LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Jidinum
(sitagliptin hydrochloride monohydrate)

SE/H/2105/01-03/DC

This module reflects the scientific discussion for the approval of Jidinum. The procedure was finalised on 2021-12-22. 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 Jidinum, 25 mg, 50 mg, 100 mg, Film-coated tablet.

The active substance is sitagliptin, sitagliptin hydrochloride 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 Jidinum, 25 mg, 50 mg and 100 mg, film- coated tablet, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Medochemie Ltd, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and BG, CY, CZ, EL, ES, LT, MT, PT, RO, SK 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, 50 mg, 100 mg, film-coated tablet authorised in the Union since 2007, with Merck Sharp & Dohme BV 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

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, and the applicant provides none. Overview based on literature review is, thus, appropriate**.**

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

IV. CLINICAL ASPECTS

Pharmacokinetics
BCS-based biowaiver
The application is based on a Biopharmaceutical Classification System (BCS) based biowaiver and no bioequivalence study has been submitted.

According to the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr), a BCS class I-based biowaiver is applicable for an immediate release product if the drug substance is not considered to have a narrow therapeutic index and has been proven to exhibit high solubility and complete absorption (BCS class I). 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 and qualitatively the same.

From a quality perspective, a BCS-class I based biowaiver is acceptable if the solubility of the substance is high and if very rapid or similarly rapid dissolution characteristics of the test and reference products have been demonstrated. For quality aspects of biowaiver, see the quality assessment report.

Discussion and overall conclusion
The extent of absorption of sitagliptin is >85 % and the absorption/permeability criteria for a BCS class I biowaiver is fulfilled. The qualitative composition of the test and reference products is identical. However, the proposed product contains sitagliptin HCl as opposed to Januvia where sitagliptin phosphate is used. Furthermore, composition of colouring agents varies between different strength. None of the excipients are known to affect the bioavailability and the composition of colouring agents and the use of different salts is considered acceptable. In addition, sitagliptin is not considered to be a narrow therapeutic index drug. Hence, the justification for a BCS class I (Biopharmaceutics Classification System) based biowaiver can be accepted from a clinical 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 Jidinum.

Safety specification
The MAH has submitted the version 0.3 RMP dated April 2021 and proposed the following summary safety concerns:

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

The proposed safety concerns in the RMP for Jidinum is in line with that of the reference product Januvia.

Pharmacovigilance Plan

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

Risk minimisation measures

Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Summary of the RMP
The submitted Risk Management Plan, version 0.3 signed April 2021 is considered acceptable.

The MAH has satisfactorily responded to the questions raised and updated the RMP accordingly. The Safety concerns have been updated with “and lactation” under point Missing information, and the document has been further corrected as requested.
Issue resolved.

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 Januvia film-coated tablets, EMEA/H/C/000722, regarding text content and to Areston 12.5 mg film-coated tablets, NL/H/3773/001/DC, regarding design and layout. 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 Jidinum is found adequate. There are no objections to approval of Jidinum from a non-clinical and clinical point of view. The product information is acceptable. 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 Jidinum, 25 mg, 50 mg, 100 mg, Film-coated tablet was positively finalised on 2021-12-22.

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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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