COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Rosuvastatine Glenmark 5 mg, 10 mg, 20 mg and 40 mg film-coated tablets (rosuvastatin calcium)

NL/H/4832/001-004/DC

Date: 13 February 2023

This module reflects the scientific discussion for the approval of Rosuvastatine Glenmark 5 mg, 10 mg, 20 mg and 40 mg film-coated tablets. The procedure was finalised at 18 July 2014 in Portugal (PT/H/1127/001-004/DC). After a transfer on 16 May 2019, the current RMS is the Netherlands. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Rosuvastatine Glenmark 5 mg, 10 mg, 20 mg and 40 mg film-coated tablets from Glenmark Arzneimittel GmbH.

A comprehensive description of approved indications and posology is given in the SmPC.

This decentralised procedure concerns a generic application claiming essential similarity with the innovator product Crestor 10 mg film-coated tablets which has been registered in The Netherlands by AstraZeneca B.V since 6 November 2002.

The concerned member states (CMS) involved in this procedure were Germany, The Netherlands and United Kingdom.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC.

II. QUALITY ASPECTS

II.1 Introduction

All four strengths of Rosuvastatine Glenmark tablets are pink, circular and film-coated.

- Rosuvastatine Glenmark 5 mg film-coated tablets are debossed with “G” on one side and “C” on the other side of the tablet. Each tablet contains 5 mg rosuvastatin (as rosuvastatin calcium).
- Rosuvastatine Glenmark 10 mg film-coated tablets debossed with “G” on one side and “D” on the other side of the tablet. Each tablet contains 10 mg rosuvastatin (as rosuvastatin calcium).
- Rosuvastatine Glenmark 20 mg film-coated tablets are debossed with “G” on one side and “O” on the other side of the tablet. Each tablet contains 20 mg rosuvastatin (as rosuvastatin calcium).
- Rosuvastatine Glenmark 40 mg film-coated tablets are debossed with “G 264” on one side and “40” on the other side of the tablet.

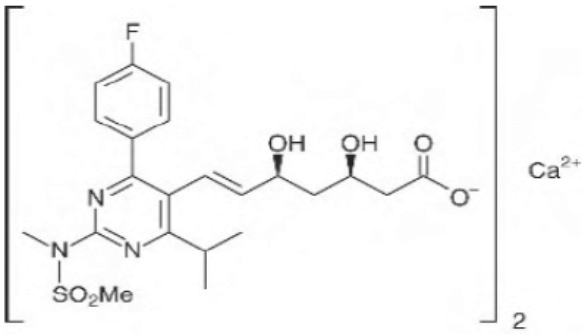
Each tablet contains 40 mg rosuvastatin (as rosuvastatin calcium).

The tablets packed in OPA/Aluminium/PVC and aluminium blisters or HDPE-bottles with a PP-cap and induction seal.

The excipients are:
Tablet core- lactose monohydrate, microcrystalline cellulose, crospovidone, sodium hydrogen carbonate and magnesium stearate.

Tablet coat- hypromellose, lactose monohydrate, titanium dioxide (E171), triacetin (E1518) and iron oxide, red (E172).

II.2 Drug Substance



Molecular formula
$C_{44}H_{54}F_2N_6O_{12}S_2\,Ca$

Relative molecular mass:
1001.14

A white to off-white powder. Soluble in dimethyl formamide, dimethyl sulphoxide and acetonitrile. Slightly soluble in acetone, water and methanol.

The chemical-pharmaceutical documentation and expert report in relation to rosuvastatin calcium are of sufficient quality in view of the present European regulatory requirements.

II.3 Medicinal Product

Pharmaceutical development
The documentation provided complies with relevant EU guidelines and directives. The development of the product has been described, the choice of excipients is justified and their functions explained.

Manufacturing process
Manufacture is performed in accordance with cGMP and consistency in quality and homogeneity is demonstrated.

Quality control of drug product

The finished product specification is based on relevant development and stability studies. Appropriate validation data have been provided for the analytical methods. Batch analyses data support the proposed finished product specification.

Stability of drug product

The conditions used in the stability studies are according to the ICH stability guideline. The control tests and specifications for drug product are adequately drawn up. The proposed shelf-life of 24 months with store in the original package in order to protect from light (blisters) and store in the original package in order to protect from light. Use within 30 days of opening (HDPE bottles) as conditions is considered acceptable.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Rosuvastatine Glenmark has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.

No post-approval commitments were made.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

Since Rosuvastatine Glenmark is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.2 Discussion on the non-clinical aspects

This product is a generic formulation of Crestor which is available on the European market. Reference is made to the preclinical data obtained with the innovator product. A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which is based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. Therefore, the member states agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

To support the application, the applicant has submitted data from a single-dose bioequivalence study conducted under fasting conditions with the strength of Rosuvastatin

40 mg, film-coated tablets.

Based on acceptable bioequivalence study for Rosuvastatin Calcium 40 mg tablets, a biowaiver is requested for 5 mg, 10 mg & 20 mg tablets. The results can be extrapolated to other proposed strengths.

IV.2 Pharmacokinetics

The RMS considers that the pharmacovigilance system, as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the community or in a third country.

IV.3 Risk Management Plan

The MAH has provided a revised documentation regarding the summary risk management plan (RMP) for rosuvastatin calcium in order to comply with the member states comments. The RMS considers that the current regulatory requirements for the RMP were adequately fulfilled.

IV.4 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Crestor. No new clinical studies were conducted. The MAH demonstrated through a bioequivalence study that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of this reference product. Risk management is adequately addressed. This generic medicinal product can be used instead of the reference product.

V. USER CONSULTATION

The package leaflet has been evaluated 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 PIL 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

Based on the review of the data on quality, safety and efficacy, the RMS considered that the application for Rosuvastatin Glenmark, 5 mg, 10 mg, 20 mg and 40 mg, film-coated tablets, is approvable.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
NL/H/4832/1-4/IB/0008	Changes in the SmPC and PIL intended to implement the outcome of a procedure concerning a PSUR follow-up assessment report.	Yes	23-10-2019	Approved	N/A
NL/H/4832/1-4/IA/0009	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph. New certificate from an already approved manufacturer	No	06-01-2020	Approved	N/A
NL/H/4832/1-4/IA/0010	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph New certificate from a new manufacturer (replacement or addition)	No	14-04-2020	Approved	N/A
NL/H/4832/1-4/IB/0011	Change(s) in the SmPC, labelling or PIL of a generic/hybrid/biosimilar medicinal products following assessment of the same change for the reference product Implementation of change(s) for which no new additional data are submitted by the MAH	Yes	20-03-2021	Approved	N/A
NL/H/4832/1-4/IA/0012	Change(s) in the SmPC, Labelling or PIL of human medicinal products intended to implement the outcome of a procedure concerning PSUR or PASS, or the outcome of the assessment done by the competent authority under Articles 45 or 46 of Regulation 1901/2006SmPCSmPC Implementation of wording agreed by the competent authority	Yes	20-01-2022	Approved	N/A
NL/H/4832/1-4/IA/0013	Change in finished product specifications and test methods in line with Ph.Eur. Monograph.	No	06-04-2022	Approved	N/A
NL/H/4832/1-4/IA/0013/G	Submission of updated Ph. Eur. certificates of suitability for rosuvastatin calcium from an already approved manufacturer Submission of a new Ph. Eur. certificate of suitability for rosuvastatin calcium from a new manufacturer as an additional API source	No	15-04-2022	Approved	N/A