Public Assessment Report

Decentralised Procedure

Rosuvastatin 5 mg Film-coated Tablets
Rosuvastatin 10 mg Film-coated Tablets
Rosuvastatin 20 mg Film-coated Tablets
Rosuvastatin 40 mg Film-coated Tablets
(rosuvastatin calcium)

Procedure No: UK/H/6734/001-004/DC
UK Licence Number/s: PL 20075/1227-1230

ACCORD HEALTHCARE LIMITED
This is a summary of the Public Assessment Report (PAR) for Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets (PL 20075/1227-1230; UK/H/6734/001-004/DC). It explains how Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

The products will be collectively referred to as Rosuvastatin Tablets throughout the Lay Summary.

For practical information about using Rosuvastatin Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

**What are Rosuvastatin Tablets and what are they used for?**

Rosuvastatin Tablets are ‘generic medicines’. This means that Rosuvastatin Tablets are similar to ‘reference medicines’ already authorised in the European Union (EU) called Crestor 5 mg, 10 mg, 20 mg and 40 mg film-coated tablets (AstraZeneca UK Ltd)

Rosuvastatin Tablets are for:

- patients with a high cholesterol level. This means they are at risk from a heart attack or stroke. Rosuvastatin Tablets are used in adults, adolescents and children 6 years or older to treat high cholesterol.

Patients may be advised to take a statin, because changing their diet and taking more exercise were not enough to correct their cholesterol levels. Patients should continue with a cholesterol-lowering diet and exercise while taking Rosuvastatin Tablets

Or

- Patients with other factors that increase their risk of having a heart attack, stroke or related health problems. Heart attack, stroke and other problems can be caused by a disease called Atherosclerosis. Atherosclerosis is due to a build-up of fatty deposits in the arteries.

**How do Rosuvastatin Tablets work?**

Rosuvastatin Tablets belong to a group of medicines called statins.

Rosuvastatin Tablets are used to correct the levels of fatty substances in the blood called lipids, the most common of which is cholesterol.

There are different types of cholesterol found in the blood – “bad” cholesterol (LDL-C) and “good” cholesterol (HDL-C).

- Rosuvastatin Tablets can reduce the “bad” cholesterol and increase the “good” cholesterol.

- It works by helping to block your body’s production of “bad” cholesterol. It also improves your body’s ability to remove it from your blood.

For most people, high cholesterol does not affect the way they feel because it does not produce any symptoms. However, if it is left untreated, fatty deposits can build up in the walls of your blood vessels causing them to narrow.

Sometimes, these narrowed blood vessels can get blocked which can cut off the blood supply to the heart or brain leading to a heart attack or a stroke. If you correct your cholesterol levels, you can reduce your risk of having a heart attack or stroke.

You need to keep taking Rosuvastatin Tablets, even if it has got your cholesterol to the right level, because it prevents your cholesterol levels from creeping up again and causing buildup of fatty deposits. However, you should stop if your doctor tells you to do so, or if you have become pregnant.
How are Rosuvastatin Tablets used?
The pharmaceutical form of this medicine is a film-coated tablet and the route of administration is oral (by mouth).

This medicine should always be taken exactly as the doctor has told their patient. The patient should check with their doctor or pharmacist if they are unsure.

Each tablet should be swallowed whole with a drink of water and taken once daily. Rosuvastatin Tablets can be taken at any time of the day. Patients should try to take their tablet at the same time every day to help remind themselves to keep taking their tablets.

The patient should stay on a cholesterol-lowering diet while taking Rosuvastatin Tablets.

Rosuvastatin Tablets for high cholesterol:
Starting dose:
Treatment with Rosuvastatin Tablets must start with the 5mg or the 10mg dose, even if the patient has taken a higher dose of a different statin before. The choice of starting dose (5 or 10 mg) will depend upon:

- The patient's cholesterol level.
- The level of risk the patient has of experiencing a heart attack or stroke.
- Factors that may make a patient more sensitive to possible side effects.

