Public Assessment Report

Decentralised Procedure

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

(Rosuvastatin zinc)

Procedure No: UK/H/6263/01-04/DC

UK Licence No: PL 30306/0777-0780

Actavis Group PTC ehf.
LAY SUMMARY
Rosuvastatin 5 mg, 10 mg, 20 mg and 40 mg Film-coated Tablets
(Rosuvastatin zinc)

This is a summary of the public assessment report (PAR) for Rosuvastatin 5 mg, 10 mg, 20 mg and 40 mg Film-coated Tablets (PL 30306/0777-0780: UK/H/6263/01-04/DC). These products will be referred to as Rosuvastatin Tablets in the remainder of this summary, for ease of reading.

This summary explains how Rosuvastatin Tablets were assessed and their authorisation recommended, as well as the conditions of use. It is not intended to provide practical advice on how to use these products.

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 UK called Crestor 5mg, 10mg, 20mg & 40mg tablets (AstraZeneca UK Limited; PL 17901/0201-0203 & PL 17901/0243).

Rosuvastatin tablets are used for the following in adults, adolescents and children 6 years or older:

- To treat high cholesterol levels, when there is a risk of a heart attack or stroke, and where changing diet and taking more exercise are not enough to correct the cholesterol levels
- To reduce the risk of heart attack, stroke or related health problems in patients with other risk factors. Heart attack, stroke and other problems can be caused by atherosclerosis, a build-up of fatty deposits in the arteries.

How are Rosuvastatin Tablets used?
Rosuvastatin Tablets should be taken once daily and swallowed whole with a drink of water. They can be taken at anytime of the day, with or without food; however, patients should try and take the tablets at the same time every day.

Please read Section 3 of the Package Leaflet for detailed information on dosing recommendations, the route of administration and the duration of treatment.

Rosuvastatin Tablets can only be obtained on prescription from a doctor.

How do Rosuvastatin Tablets work?
Rosuvastatin Tablets contain the active ingredient rosuvastatin zinc which belongs to a group of medicines called statins. Rosuvastatin is 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 the body’s production of ‘bad’ cholesterol. It also improves the body’s ability to remove it from the 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 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. By lowering cholesterol levels, this reduces the risk of having a heart attack, a stroke or related health problems.
How have Rosuvastatin Tablets been studied?
Because Rosuvastatin Tablets are generic medicines, studies in patients have been limited to tests to
determine that they are bioequivalent to the reference products, Crestor® 5 mg, 10 mg, 20 mg and 40 mg
Tablets. Two medicines are bioequivalent when they produce the same levels of the active substance in
the body.

What are the benefits and risks of Rosuvastatin Tablets?
As Rosuvastatin Tablets are generic medicines that are bioequivalent to Crestor® 5 mg, 10 mg, 20 mg
and 40 mg Tablets, their benefits and risks are taken as being the same as Crestor® 5 mg, 10 mg, 20 mg
and 40 mg Tablets.

Why are Rosuvastatin Tablets approved?
It was concluded that, in accordance with EU requirements, Rosuvastatin Tablets have been shown to
have comparable quality and are bioequivalent to Crestor® 5 mg, 10 mg, 20 mg and 40 mg Tablets.
Therefore, the view was that, as for Crestor® 5 mg, 10 mg, 20 mg and 40 mg Tablets the benefits
outweigh the identified risks.

What measures are being taken to ensure the safe and effective use of Rosuvastatin Tablets?
A risk management plan 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 and the package leaflet for Rosuvastatin Tablets, including the appropriate precautions to
be followed by healthcare professionals and patients.

Other information about Rosuvastatin Tablets
Spain, Italy and the UK agreed to grant Marketing Authorisations for Rosuvastatin Tablets on 23 August
2016. Marketing Authorisations were granted in the UK on 21 September 2016.

