COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

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

NL/H/6446/001-004/DC

Date: 13 August 2025

This module reflects the scientific discussion for the approval of Rosuvastatine Aurobindo 5 mg, 10 mg, 20 mg and 40 mg film-coated tablets. The procedure was finalised at 27 June 2012 in Portugal (PT/H/0689/001-004/DC). After a transfer on 3 June 2025, the current RMS is the Netherlands. For information on changes after the finalisation 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
EMA	European Medicines Agency
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
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Aurobindo Pharma B.V. has applied for a marketing authorisation for Rosuvastatine Aurobindo 5 mg, 10 mg, 20 mg and 40 mg, film-coated tablets, containing rosuvastatin as the active substance, indicated in:

Treatment of hypercholesterolaemia
Adults, adolescents and children aged 10 years or older with primary hypercholesterolaemia (type IIa including heterozygous familial hypercholesterolaemia) or mixed dyslipidaemia (type IIb) as an adjunct to diet when response to diet and other non-pharmacological treatments (e.g. exercise, weight reduction) is inadequate.

Homozygous familial hypercholesterolaemia as an adjunct to diet and other lipid lowering treatments (e.g. LDL apheresis) or if such treatments are not appropriate.

Prevention of Cardiovascular Events
Prevention of major cardiovascular events in patients who are estimated to have a high risk for a first cardiovascular event (see Section 5.1), as an adjunct to correction of other risk factors.

A comprehensive description of the up-to-date indications and posology is given in the current SmPC.

This decentralised application concerns a generic version claiming essential similarity with the reference product Crestor 5 mg, 10 mg, 20 mg, 40 mg, film-coated tablets, registered since 23-04-2003.

This type of application refers to information that is contained in the pharmacological-toxicological and clinical part of the dossier of the authorisation of the reference product. A reference product is a medicinal product authorised and marketed on the basis of a full dossier, i.e. including chemical, biological, pharmaceutical, pharmacological-toxicological and clinical data. Authorisations for generic products re therefore only allowed once the data protection time of the dossier of the reference product has expired. For this kind of application, it has to be demonstrated that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of the reference product. This generic product can be used instead of its reference product.

The marketing authorization was granted on 27-07-2012 based on Directive 2001/83/EC article 10.1 (a) (iii) first paragraph.

The Concerned Member States for this application were Belgium, Cyprus, Finland, France, Germany, Luxembourg, Malta and Romania.

II. QUALITY ASPECTS

II.1 Introduction

Rosuvastatine Aurobindo contains rosuvastatin as the active substance.

The core tablets excipients are: lactose monohydrate, calcium hydrogen phosphate anhydrous, microcrystalline cellulose, crospovidone (type B), magnesium stearate.
Film-coating excipients are: hypromellose (15cP) (E464), lactose monohydrate, titanium dioxide (E171), allura red AC aluminium lake (E129), sunset Yellow FCF (E110) aluminium lake, indigo carmine aluminium lake (E132), triacetin.

II.2 Drug Substance

The chemical-pharmaceutical documentation and Expert Report in relation to Rosuvastatine Aurobindo are of sufficient quality in view of the present European regulatory requirements.

Quality control of drug substance
The control tests and specifications for drug substance product are adequately drawn up.

Stability of drug substance
The proposed retest period of 2 years for the active substance is justified.

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 product specifications cover appropriate parameters for this dosage form. Validations of the analytical methods have been presented. Batch analysis has been performed on 3 batches each strength. The batch analysis results show that the finished products meet the specifications proposed.
The control tests and specifications for drug product are adequately drawn up.

Stability of drug product
The conditions used in the stability studies are according to the ICH stability guideline.

The proposed shelf-life of 2 years without any special temperature storage conditions and storing in the original package in order to protect from light is considered acceptable.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of rosuvastatin are well known. As rosuvastatin is a widely used, well-known active substance, no further studies are required and the applicant provides none. An overview based on literature review is, thus, appropriate.

IV. CLINICAL ASPECTS

IV.1 Introduction

Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the ratelimiting enzyme that converts 3-hydroxy-3-methylglutaryl coenzyme A to mevalonate, a precursor for cholesterol. The primary site of action of rosuvastatin is the liver, the target organ for cholesterol lowering.

Rosuvastatin increases the number of hepatic LDL (low density lipoprotein) receptors on the cell-surface, enhancing uptake and catabolism of LDL and it inhibits the hepatic synthesis of VLDL (very low density lipoprotein), thereby reducing the total number of VLDL and LDL particles.

Rosuvastatin is effective in adults with hypercholesterolaemia, with and without hypertriglyceridaemia, regardless of race, sex, or age and in special populations such as diabetics, or patients with familial hypercholesterolaemia.

