TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR RUISUFA® 5 MG (ROSUVASTATIN CALCIUM EQUIVALENT TO ROSUVASTATIN 5 MG) FILM COATED TABLETS

Version number 1.0

14 April, 2022

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1. Introduction

RUISUFA® 5 mg is a generic medicine of Crestor 5 mg film- coated tablets of Astra Zeneca is a blood cholesterol-lowering drug of statin family. 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. RUISUFA® 5 mg is approved in Tanzania for use in adults, adolescents, and children aged 6 years or older.

1.1 Product details

Registration number	TAN 21 HM 0176
Brand name	RUISUFA® 5 mg
Generic name, strength, and form	Each film coated tablet contains: Rosuvastatin Calcium Equivalent to Rosuvastatin 5 mg
ATC classification	ATC code: C10A A07- HMG-CoA reductase inhibitors
Distribution category	POM
Country of origin	India
Associated product	RUISUFA® 10 mg Film-Coated Tablets
Marketing Authorization Holder	B&O PHARM ZAC de la Masquère - 500 rue de l'Hers - 31750 ESCALQUENS, France Email address: l.serena@tridem-pharma.com
Local Technical Representative	Tridem Pharma Tanzania Limited P.O. Box 23145, Dar es Salaam, Tanzania E-Mail: b.aloyce@tridem-pharma.com

1.2 Assessment procedure

The application for registration of RUISUFA® 5 mg was submitted on 02 June 2020. The product underwent full assessment. Assessment was completed in 3 (three) rounds of evaluation and the product was registered on 29 March 2021.

1.3 Information for users

Visual description of the finished product	Film-coated tablet with peach color (from orange to peach for visual difference), biconvex and round tablet, two sides are both smooth.
Primary packing material	Al-PA/Al/PVC blister
Secondary packing materials	A printed carton box
Shelf-life and storage condition	24 months, Do not store above 30°C.Store in the original package in order to protect from moisture
Route of administration	Oral
Therapeutic indications	Treatment of hypercholesterolaemia

	Adults, adolescents and children aged 6 years or older with primary hypercholesterolaemia (type IIa includingheterozygous 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, as an adjunct to correction of other risk factors.

2. Labelling and product information

Summary of product characteristics
The SmPC included all the relevant information to ensure correct and safe use of the medicine by healthcare providers. The complete SmPC can be accessed here.

Package insert/leaflet
The package insert is confirmed to be derived from the SmPC and contains sufficient data for the end user. Since the product is POM, the package insert contains full prescribing information as per SmPC.

Container labels
The product label information is presented in English. Details in the secondary pack label include:
Brand name: RUISUFA® 5 mg

Composition: Rosuvastatin calcium equivalent to 5 mg Rosuvastatin

Pack size:28 tablets

Manufacturing details: batch number, manufacturing date, and expiry date

Storage conditions: Do not store above 30°C. Store in the original package in order to protect from moisture

Manufacturer address: physical address of release site

Unique identifier: Not applicable

Special warnings/precautions or instructions for use: Excipient with notorious effects: lactose monohydrate -For details please see the leaflet

The details of the primary pack include:

Brand name and strength: RUISUFA® 5 mg

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: ZHEJIANG JINGXIN PHARMACEUTICAL CO., LTD

The content of the primary and secondary labels was aligned to the requirements of the Part V of the Compendium: Guidelines on Format and Content of Product Labels for Medicinal products. The label contains sufficient information for proper identification of the medicine and post marketing follow up of the product.

Mock labels are appended as annex I.

3. Scientific discussion

Quality of Active Pharmaceutical Ingredients

Information on the quality of the API was submitted in form of DMF.

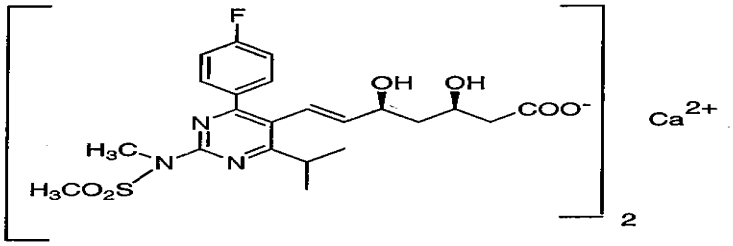
General Information

Rosuvastatin calcium API is compendia in USP and BP/Ph. Pharmacopeia.