Patients should check with the doctor or pharmacist which starting dose of Rosuvastatin Tablets will best suit their needs.

The doctor may decide to give their patient the lowest dose (5mg) if they are:

- of Asian origin (Japanese, Chinese, Filipino, Vietnamese, Korean and Indian).
- are over 70 years of age.
- have moderate kidney problems.
- are at risk of muscle aches and pains (myopathy).

Rosuvastatin Tablets to reduce your risk of having a heart attack, stroke or related health problems:
The recommended dose is 20mg daily. However, the doctor may decide to use a lower dose if the patient has any of the factors mentioned above.

Please read section 3 of the package leaflet for detailed dosing recommendations, the route of administration, and the duration of treatment.

For further information on how Rosuvastatin Tablets are used, refer to the package leaflet and Summaries of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

What benefits of Rosuvastatin Tablets have been shown in studies?
Because Rosuvastatin Tablets are generic medicines, considerations have been limited to determine whether they can be expected to bioequivalent, and therefore therapeutically equivalent to the reference products, Crestor 5 mg, 10 mg, 20 mg & 40 mg film-coated tablets. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

What are the possible side effects of Rosuvastatin Tablets?
Because Rosuvastatin Tablets are generic medicines and are considered to be bioequivalent to the reference medicines Crestor 5 mg, 10 mg, 20 mg & 40 mg film-coated tablets their benefits and possible side effects are taken as being the same as those for the reference products.
For the full list of all side effects reported with Rosuvastatin Tablets, see section 4 of the package leaflet available on the MHRA website.

**Why were Rosuvastatin Tablets approved?**

It was concluded that, in accordance with EU requirements, Rosuvastatin Tablets have been shown to have comparable quality and to be comparable to Crestor 5 mg, 10 mg, 20 mg & 40 mg film-coated tablets. Therefore, the MHRA decided that, as for Crestor 5 mg, 10 mg, 20 mg and 40 mg film-coated tablets; the benefits are greater than the risks and recommended that they can be approved for use.

**What measures are being taken to ensure the safe and effective use of Rosuvastatin Tablets?**

A risk management plan (RMP) has been developed to ensure that Rosuvastatin Tablets are used as safely as possible. Based on this plan, safety information has been included in the Summaries of Product Characteristics (SmPCs) and the package leaflet for Rosuvastatin Tablets including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

**Other information about Rosuvastatin Tablets**

Denmark, Austria, Republic of Ireland, Malta, Sweden, Slovenia and the UK agreed to grant Marketing Authorisations for Rosuvastatin Tablets on 18 January 2017. On 18 May 2017 the RMS was transferred from Denmark to the UK, the following procedure number UK/H/6734/001-004 was assigned.

The full PAR for Rosuvastatin Tablets follows this summary.

This summary was last updated in December 2018.
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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Member States considered that the applications for Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets (PL 20075/1227-1230; UK/H/6734/001-004). These products were previously authorised with Denmark as the RMS, with the product name Lyklarzu (DK/H/2553/001-004/DC).

Rosuvastatin Tablets are Prescription-Only Medicines (POM) indicated for the:

Treatment of hypercholesterolaemia

Adults, adolescents and children aged 6 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.

Adults, adolescents and children aged 6 years or older with 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.

Mechanism of action

Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting 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 receptors on the cell-surface, enhancing uptake and catabolism of LDL and it inhibits the hepatic synthesis of VLDL, thereby reducing the total number of VLDL and LDL particles.

The applications were submitted using the Decentralised Procedure (DCP), with the Denmark as Reference Member State (RMS), and the United Kingdom, Austria, Republic of Ireland, Malta, Sweden, and Slovenia as Concerned Member States (CMS). The applications were submitted under Article 10(1) of Directive 2001/83/EC, as amended, as generic applications. The reference products are Crestor 5 mg, 10 mg, 20 mg and 40 mg film-coated tablets authorised to AstraZeneca UK Ltd on 24 March 2003.