From pooled phase III data, Rosuvastatin has been shown to be effective at treating the majority of patients with type IIa and IIb hypercholesterolaemia to recognised European Atherosclerosis Society (EAS; 1998) guideline targets.

IV.2 Pharmacokinetics

The application concerns 5 mg, 10 mg, 20 mg and 40 mg, film-coated tablets proposed for marketing. The bioequivalence study was carried out with the 40 mg strength. The conditions for bio-waivers in sections 5.4 of the Bioequivalence Guideline have been fulfilled: same manufacturer and process, drug input has been shown to be linear over the therapeutic dose

range, same qualitative composition, same ratio between active and excipients and similar dissolution profile under identical conditions between the 40 mg and 5 mg, 10 mg and 20 mg strengths.

IV.3 Clinical efficacy and Clinical safety

Rosuvastatin has a well-recognised efficacy and acceptable level of safety in the indications approved for 5 mg, 10 mg, 20 mg and 40 mg, film-coated tablets and has been widely used in many countries.

IV.4 Pharmacovigilance System

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.5 Risk Management Plan

The innovator product Crestor has risk minimisation activities. This risk minimisation activities are aimed at minimising skeletal muscle effects, hepatic effects and renal effects, by ensuring use of the appropriate starting dose (5 mg) and cautious use of the 40 mg dose (in accordance with contraindication and warnings in the summary of product characteristics). The MAH will conduct route risk minimisation activities by ensuring the proposed generic product information is similar to the reference product. Safety issues associated with rosuvastatin i.e. “minimizing the skeletal muscle effects, hepatic effects and renal effects, by ensuring the use of appropriate starting dose (5 mg) and cautious use of the 40mg dose” are addressed in the proposed summary of product characteristics SPC and package information leaflet respective sections to be in line with the reference product information.

V. USER CONSULTATION

The readability of the package leaflet was successfully demonstrated.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The application for Rosuvastatine Aurobindo contains adequate quality, non-clinical and clinical data and the bioequivalence has been shown. A benefit/risk ratio comparable to the reference product can therefore be concluded.

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
PT/H/0689/001-4/IA/001/G	Changes (Safety/Efficacy) to Human and Veterinary Medicinal Products Other variation	Yes	31-7-2013	Approved	N.A.
PT/H/0689/001-4/IB/002	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	30-5-2014	Approved	N.A.
PT/H/0689/001-4/IB/003	Change(s)in the Summary of Product Characteristics, Labelling or Package Leaflet of (union referral procedure) The medicinal product is covered by the defined scope of the procedure	Yes	21-1-2016	Approved	N.A.
PT/H/0689/001-4/IA/004/G	Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product Secondary packaging sites	No	13-12-2014	Approved	N.A.
PT/H/0689/001-4/IB/005/G	Change in pack size of the finished product Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes - Change outside the range of the currently approved pack sizes	Yes	28-4-2015	Partially approved	N.A.
PT/H/0689/001-4/IA/006	Change in pack size of the finished product Change in the number of units (e.g. tablets, ampoules, etc.) in a pack	Yes	9-3-2015	Approved	N.A.

	- Change within the range of the currently approved pack sizes				
PT/H/0689/001-4/II/007	Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the risk management plan Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment by the competent authority is required	No	27-6-2015	Approved	N.A.
PT/H/0689/001-4/IA/008/G	Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product -Secondary packaging site -Primary packaging site Change to importer, batch release arrangements and quality control testing of the finished product Replacement or addition of a site where batch control/testing takes place	No No	17-4-2015	Approved	N.A.
PT/H/0689/001-4/IB/009	Changes (Safety/Efficacy) to Human and Veterinary Medicinal Products Other variation: update of Summary of Product Characteristics and Package Leaflet	Yes	14-12-2015	Approved	N.A.
PT/H/0689/001-4/IA/010	Change in the name and/or address of a	Yes	9-10-2015	Approved	N.A.

	manufacturer/importer of the finished product (including batch release or quality control testing sites) The activities for which the manufacturer/importer is responsible do not include batch release				
PT/H/0689/001-4/IB/011	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet 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	20-10-2016	Approved	N.A.
PT/H/0689/001-4/IB/012	Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the risk management plan Other variation: update of the Risk Management Plan in line with innovator safety concerns by incorporating the new safety changes	No	20-10-2016	Approved	N.A.
PT/H/0689/001-4/R/001	Renewal	No	6-4-2018	Approved	N.A.
PT/H/0689/001-4/II/014	Change in the specification parameters and/or limits of the finished product Other variation: Change in the limits of related substances test in the finished product specifications	No	17-3-2017	Approved	N.A.
PT/H/0689/001-4/IB/013	Submission of a new or updated Ph. Eur. certificate	No	9-2-2017	Approved	N.A.