Molecular formula: $C_{44}H_{54}F_2N_6O_{12}S_2.Ca$

Chemical name:
(3R,5S)-7-[4-(4-phlorophenyl)-6-isopropyl-2-[methyl(methylsulphonyl)amino]pirimidyn-5-yl]-3,5-dihydroxy-6(E)-heptenoicacid calcium salt (2:1)
Or
6-Heptanoic acid-7-[4-(4-phloropheny)-6-(1-methylethyl)-2-[methyl(methylsulphonyl)amino]-5-primidinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)
Or
Bis[(E)-7[4-(4-phlorophenyl)-6-isopropyl-2-methyl(methylsulphonyll)amino]pirimidyn-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid] calcium salt

Structure:



General properties

The active substance is a white to light yellow powder and is soluble in dimethylformamide, acetone and acetonitrile and is insoluble in water. It shows polymorphism. The molecule has 2 chiral centres; the manufacturer consistently produces the correct isomer and the same polymorphic form. Enantiomeric purity is controlled routinely by suitable analytical methods.

According to Biopharmaceutics Classification System (BCS), Rosuvastatin calcium is classified as Class 2 compound (low solubility, high permeability) hence particle size distribution (PSD) is considered critical parameter and form part of the API specifications.

Manufacture

Rosuvastatin calcium API manufacturer is Shangyu Jingxin Pharmaceutical Co., Ltd, No.31 Weisan Road, Zhejiang Hangzhou Bay, Shangyu Economic and Technological Development Area, Shangyu, Zhejiang Province, the People's Republic of China. The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by the Food and Drugs Administration, Republic of China. Rosuvastatin calcium API is manufactured by chemical synthesis using conventional techniques. Sufficient controls of quality of materials and in-process checks were employed throughout the manufacturing process.

Specifications

The API specifications were set as per in-house standards and ICHQ3A. The parameters monitored during quality control are: appearance, optical rotation, identification of API and calcium, test for calcium content, test for chloride, heavy metals, water content, enantiomeric purity, related substances, assay, residual solvents, and particle size. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Rosuvastatin calcium API is 36 months when packed in low density polythene bag in an aluminum foil bag filled with nitrogen contained inside a fiber drum when store at 10-20°C.

Quality of the Finished Pharmaceutical Product

Formulation

RUISUFA® 5 mg is a film-coated tablet with peach color (from orange to peach for visual difference), biconvex and round tablet, two sides are both smooth

RUISUFA® 5 mg contains the Rosuvastatin calcium and other ingredients listed here after: lactose monohydrate, microcrystalline cellulose, crospovidone, magnesium oxide, silicon dioxide magnesium stearate, hypromellose, titanium dioxide, triacetin, lactose monohydrate, FD&C yellow# sunset yellow, FCF aluminum lake, FD&C red# allura red AC aluminum lake, FD&C blue# indigo carmine FCF aluminum lake. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, 8th Edition in terms of function and quantities.

Manufacture

The finished product manufacturer is Zhejiang Jingxin Pharmaceutical Co., Ltd., No.800 Xinchang East Road, Yulin Subdistrict, Xinchang County, Zhejiang, China. The compliance of the site to TMDA GMP standards was confirmed through site inspection on 18-19 December, 2016.

Specifications

The FPP is compendia in BP and USP. The manufacturer controls the quality of the finished product as per in-house standards and ICH requirements. The parameters monitored during quality control are: appearance, identification, uniformity of dosage units, dissolution, related substances, assay, microbial enumeration tests, and test for specified microorganisms. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on a 3 (three) batches of the finished product stored at 30 ± 2°C & RH: 75 ± 5% RH for 24 months and 40± 2°C & RH: 75% ± 5% RH for 6 months. Based on the stability data presented, the approved shelf-life is 36 months when stored in Al-PA/Al/PVC blister with storage condition ‘Do not store above 30°C. Store in the original package in order to protect from moisture’.

Safety and efficacy information

The biowaiver was approved based on additional strength.

RUISUFA® 5 mg fulfilled the criteria for waiving an in-vivo bioequivalence study as per relevant TMDA guidance. Dissolution profiles of lower strength-RUISUFA® 5 mg (Rosuvastatin 5 mg) Tablets manufactured by Zhejiang Jingxin Pharmaceutical Co., Ltd, was compared higher strength used in the in vivo bioequivalence study-RUISUFA® 10 mg (Rosuvastatin 10 mg) manufactured by Zhejiang Jingxin Pharmaceutical Co., Ltd.At least 85% of the labelled amount of Rosuvastatin had dissolved within 15 minutes in three different media (pH 1.2, pH 4.5 and pH 6.6). Therefore, confirming similarity.