The applicant has submitted a bioequivalence study in which the pharmacokinetic profile of the product 40mg film-coated tablets is compared with the pharmacokinetic profile of the reference product Crestor 40 mg film-coated tablets (AstraZeneca UK Ltd) and also with Rosuvastatin 5 mg film-coated tablets vs. Crestor® 5 mg film-coated tablets (AstraZeneca UK Ltd). This generic product can be used instead of its reference product.

The RMS has been assured that acceptable standards of Good Manufacturing Practice are in place for this product type at all sites responsible for the manufacture, assembly and batch release of these products.

The RMS has been assured that acceptable standards of GMP (see Directive 2003/94/EC) are in place for this product type at all sites responsible for the manufacture and assembly of this product prior to granting its national authorisation.
QII QUALITY ASPECTS

II.1 Introduction

Rosuvastatin 5mg Film-coated Tablets are Yellow, round, 7mm, biconvex with “RU5” engraved on one side and blank on the other side.

Rosuvastatin 10mg Film-coated Tablets are Pink, round, 7mm, biconvex with “RU10” engraved on one side and blank on the other side.

Rosuvastatin 20mg Film-coated Tablets are Pink, round, 9mm, biconvex with “RU20” engraved on one side and blank on the other side.

Rosuvastatin 40mg Film-coated Tablets are Pink, oval, 15.5mm x 8mm, biconvex with “RU40” engraved on one side and blank on the other side.

The active substance in Rosuvastatin Tablets is rosuvastatin. Rosuvastatin Film-coated Tablets contain rosuvastatin calcium equivalent to 5mg, 10mg, 20mg or 40mg of rosuvastatin.

Other ingredients consist of the pharmaceutical excipients as follows:

Tablet core: lactose monohydrate, microcrystalline cellulose, crospovidone type A, sodium carbonate monohydrate, sodium laurilsulfate, magnesium stearate,

Tablet coat 5mg: Opadry II 85F62533 Yellow: polyvinyl alcohol part hydrolysed, titanium dioxide (E171), polyethylene glycol, talc, iron oxide yellow (E172),

Tablet coat 10mg, 20mg, 40mg: Opadry II 85F64743 Pink: polyvinyl alcohol part hydrolysed, titanium dioxide (E171), polyethylene glycol, talc, iron oxide yellow (E172), iron oxide red (E172), Allura red AC (E129), Indigo carmine (E132).

Rosuvastatin 5, 10, 20, 40 mg Tablets are packaged in Aluminium / Aluminium (Al/Al) blister packs containing 28 tablets.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

II.2 Drug Substance

INN: Rosuvastatin calcium

Chemical name: Calcium bis[(3R,5S,6E)-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl (methylsulfonyl)amino]pyrimidin-5-yl]-3,5-dihydroxyhept-6-enoate]

Structure:

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\text{\begin{align*}
\text{Ca}^{2+} & \\
\text{CH}_3 & \\
\text{CH}_3 & \\
\text{OH} & \\
\text{OH} & \\
\text{COO}^{-} & \\
\end{align*}}
\]
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Molecular formula: \((C_{22}H_{27}F\text{N}_3\text{O}_6\text{S})_2\text{Ca}\)
Molecular weight: 1001.14 g/mol

Appearance: White or almost white powder.

Solubility: It is slightly soluble in water, freely soluble in methylene chloride, practically insoluble in anhydrous ethanol. It is optically active.

All aspects of the manufacture and control of the active substance, rosuvastatin calcium, are covered by the European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

The finished product manufacturer’s specification on the drug substance includes all tests as included in the active substance manufacturer’s specification and additional test for particle size. Certificates of analysis of the active substance issued by the finished product manufacturer are presented.

II.3. Medicinal Product

Pharmaceutical Development
The objective of the development programme was to formulate safe, efficacious, tablets containing 5, 10, 20 or 40 mg rosuvastatin calcium that are generic versions of the reference products Crestor® 5 mg, 10 mg, 20 mg & 40 mg film-coated tablets (AstraZeneca UK Ltd).