The full PAR for Rosuvastatin Tablets follows this summary. For more information about treatment with
Rosuvastatin Tablets, read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in October 2016.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Introduction</td>
<td>5</td>
</tr>
<tr>
<td>II Quality aspects</td>
<td>6</td>
</tr>
<tr>
<td>III Non-clinical aspects</td>
<td>8</td>
</tr>
<tr>
<td>IV Clinical aspects</td>
<td>8</td>
</tr>
<tr>
<td>V User consultation</td>
<td>11</td>
</tr>
<tr>
<td>VI Overall conclusion, benefit/risk assessment and recommendation</td>
<td>11</td>
</tr>
</tbody>
</table>

Table of content of the PAR update for MRP and DCP Page 20
I INTRODUCTION

Based on the review of the data on quality, safety and efficacy the Member States considered that the applications for Rosuvastatin 5 mg, 10 mg, 20 mg and 40 mg Film-coated Tablets (PL 30306/0777-0780: UK/H/6263/01-04/DC), are approvable. The products are prescription-only medicines (POM) indicated for the following:

Treatment of hypercholesterolemia

Adults, adolescents and children aged 6 years or older with primary hypercholesterolemia (type IIa including heterozygous familial hypercholesterolemia) 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 hypercholesterolemia 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, as an adjunct to correction of other risk factors.

The applications were submitted using the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS), and Spain and Italy 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 medicinal products for these applications are Crestor 5mg, 10mg, 20mg and 40mg tablets, which were authorised to AstraZeneca B.V., The Netherlands (PL 17901/0201-0203 & PL 17901/0243) on 21 March 2003. The products used for the purpose of bioequivalence studies are Rosuvastatin 20 mg and 40 mg Tablets (AstraZeneca Reims, France).

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

With the exception of the bioequivalence studies, no new non-clinical or clinical studies were conducted, which is acceptable given that the applications were based on being generic medicinal products of originator products that have been licensed for over 10 years. Bioequivalence studies were carried out in accordance with Good Clinical Practice (GCP).

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.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

Both Member States agreed to grant Marketing Authorisations for the above products at the end of the procedure (Day 201 – 23 August 2016). After a subsequent national phase, the UK granted Marketing Authorisations (PL 30306/0777-0780) for these products on 21 September 2016.
II QUALITY ASPECTS

II.1 Introduction

The products are film-coated tablets. Each film-coated tablet contains 5 mg, 10 mg, 20 mg and 40 mg rosvastatin (corresponding to 5.34 mg, 10.68 mg, 21.36 mg or 42.72 mg rosvastatin zinc).

Other ingredients consist of the pharmaceutical excipients lactose monohydrate, crospovidone type A and B (E1202), povidone (E1201), magnesium stearate (E572) making up the tablet core, and the tablet coat composed of opadry II white 85F 18422 (polyvinyl alcohol (E1203), talc (E553b), macrogol 3350 (E1521) and titanium dioxide (E171)). Appropriate justification for the inclusion of each excipient has been provided.

All excipients comply with their respective European Pharmacopoeia monographs with the exception of opadry II white 85F 18422 which complies with an in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

The only excipient used that contains material of animal or human origin is lactose monohydrate. The applicant has provided a declaration that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption. Confirmation has also been given that the magnesium stearate used in the tablets is of vegetable origin.

The finished product is packed in oriented polyamide (OPA)/polyvinylchloride (PVC)/aluminium blisters. The pack sizes are 28, 56 and 84 tablets.

Not all pack sizes may be marketed.

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 zinc

Chemical name:

1) \((3R,5S,6E)-7-[4-(4-Fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-6-heptenoic acid zinc salt (2:1)\)

2) \(7-[4-(4-Fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-(3R,5S,6E)-6-heptenoic acid zinc salt (2:1)\)

3) \(3R,5S,6E)-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-3,5-dihydroxyhept-6-enoic acid zinc salt\)

Structural formula:

![Structural formula image]
Molecular formula: $\text{C}_{44}\text{H}_{54}\text{F}_2\text{N}_6\text{O}_{12}\text{S}_2\text{Zn}$
Molecular mass: 1026.46 g/mol
Appearance: White to off-white powder.
Solubility: Rosuvastatin zinc salt is freely soluble in ethanol, methylene chloride and dimethyl formamide at 37°C and slightly soluble in water and 2-propanol.

Rosuvastatin zinc is the subject of an active substance master file (ASMF).

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis. No materials of animal or human origin are used in the production of the active substance.