4. Benefit-Risk Assessment and Conclusion

On basis of the data submitted, the current state of knowledge and compliance to Good Manufacturing Practice, the benefit of the product outweighs the risks associated with its use when used in accordance to the summary of product characteristics. RUISUFA® 5 mg is recommended for registration.

5. Post-approval updates

Variation applications

Reference number	Date submitted	Change requested	Recommendation	Granting date

Feedback from pharmacovigilance, post marketing surveillance and enforcement activities

Type of feedback	Impact	Response

Re-registration applications

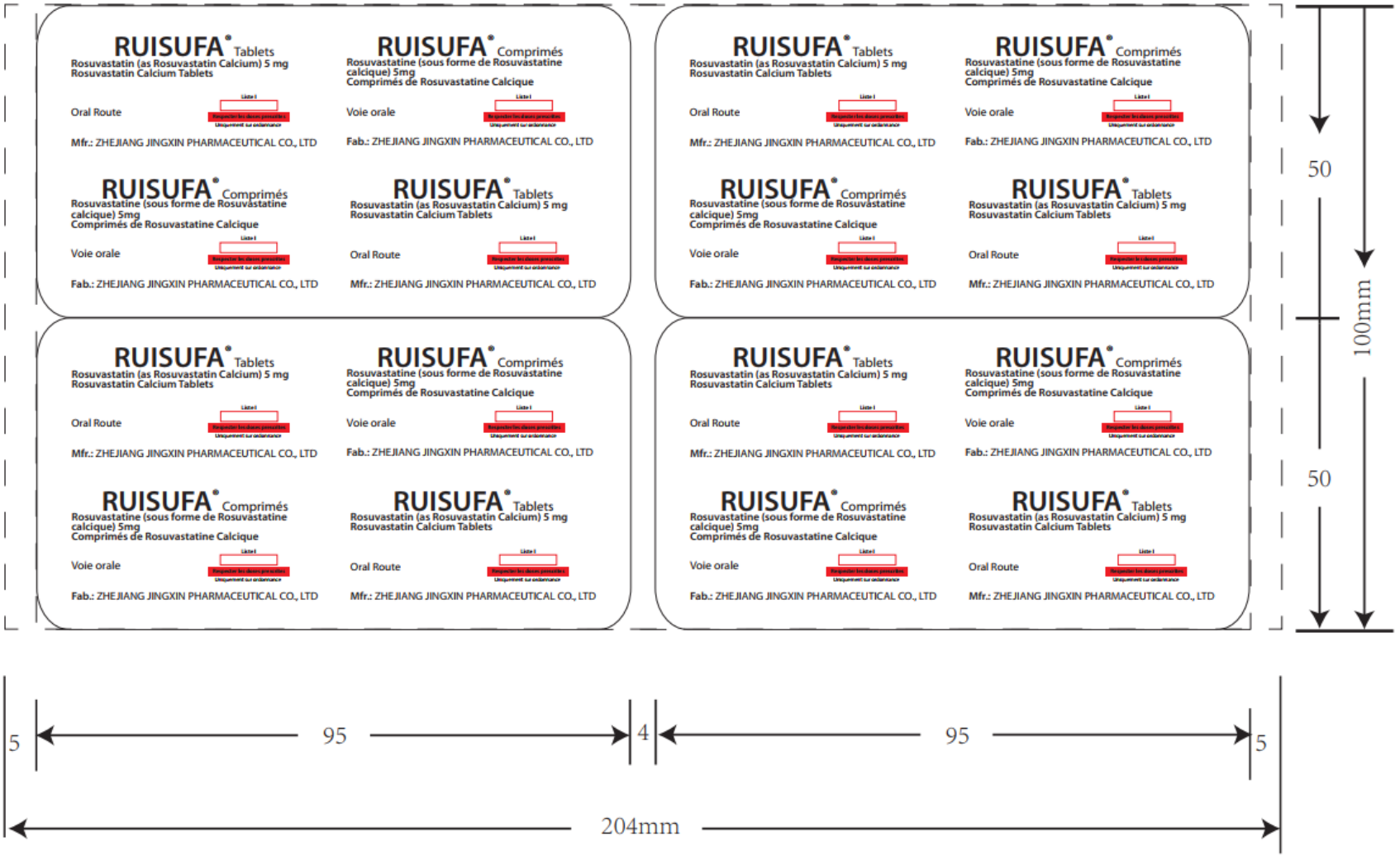
NA

PART 5: CHANGE HISTORY

Version number	Date	Description of update	Section(s) Modified	Approval date

Annex I: Mock up labels;

Primary pack label;



Secondary pack label;