The strengths applied for are 5, 10, 20 and 40 mg. The 10, 20 and 40 mg strengths are dose proportional, whereas the 5 mg strength is not proportional to the other strengths, but it has the same tablet core weight as the 10 mg strength. The development of the product has been adequately described, the choice of excipients is justified and their functions explained.

Comparative in-vitro dissolution profiles have been provided for the proposed and originator products.

All excipients comply with their respective European Pharmacopoeia monographs with the exception of the colourants which comply with the EU regulation EU 231/2012 on food colourants and additives. Satisfactory Certificates of Analysis have been provided for all excipients. Suitable specifications and certificates of analysis data have been provided for each excipient.

With the exception of lactose monohydrate, none of the excipients used contain material of animal or human origin. The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption. The Magnesium Stearate used in the formulation is of vegetable origin. A statement by the current supplier has been provided.

Manufacture of the products
Satisfactory batch formulae have been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated at commercial-scale batch size and shown satisfactory results.

Finished Product Specifications
The finished product specifications cover appropriate parameters for this dosage form. The limit for dissolution testing reflects the dissolution profiles obtained with the biobatches. The analytical methods used to control the finished product has been adequately validated. Batch analysis results are provided showing that the finished products meet the specifications proposed.

Stability of the Product
Finished product stability studies were performed in accordance with current guidelines on batches of the finished products in the packaging proposed for marketing. The data from these studies, for all packaging presentations support a shelf-life of 3 years, this medicinal product does not require any special storage conditions.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.
II.4 Discussion on chemical, pharmaceutical and biological aspects
There are no objections to the approval of these applications from a pharmaceutical viewpoint.
III  NON-CLINICAL ASPECTS

III.1  Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of rosuvastatin calcium are well-known, no new non-clinical studies are required and none have been provided. An overview based on the literature review is, thus, appropriate.

The applicant’s non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.

III.2  Pharmacology
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.3  Pharmacokinetics
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.4  Toxicology
The impurities associated with the drug substance and drug product appear to be well controlled and the relevant limits in the specifications are acceptable.

III.5  Ecotoxicity/environmental risk assessment (ERA)
Since Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets are 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.6  Discussion on the non-clinical aspects
There are no objections to the approval of these applications from a non-clinical viewpoint.

IV  CLINICAL ASPECTS

IV.1  Introduction
The clinical pharmacology of rosuvastatin calcium is well-known.

No new efficacy or safety studies have been performed and none are required for this type of application. A comprehensive review of the published literature has been provided by the applicant, citing the well-established clinical pharmacology, efficacy and safety of rosuvastatin calcium.

IV.2  Pharmacokinetics
For this generic application, the MAH has submitted two bioequivalence studies in which the pharmacokinetic profile of the test product Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets is compared with the pharmacokinetic profile of the reference product Crestor® 40 mg film-coated tablets (AstraZeneca UK Ltd) and Crestor® 5 mg film-coated tablets (AstraZeneca UK Ltd).

Bioequivalence
To support the application, the applicant has submitted as report two bioequivalence studies; single dose, fasting conditions for the 5 and 40 mg strength. All studies were 2 way cross over studies.

First study
A single centre, open label, randomized, 2-period, 2-sequence, single dose, crossover bioequivalence study performed under fasting conditions. The treatment periods were separated by a washout period of 10 days. A single oral dose of rosuvastatin as one 40 mg tablet was administered in each study period.

Bioequivalence between the test and the reference product was demonstrated since 90% confidence intervals for the log-transformed AUC_{0-t} and C_{max} were within the acceptance range of 80-125%:
Second study
The single centre, open label, randomized, 2-period, 2-sequence, single dose, crossover bioequivalence study was performed under fasting conditions. The study included Rosuvastatin 5 mg film coated tablets and Crestor 5 mg film coated tablets. The treatment periods were separated by a washout period of 10 days.

