMA/CHMP/ICH/493213/2018), a BCS class I based biowaiver is applicable for an immediate release orally administered product with systemic action if the drug substance is not considered to have a narrow therapeutic index and has been proven to exhibit high solubility and high permeability. Also, *in vitro* dissolution characteristics of the test and the reference product should be either very rapid or similarly rapid and the excipients that might affect bioavailability should be quantitatively the same and qualitatively similar.

Discussion and overall conclusion
The extent of absorption of sitagliptin is ≥85 % and the absorption/permeability criteria for a BCS class I biowaiver is considered fulfilled. Both the applied for and the approved medicinal product have the same qualitative and similar quantitative composition in excipients. The quantitative difference in excipients is acceptable for a BCS class I-biowaiver. None of the excipients are known to affect the bioavailability. In addition, sitagliptin is not considered to be a narrow therapeutic index drug in the sense that narrowed acceptance ranges would be necessary in bioequivalence studies performed with sitagliptin. Hence, the justification for a BCS class I- based biowaiver can be accepted from a pharmacokinetic point of view.

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 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 Sitagliptin Devatis.

Part II Safety specification

List of important risks and missing information	
Important identified risks	None
Important potential risks	Pancreatic cancer
Missing information	Exposure during pregnancy and lactation

Part III Pharmacovigilance Plan
Routine pharmacovigilance is suggested and 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 0.1 signed 2024-07-12 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

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PL was English.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Sitagliptin Devatis, is found adequate. There are no objections to approval of Sitagliptin Devatis, 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 Sitagliptin Devatis, 25 mg, 50 mg, 100 mg, Film-coated tablet was positively finalised on 2025-09-10.

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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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