

Public Assessment Report

Scientific discussion

Sitagliptin Aspire **(sitagliptin phosphate monohydrate, sitagliptin)**

SE/H/2501/001-003/DC

This module reflects the scientific discussion for the approval of Sitagliptin Aspire. The procedure was finalised on 2024-12-04. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Sitagliptin Aspire, 25 mg, 50 mg, 100 mg, Film-coated tablet.

The active substance is sitagliptin phosphate monohydrate, sitagliptin. 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 Aspire, 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, ES, 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 BV 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 this product 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 Aspire from a non-clinical point of view.

IV. CLINICAL ASPECTS

BCS-based biowaiver

The application is based on a Biopharmaceutical Classification System (BCS)-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-based biowaiver is applicable for an immediate release oral dosage form with systemic action, and the drug product is the same dosage form and strength as the reference product. Drug products having a narrow therapeutic index are excluded from consideration for a BCS-based biowaiver. BCS-based biowaivers are applicable for drug products where the drug substance(s) exhibit high solubility and, either high permeability (BCS class I) or low permeability (BCS class III). Also, *in vitro* dissolution characteristics of the test and the reference product should be either very rapid or similarly rapid. For BCS class I drugs, qualitative and quantitative differences in excipients are permitted, except for excipients that may affect absorption, which should be qualitatively the same and quantitatively similar, i.e., within $\pm 10\%$ of the amount of excipient in the reference product. Additionally, the cumulative difference for excipients that may affect absorption should be within $\pm 10\%$.

Discussion and overall conclusion

Sitagliptin Aspire is not considered to have a narrow therapeutic index in the sense that narrowed acceptance ranges would be necessary in bioequivalence studies performed with sitagliptin.

The product-specific bioequivalence guidance for Sitagliptin Aspire film-coated tablets 25, 50 and 100 mg (EMA/CHMP/158934/2016) concludes that sitagliptin is a high soluble compound with complete absorption and belongs to BCS class I.

All the excipients are considered qualitatively the same. The quantitative difference in excipients is acceptable for a BCS class I-biowaiver. None of the excipients are likely to affect absorption.

The quality criteria for biowaiver (solubility and dissolution) have also been fulfilled. Similar *in vitro* dissolution characteristics of the test and the reference product has been demonstrated.

In conclusion, the justification for a BCS-based biowaiver can be accepted.

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 Sitagliptin Aspire.

Part II Safety specification

The MAH has submitted the version 2.0 RMP dated 20-Nov-2023 and proposed the following summary of safety concerns:

Summary of safety concerns*	
Important identified risks	• None
Important potential risks	• Pancreatic cancer
Missing information	• Exposure during pregnancy and lactation

The proposed summary of safety concerns is in line with the summary of safety concerns of the originator Januvia and is acceptable.

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 2.0 signed 20-Nov-2023 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 Aspire is found adequate. There are no objections to approval of Sitagliptin Aspire, 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 Aspire, 25 mg, 50 mg, 100 mg, Film-coated tablet was positively finalised on 2024-12-04.

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)