Bioequivalence between the test and the reference product was demonstrated since 90% confidence intervals for the log-transformed AUC$_{0-t}$ and C$_{max}$ were within the acceptance range of 80-125%:

**Table 1 - Summary of Pharmacokinetic Data for Rosuvastatin**

<table>
<thead>
<tr>
<th>Pharmacokinetic parameter</th>
<th>Geometric mean</th>
<th>Arithmetic mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC$_{0-t}$ (ng.h/mL)</td>
<td>63.19</td>
<td>68.07</td>
<td>27.685</td>
</tr>
<tr>
<td>C$_{max}$ (ng/mL)</td>
<td>7.53</td>
<td>8.13</td>
<td>3.405</td>
</tr>
</tbody>
</table>

**Table 2 - Ratio and 90% Confidence Intervals of Test Product versus Reference Product**

<table>
<thead>
<tr>
<th>Pharmacokinetic parameter</th>
<th>Ratio (%)</th>
<th>90% Confidence Intervals</th>
<th>Intra Subject Variability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower 90% CI (%)</td>
<td>Upper 90% CI (%)</td>
</tr>
<tr>
<td>AUC$_{0-t}$</td>
<td>112.49</td>
<td>105.53</td>
<td>119.91</td>
</tr>
<tr>
<td>C$_{max}$</td>
<td>112.11</td>
<td>104.35</td>
<td>120.44</td>
</tr>
</tbody>
</table>

**Conclusion on bioequivalence studies:**
Based on the submitted bioequivalence studies Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets is considered bioequivalent to Crestor.

**IV.3 Pharmacodynamics**
No new pharmacodynamic data were submitted and none were required for applications of this type.

**IV.4 Clinical efficacy**
No new efficacy data were submitted, and none were required for applications of this type.

**IV.5 Clinical safety**
No new safety data were submitted and none are required.
IV.6 Risk Management Plan (RMP) and Pharmacovigilance System

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 Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets.

The agreed summary list of safety concerns with no additional pharmacovigilance or risk minimisation measures is as follows:

<table>
<thead>
<tr>
<th>Important identified risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Rhabdomyolysis</td>
</tr>
<tr>
<td>• Myopathy, myositis, myalgia, CK increases, myoglobinuria and myoglobinuaemia (in the setting of rhabdomyolysis and myopathy)</td>
</tr>
<tr>
<td>• Increase transaminases, hepatitis, jaundice</td>
</tr>
<tr>
<td>• Pancreatitis</td>
</tr>
<tr>
<td>• Memory loss</td>
</tr>
<tr>
<td>• Proteinuria</td>
</tr>
<tr>
<td>• Diabetes mellitus</td>
</tr>
<tr>
<td>• Depression</td>
</tr>
<tr>
<td>• Sleep disorders (including insomnia and nightmares)</td>
</tr>
<tr>
<td>• Immune Mediated Necrotizing Myopathy (IMNM)</td>
</tr>
<tr>
<td>• Thrombocytopenia/decreased platelet count</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Important potential risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>• SJS/TEN (Stevens-Johnson syndrome and toxic epidermal necrolysis)</td>
</tr>
<tr>
<td>• Tendon disorders</td>
</tr>
<tr>
<td>• Peripheral neuropathy</td>
</tr>
<tr>
<td>• Drug interaction: ciclosporin, various protease inhibitor combinations with ritonavir, clopidogrel, gemfibrozil, eltrombopag, dronedarone, warfarin, other vitamin K antagonists, fusidic acid, ezetimibe and simprevir.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Missing information</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Children &lt; 6 years of age</td>
</tr>
<tr>
<td>• DDI studies in the paediatric population</td>
</tr>
</tbody>
</table>

IV.7 Discussion on the clinical aspects

The grant of marketing authorisations is recommended for these applications from a clinical viewpoint.

V User consultation

The package leaflet has been evaluated via a user consultation study 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**

Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets have a proven chemical pharmaceutical quality and are generic of Crestor. Crestor is a well-known medicinal product with an established favourable efficacy and safety profile. Bioequivalence has been shown to be in compliance with the requirements of European guidance documents. Agreement between Member States was reached during a written procedure. There was no discussion in the CMD(h). The Concerned Member States, on the basis of the data submitted, considered that essential similarity has been demonstrated for Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised on 18-01-2017.

Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets were authorised in RMS Denmark on 23 March 2017 with the product name Lyklarzu (DK/H/2553/01-04/DC). There were no post-approval commitments made during the procedure. On 18 May 2017 the RMS was transferred from Denmark to the UK, the following procedure number UK/H/6734/001-004 was assigned.

According to the List of Union reference dates and frequency of submission of periodic safety update reports (PSURs), no routine PSURs are required for this product. The date for the first renewal will be: 18 January 2022.
Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The following text is the approved label text for this medicine, no label mock-ups have been provided. In accordance with medicines legislation, the product shall not be marketed in the UK until approval of the label mock-ups has been obtained:
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Carton

1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 5mg Film-coated Tablets

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 5mg rosuvastatin (as rosuvastatin calcium).

3. LIST OF EXCIPIENTS

Also contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

28 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.
Read the package leaflet before use.
Use as directed by your doctor.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE
11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MA holder
Accord Healthcare Ltd, North Harrow, HA1 4HF, UK

12. MARKETING AUTHORISATION NUMBER(S)

PL 20075/1227

13. BATCH NUMBER\*, DONATION AND PRODUCT CODES\*

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

rosuvastatin 5mg film-coated tablets

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included>

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:
MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister

1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 5mg Film-coated Tablets

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Accord logo

3. EXPIRY DATE

EXP

4. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Batch

5. OTHER
### MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

<table>
<thead>
<tr>
<th>Blister</th>
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<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT</th>
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<tbody>
<tr>
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<table>
<thead>
<tr>
<th>2. NAME OF THE MARKETING AUTHORIZATION HOLDER</th>
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<tr>
<td>Accord logo</td>
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<table>
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<tr>
<th>3. EXPIRY DATE</th>
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<td>EXP</td>
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<th>4. BATCH NUMBER&lt;, DONATION AND PRODUCT CODES&gt;</th>
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<tr>
<td>Batch</td>
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<td></td>
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</tbody>
</table>
## PARTICULARS TO APPEAR ON THE OUTER PACKAGING

### Carton

### 1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 10mg Film-coated Tablets

### 2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 10mg rosuvastatin (as rosuvastatin calcium).

### 3. LIST OF EXCIPIENTS

Also contains lactose and Allura red AC (E129). See leaflet for further information.

### 4. PHARMACEUTICAL FORM AND CONTENTS

28 tablets

### 5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.
Read the package leaflet before use.
Use as directed by your doctor.

### 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

### 7. OTHER SPECIAL WARNING(S), IF NECESSARY

### 8. EXPIRY DATE

EXP

### 9. SPECIAL STORAGE CONDITIONS

### 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE
DCPAR Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets  
UK/H/6734/001-004

11. NAME AND ADDRESS OF THE MARKETING AUTHORIZATION HOLDER

MA holder
Accord Healthcare Ltd, North Harrow, HA1 4HF, UK

12. MARKETING AUTHORIZATION NUMBER(S)

PL 20075/1228

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

rosuvastatin 10mg film-coated tablets

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:
<table>
<thead>
<tr>
<th>MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS</th>
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</thead>
<tbody>
<tr>
<td>Blister</td>
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<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT</th>
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<tbody>
<tr>
<td>Rosuvastatin 20mg Film-coated Tablets</td>
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<table>
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<tr>
<th>2. NAME OF THE MARKETING AUTHORISATION HOLDER</th>
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<tr>
<td>Accord Logo</td>
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<table>
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<tr>
<th>3. EXPIRY DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXP</td>
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</table>

<table>
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<tr>
<th>4. BATCH NUMBER&lt;, DONATION AND PRODUCT CODES&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Batch</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. OTHER</th>
</tr>
</thead>
</table>
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Carton

1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 20mg Film-coated Tablets

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 20mg rosvastatin (as rosvastatin calcium).