	of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph -New certificate from an already approved manufacturer				
PT/H/0689/001-3/IB/015/G	Change in the (invented) name of the medicinal product for Nationally Authorised Products Introduction of , or changes to, a summary of pharmacovigilance system for medicinal products for human use Introduction of a summary of pharmacovigilance system, changes in QPPV (including contact details) and/or changes in the Pharmacovigilan-ce System Master File (PSMF) location	Yes No	17-4-2017	Approved	N.A.
PT/H/0689/002-4/IB/016	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	6-4-2018	Approved	N.A.
PT/H/0689/001-4/IB/017	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet of a generic/hybrid/biosimilar medicinal products following assessment of the same change for the reference product	Yes	16-8-2018	Approved	N.A.

	Implementation of change(s) for which no new additional data are submitted by the MAH				
PT/H/0689/001-4/IA/018	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph -Updated certificate from an already approved manufacturer	No	11-5-2018	Approved	N.A.
PT/H/0689/001-4/IA/019	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet 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 1901/2006SmPC Implementation of wording agreed by the competent authority	Yes	24-4-2019	Approved	N.A.
PT/H/0689/001-4/IA/021	Change to importer, batch release arrangements and quality control testing of the finished product Replacement or addition of a site where batch control/testing takes place	No	13-5-2019	Approved	N.A.
PT/H/0689/001-3/IA/022	Change in the batch size (including batch size	No	14-5-2019	Approved	N.A.

	ranges) of the finished product Up to 10-fold compared to the originally approved batch size				
PT/H/0689/001-4/IB/023	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet 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 1901/2006SmPC Other variation: update of Summary of Product Characteristics and Package Leaflet	Yes	6-7-2020	Approved	N.A.
PT/H/0689/001-4/IA/024	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph -New certificate from a new manufacturer (replacement or addition)	No	29-1-2020	Approved	N.A.
PT/H/0689/001-4/IB/025/G	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet of a generic/hybrid/biosimilar medicinal products	Yes	22-3-2021	Approved	N.A.

	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 Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the risk management plan Other variation	 No			
PT/H/0689/001-4/IA/026/G	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph -Updated certificate from an already approved manufacturer	No	6-8-2021	Approved	N.A.
PT/H/0689/001-4/IA/027	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet 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 1901/2006SmPC Implementation of wording agreed by the competent authority	Yes	6-8-2021	Approved	N.A.

PT/H/0689/001-4/IA/028	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph -Updated certificate from an already approved manufacturer	No	14-10-2021	Approved	N.A.
PT/H/0689/001-4/IA/029	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph -Updated certificate from an already approved manufacturer	No	7-12-2021	Approved	N.A.
PT/H/0689/001-4/IA/030	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet 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	Yes	14-2-2022	Approved	N.A.

	or 46 of Regulation 1901/2006SmPC Implementation of wording agreed by the competent authority				
PT/H/0689/004 /IA/031	Change in the batch size (including batch size ranges) of the finished product Up to 10-fold compared to the originally approved batch size	No	27-5-2022	Approved	N.A.
PT/H/0689/001 -4/IB/032	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet 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	11-5-2023	Approved	N.A.
PT/H/0689/001 -4/IA/033	Change in name of the active substance or of an excipient	Yes	14-7-2023	Approved	N.A.
PT/H/0689/001 -4/IA/034	Deletion of manufacturing sites (including for an active substance, intermediate or finished product, packaging site, manufacturer responsible for batch release, site where batch control takes place, or supplier of a starting material, reagent or excipient (when mentioned in the dossier) Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product Secondary packaging site	Yes No	14-7-2023	Approved	N.A.

	Changes (Safety/Efficacy) to Human and Veterinary Medicinal Products Other variation: update of product information to be in line with recently published PRAC safety recommendations	Yes			
PT/H/0689/001-4/IA/035	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph -Updated certificate from an already approved manufacturer	No	1-9-2023	Approved	N.A.
PT/H/0689/001-4/IB/036/G	Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product - Secondary packaging site - Primary packaging site - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products.	No	7-12-2023	Approved	N.A.

PT/H/0689/001-4/IA/037	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph -Updated certificate from an already approved manufacturer	No	4-7-2024	Approved	N.A.
PT/H/0689/001-4/IB/038	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet 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	28-10-2024	Approved	N.A.
PT/H/0689/001-4/IB/039	Change in the shelf-life or storage conditions of the finished product Extension of the shelf life of the finished product – As packaged for sale (supported by real time data)	Yes	2-9-2024	Approved	N.A.