Appropriate proof-of-structure data have been supplied for the active substance. All potential impurities have been identified and monitored appropriately.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analysis data are provided and comply with the proposed specification.

Satisfactory Certificates of Analysis have been provided for all working standards.

Suitable specifications have been provided for all packaging used. The primary packaging has been shown to comply with current guidelines concerning contact with food.

Appropriate stability data have been provided supporting a suitable retest period when stored in the proposed packaging.

II.3. Medicinal Product
Pharmaceutical Development
The objective of the development programme was to formulate safe, efficacious tablets containing 5 mg, 10 mg, 20 mg or 40 mg of rosuvastatin per tablet that are generic versions of the reference products, Crestor 5mg, 10mg, 20mg & 40mg tablets (AstraZeneca UK Limited).

Comparative impurity and dissolution profiles have been presented for test and reference products.

Manufacture of the products
Satisfactory batch formulae have been provided for the manufacture of the products, along with an appropriate account of the manufacturing processes. The manufacturing processes have been validated and have shown satisfactory results. Process validation data on commercial scale batches have been provided.

Finished Product Specifications
The finished product specifications proposed are acceptable. The test methods that have been described have been adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for all working standards used.
Stability of the Products
Finished product stability studies were performed in accordance with current guidelines on batches of finished product in the packaging proposed for marketing. The data from these studies support a shelf life of 3 years with storage conditions “Store in the original package in order to protect from light”.

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 point of view.

III NON-CLINICAL ASPECTS

III.1 Introduction
The pharmacodynamic, pharmacokinetic and toxicological properties of rosuvastatin zinc are well-known. As this is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. An overview based on literature review is, thus, appropriate.

The non-clinical overview has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetic 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
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.5 Ecotoxicity/environmental risk assessment (ERA)
Since these products are intended for substitution of originator products, their use 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 point of view.

IV CLINICAL ASPECTS
These are generic applications submitted under the Decentralised Procedure according to Article 10(1) of Directive 2001/83/EC, as amended, for Rosuvastatin 5 mg, 10 mg, 20 mg and 40 mg Film-coated Tablets.

The pharmacodynamic, pharmacokinetic, clinical efficacy and safety properties of rosuvastatin are well known. As rosuvastatin is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. An overview based on literature review is considered appropriate.

The Applicant submitted two bioequivalence studies (Rosuvastatin 20 mg and 40 mg Tablets versus Crestor® 20mg and 40 mg Tablets) in support of these applications. A waiver from additional bioequivalence studies was requested for Rosuvastatin 5 mg and 10 mg Tablets.
The bioequivalence study with the 20 mg formulation was a repeat study that was conducted in 2013 in order to fulfil the additional requirement for performing an investigator-sponsored research (ISR) which was not a requirement when the study for the 40 mg formulation was performed in 2009. The Applicant explained that selection of the 20 mg strength is acceptable under CPMP/EWP/QWP/1401/98 Rev. 1/Corr**, which states that for products with linear pharmacokinetics and where the drug substance is highly soluble selection of a lower strength is also acceptable. Rosuvastatin belongs to BCS class III (high solubility substance) and has linear pharmacokinetics.

In addition, the Applicant discussed the increased reporting rate of adverse reactions with the 40 mg dose compared to lower doses. When designing the second bioequivalence study (20 mg formulation) it was considered that as the 40 mg dose is only indicated in patients with severe hypercholesterolaemia at high cardiovascular risk, who do not achieve their treatment goal on 20 mg and in whom routine follow-up will be performed, the 20 mg dose was more appropriate for the bioequivalence study in terms of subject safety, as well as being more representative of the product’s real-world clinical application.

With the exception of the bioavailability studies, no new clinical data have been submitted and none are required for applications of this type. The applicant’s clinical overview has been written by an appropriately qualified person and is considered acceptable.

IV.2 Pharmacokinetics
In support of these applications, the Marketing Authorisation Holder has submitted the following two bioequivalence studies:

**Study 1**
This is a single center, randomised, single dose, laboratory-blinded, 2-period, two-sequence, crossover comparative bioavailability study of Rosuvastatin 20mg Tablet and Crestor® 20mg Tablets (AstraZeneca Reims, France) in healthy, male subjects under fasting conditions.

