LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Vildagliptin Accord

(vildagliptin)

SE/H/1962/01/DC

This module reflects the scientific discussion for the approval of Vildagliptin Accord. The procedure was finalised on 2020-04-30. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Vildagliptin Accord, 50 mg, tablet, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Accord Healthcare S.L.U., applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and AT, CY, CZ, DK, ES, FI, FR, IT, MT, NL, NO, PT and SK as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Galvus, 50 mg, tablet authorised in the Community since 2007, with Novartis Europharm Limited as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

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

III.1 Discussion on the non-clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to preclinical data, no further such data have been submitted or are considered necessary.

IV. CLINICAL ASPECTS

IV.1 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.

Discussion and overall conclusion
The extent of absorption of vildagliptin 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 and none of the excipients are known to affect the bioavailability. In addition, vildagliptin 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.

The quality criteria for biowaiver (solubility and dissolution) have also been fulfilled. For quality aspects of biowaiver, see section Quality aspects.

IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to clinical efficacy/safety data, no further such data have been submitted or are considered necessary.

IV.3 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 Vildagliptin Accord.

The MAH has submitted an updated version 1.1 RMP dated 2019-09-12 and proposed the following summary safety concerns:

Safety specification

Important identified risk (s)

- Transaminase elevationsand Drug-induced liver injury (DILI)
- Angioedema
- Acute pancreatitis
- Skin lesions
- Hypoglycaemia

Important potential risk (s)

□ Serious infections
□ Cardiac events in CHF (NYHA Functional Class III) patients
□ Muscle events /myopathy /rhabdomyolysis, in particular with current statin use
□ Neuropsychiatric events
□ Breast cancer
□ Pancreatic cancer

Missing information

□ Patients with severe hepatic impairment
□ Patients with compromised cardiac function (NYHA functional class IV)
□ Pregnancy
□ Gender incidence/frequency differences

Pharmacovigilance Plan

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

Routine pharmacovigilance activities including collection and reporting of adverse reactions and signal detection as stated in the pharmacovigilance system master file are sufficient for the safety concerns.
The MAH has proposed specific adverse reaction targeted follow-up questionnaire for following safety concerns.

- Transaminase elevations and Drug-induced liver injury (DILI) –identified risk
- Angioedema
- Skin lesions
- Hypoglycemia
- Muscle events/myopathy/rhabdomyolysis, in particular with current statin use –potential risk
- Pancreatic cancer

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 1.1 signed 2019-09-12 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 an 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 Galvus, EMEA/H/C/000771 (regarding content) and Mycophenolic acid 180 mg and 360mg gastro-resistant Tablets, ES/H/0183/001-002/DC (regarding 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, Vildagliptin Accord, is found adequate. There are no objections to approval of product name, from a non-clinical and clinical point of view. The product information is acceptable.

The benefit/risk ratio is considered positive and Vildagliptin Accord, 50 mg, tablet, is recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

The decentralised procedure for Vildagliptin Accord, 50 mg, tablet, was positively finalised on 2020-04-30.

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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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