3. LIST OF EXCIPIENTS

Also contains lactose and Allura red AC (E129). See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

28 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.
Read the package leaflet before use.
Use as directed by your doctor.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS
10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MA holder
Accord Healthcare Ltd, North Harrow, HA1 4HF, UK

12. MARKETING AUTHORISATION NUMBER(S)

PL 20075/1229

13. BATCH NUMBER, DONATION AND PRODUCT CODES

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

rosuvastatin 20mg film-coated tablets

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included>

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:
### Minimum Particulars to Appear on Blisters or Strips

| Blister |

### 1. Name of the Medicinal Product

Rosuvastatin 40mg Film-coated Tablets

### 2. Name of the Marketing Authorisation Holder

Accord Logo

### 3. Expiry Date

EXP

### 4. Batch Number<, Donation and Product Codes>

Batch

### 5. Other
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Carton

1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 40mg Film-coated Tablets

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 40mg rosuvastatin (as rosuvastatin calcium).

3. LIST OF EXCIPIENTS

Also contains lactose and Allura red AC (E129). See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

28 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.
Read the package leaflet before use.
Use as directed by your doctor.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS
10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MA holder
Accord Healthcare Ltd, North Harrow, HA1 4HF, UK

12. MARKETING AUTHORISATION NUMBER(S)

PL 20075/1230

13. BATCH NUMBER<S, DONATION AND PRODUCT CODES>

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

rosuvastatin 40mg film-coated tablets

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:

Annex 1
Table of content of the PAR update for MRP and DCP
Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

<table>
<thead>
<tr>
<th>Scope</th>
<th>Procedure number</th>
<th>Product information affected</th>
<th>Date of start of procedure</th>
<th>Date of end of procedure</th>
<th>Approval/ non approval</th>
<th>Assessment report attached?</th>
<th>Y/N (version)</th>
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</thead>
<tbody>
<tr>
<td>Change of authorisation from Actavis Group PTC ehf to Accord Healthcare Limited</td>
<td>PL 30306/0790</td>
<td>Label, PIL, SmPC</td>
<td>09/03/2018</td>
<td>09/03/2018</td>
<td>Y</td>
<td>N</td>
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<tr>
<td>To update the pharmacovigilance system master file (PSMF).</td>
<td>UK/H/6734/001/IA/002</td>
<td>N</td>
<td>14/03/2018</td>
<td>13/04/2018</td>
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</tr>
<tr>
<td>To update the SmPC and PIL in line with the reference product.</td>
<td>See annex.I</td>
<td>SmPC &amp; PIL</td>
<td>See annex I</td>
<td>See annex I</td>
<td>Y</td>
<td>Y annex I</td>
<td></td>
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<tr>
<td>To update section 4.4 and 4.8 in line with the outcomes of (PSUSA/00002664/201711)</td>
<td>UK/H/6734/001/IB/004</td>
<td>PIL</td>
<td>05/12/2018</td>
<td>Y</td>
<td>N</td>
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</table>
ANNEX 1

Our Reference:  
PL 20075/1227 - 0003  
PL 20075/1228 -0003  
PL 20075/1229 -0003  
PL 20075/1230 -0003

Product:  
Rosuvastatin 5, 10, 20, and 40 mg Film-coated Tablets

Marketing Authorisation Holder:  
Accord Healthcare Limited

Active Ingredient(s):  
Rosuvastatin calcium

Type of Procedure:  
Mutual Recognition

Submission Type:  
Variation

Submission Category:  
Type IB

Submission Complexity:  
Standard

EU Procedure Number (if applicable):  
UK/H/6734/001/IB/003  
UK/H/6734/002/IB/003  
UK/H/6734/003/IB/003  
UK/H/6734/004/IB/003

Reason:  
To update section 4.2, 4.5, 4.8, 5.1, 5.2 of the SmPC and PIL in line with the reference product – Crestor film-coated tablets.

Supporting Evidence  
The applicant provided the new SPC and PIL which was compared to that of the reference product

Evaluation  
The updates to the SmPC and PIL were in line with the reference product and therefore acceptable.

Decision: Approved 9 November 2018