Subjects received the test or reference treatment after an overnight fast of at least 10 hours. Blood samples were collected before dosing and up to and including 72 hours after drug administration. The washout period was 7 days.

**Results**
Pharmacokinetic parameters for rosuvastatin (In-transformed geometric mean, 90% Confidence Interval and test/Reference ratio)

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>INTRA-SUBJECT C.V. (%)</th>
<th>GEOMETRIC LSMEANS *</th>
<th>RATIO (%)</th>
<th>90% CONFIDENCE LIMITS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TEST</td>
<td>REFERENCE</td>
<td>LOWER</td>
<td>UPPER</td>
</tr>
<tr>
<td>C_max</td>
<td>17.9</td>
<td>8.997</td>
<td>9.508</td>
<td>89.37</td>
</tr>
<tr>
<td>AUC_T</td>
<td>13.7</td>
<td>85.481</td>
<td>86.430</td>
<td>94.57</td>
</tr>
</tbody>
</table>
* units are ng/mL for C_max and ng·h/mL for AUC_T

**Conclusion**
The 90% confidence intervals for C_max and AUC_T were within the pre-defined acceptance criteria specified in “Guideline on the Investigation of Bioequivalence” (CPMP/EWP/QWP/1401/98 Rev 1/Corr**). Bioequivalence has been shown for the test formulation (Rosuvastatin 20 mg Tablets) and the reference formulation (Crestor® 20 mg Tablets) under fasting conditions.
Study 2
This is a single center, randomised, single dose, laboratory-blinded, 2-period, two-sequence, crossover comparative bioavailability study of Rosuvastatin 40mg Tablet and Crestor® 40mg Tablets (AstraZeneca Reims, France) in healthy, male subjects under fasting conditions.

Subjects received the test or reference treatment after an overnight fast of at least 10 hours. Blood samples were collected before dosing and up to and including 72 hours after drug administration. The washout period was 7 days.

Results
Pharmacokinetic parameters for rosuvastatin (In-transformed geometric mean, 90% Confidence Interval and test/Reference ratio)

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>INTRA-SUBJECT C.V. (%)</th>
<th>GEOMETRIC LSMEANS *</th>
<th>RATIO (%)</th>
<th>90% CONFIDENCE LIMITS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.max</td>
<td>23.8</td>
<td>16.998</td>
<td>17.500</td>
<td>97.13</td>
</tr>
<tr>
<td>AUCₜ</td>
<td>16.2</td>
<td>159.030</td>
<td>160.600</td>
<td>99.02</td>
</tr>
</tbody>
</table>

* units are ng/mL for C.max and ng·h/mL for AUCₜ

Conclusion
The 90% confidence intervals for C.max and AUCₜ were within the pre-defined acceptance criteria specified in “Guideline on the Investigation of Bioequivalence” (CPMP/EWP/QWP/1401/98 Rev 1/Corr**). Bioequivalence has been shown for the test formulation (Rosuvastatin 40 mg Tablets) and the reference formulation (Crestor® 40 mg Tablets) under fasting conditions.

As the 5 mg and 10 mg strength test products meet the biowaiver criteria specified in the current bioequivalence guidance, the results and conclusions of the bioequivalence studies with the 20 mg and 40 mg tablet strengths can be extrapolated to the 5 mg and 10 mg strength tablets.

IV.3 Pharmacodynamics
No new data have been submitted and none are required for applications of this type.

IV.4 Clinical efficacy
No new data on efficacy have been submitted and none are 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)
The Marketing Authorisation Holder (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 mg, 10 mg, 20 mg and 40 mg Film-coated Tablets.
A summary of safety concerns, as approved in the RMP, is listed below:

<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 myoglobinemia (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>
<tr>
<td>Stevens-Johnson syndrome and toxic epidermal necrosis (SJS/TEN)</td>
</tr>
<tr>
<td>Tendon disorders</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
</tr>
<tr>
<td>Drug-drug interactions including ciclosporin, various protease inhibitor combinations with ritonavir, clopidogrel, gemfibrozil, eltrombopag, dronedarone, warfarin; other vitamin K antagonists, fusidic acid, and ezetimibe</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Important potential risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal failure (including acute and chronic renal failure) and renal impairment</td>
</tr>
<tr>
<td>Hepatic failure (including hepatic necrosis and fulminating hepatitis)</td>
</tr>
<tr>
<td>Amyotrophic lateral sclerosis (ALS)</td>
</tr>
<tr>
<td>Interstitial lung disease (ILS)</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>

Routine pharmacovigilance and routine risk minimisation are proposed for all safety concerns.

