LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

# Public Assessment Report
# Scientific discussion

# Dalmevin
# (vildagliptin)

# SE/H/1613/01/DC

**This module reflects the scientific discussion for the approval of Dalmevin. The procedure was finalised on 2017-06-21. For information on changes after this date please refer to the module 'Update'.**

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# I. INTRODUCTION

The application for Dalmevin, 50 mg, 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, EE, EL, HR, LT, LV, MT, RO 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 Union 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 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

No bioequivalence study has been submitted, since the applicant applies for a BCS –class I biowaiver.

From a pharmacokinetic point of view, a BCS-class I based biowaiver is acceptable for an immediate release drug product if the drug substance has proven to exhibit complete absorption and the excipients that might affect bioavailability are qualitatively and quantitatively the same. It should also be confirmed that the substance is not a narrow therapeutic index drug.

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.

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.

## 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 Dalmevin.

The version of the RMP is RMP 02 and DLP is 31-08-2016.

Safety specification

Summary table of safety concerns as approved in RMP

| | |
|---|---|
| Important identified risks | • Transaminase elevations and Drug-induced liver injury (DILI)<br>• Angioedema<br>• Acute pancreatitis<br>• Skin lesions<br>• Hypoglycaemia |
| Important potential risks | • Serious infections<br>• Cardiac events in CHF (NYHA Functional Class III) patients<br>• Muscle events/myopathy with and without concurrent statin use<br>• Neuropsychiatric events<br>• Breast cancer<br>• Pancreatic cancer |
| Missing information | • Gender incidence/frequency differences<br>• Patients with severe hepatic impairment<br>• Patients with compromised cardiac function (NYHA Functional Class IV)<br>• Pregnancy |

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 MAH has satisfactory responded to the questions raised and updated the RMP accordingly. **Issue is resolved**.

*The RMP is approved.*

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 (PIL) has been performed on the basis of a bridging report making reference to Galvus 50 mg tablets (content) and Encapia 200 mg film-coated tablets (layout). The user test of the Galvus leaflet was assessed and accepted in EMEA/H/C/000771. The user test of the Encapia leaflet was assessed and accepted in NL/H/2497/001/DC.
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, Dalmevin, is found adequate. There are no objections to approval of Dalmevin, 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/22 of Directive 2001/83 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 Dalmevin, 50 mg, tablet was positively finalised on 2017-06-21.

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# Public Assessment Report – Update

| Procedure number* | Scope | Product Information affected | 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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