IV.7  Discussion on the clinical aspects
No new clinical data were submitted and none are required for applications of this type.

The grant of Marketing Authorisations is recommended for these applications.

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 Rosuvastatin Actavis 5mg, 10mg, 20mg and 40mg tablets (PT/H/0518/0535/001-4/DC). The bridging report submitted by the applicant is acceptable.

VI Overall conclusion, benefit/risk assessment and recommendation
The quality of the products is acceptable, and no new non-clinical or clinical concerns have been identified. Extensive clinical experience with rosuvastatin zinc is considered to have demonstrated the therapeutic value of the compound. The benefit risk assessment is, therefore, considered to be positive.
Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for Rosuvastatin 5 mg, 10 mg, 20 mg and 40 mg Film-coated Tablets is presented below:

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

BLISTER PACK CARTON

1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 5mg Film-coated Tablets

2. STATEMENT OF ACTIVE SUBSTANCE (S)

Each film-coated tablet contains 5mg of Rosuvastatin (as rosuvastatin zinc).

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

28 film-coated tablets
56 film-coated tablets
84 film-coated 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

Store in the original package in order to protect from light.

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
Actavis Group PTC ehf.
Reykjavíkurvegi 76-78
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER (S)

PL 30306/0777

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

rosuvastatin 5mg film-coated tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 5mg Film-coated Tablets

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Actavis Logo

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

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

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
BLISTER PACK CARTON

1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 10mg Film-coated Tablets

2. STATEMENT OF ACTIVE SUBSTANCE (S)

Each film-coated tablet contains 10mg of Rosuvastatin (as rosuvastatin zinc).

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

28 film-coated tablets
56 film-coated tablets
84 film-coated 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

Store in the original package in order to protect from light.

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
Actavis Group PTC ehf.
Reykjavikurvegi 76-78
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER (S)

PL 30306/0778

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

rosuvastatin 10mg film-coated tablets

**MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS**

**BLISTERS**

1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 10mg Film-coated Tablets

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Actavis Logo

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. OTHER
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BLISTER PACK CARTON

1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 20mg Film-coated Tablets

2. STATEMENT OF ACTIVE SUBSTANCE (S)

Each film-coated tablet contains 20mg of Rosuvastatin (as rosvastatin zinc).

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

28 film-coated tablets
56 film-coated tablets
84 film-coated 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

Store in the original package in order to protect from light.

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
Actavis Group PTC ehf.
Reykjavíkaurvægi 76-78
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER (S)

PL 30306/0779

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

rosuvastatin 20mg film-coated tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 20mg Film-coated Tablets

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Actavis Logo

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. OTHER
PARTICULARS TO APPEAR ON THE OUTER PACKAGING
BLISTER PACK CARTON

1. NAME OF THE MEDICINAL PRODUCT
Rosuvastatin 40mg Film-coated Tablets

2. STATEMENT OF ACTIVE SUBSTANCE (S)
Each film-coated tablet contains 40mg of Rosuvastatin (as rosvastatin zinc).

3. LIST OF EXCIPIENTS
Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS
28 film-coated tablets
56 film-coated tablets
84 film-coated 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
Store in the original package in order to protect from light.

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
Actavis Group PTC chf
Reykjavíkurvegi 76-78
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER (S)

PL 30306/0780

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

rosuvastatin 40mg film-coated tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Rosuvastatin 40mg Film-coated Tablets

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Actavis Logo

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. OTHER
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 the procedure</th>
<th>Date of end of procedure</th>
<th>Approval/ non approval</th>
<th>Assessment report attached Y/N (version)</th>
</tr>
</thead>
</table>
