THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR AURITZ 10 (ROSUVASTATIN CALCIUM EQUIVALENT TO ROSUVASTATIN 10 MG) FILM- COATED TABLETS

Version number 01, 06/01/2023

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1. Introduction

Auritz 10 is a generic medicine of Crestor 10 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.

Auritz 10 is approved in Tanzania for treatment of Treatment of hypercholesterolaemia in adults, adolescents and children aged 6 or older with primary hypercholesterolaemia and prevention of cardiovascular events.

1.1 Product details

Registration number	TAN 22 HM 0412
Brand name	Auritz 10
Generic name, strength and form	Each film-coated tablet contains 10 mg of rosuvastatin as rosuvastatin calcium
ATC classification	HMG-CoA reductase inhibitors ATC code: C10A A07
Distribution category	POM
Country of origin	India
Associated product	The finished product is presented as a film-coated tablet containing 10 mg & 20 mg of rosuvastatin calcium as active substance
Marketing Authorization Holder	Mega Lifesciences Public Company Limited. 384 Soi 6, Pattana 3 Road,Bangpoo Industrial Estate, Mood 4,Praeksa,Muang, Samutprakarn, Samutprakarm 10280 Thailand
Local Technical Representative	Mega Wecare Tanzania Limited, P.O.BOX 1899, Nyerere Road,10 Vingunguti Dar es Salaam

1.2 Assessment procedure

The application for registration of Auritz 10 was submitted on 22/11/2021. The product underwent full assessment. Assessment was completed in one round of evaluation. Auritz 20 was registered on 21/09/2022.

1.3 Information for users

Visual description of the finished product	Pink, round, biconvex, coated tablets, debossed "062" on one sideand plain on other side
Primary packing material	Pack of 3 x 10's tablets in Alu-Alu pack
Secondary packing materials	Carton box alongside with a package insert
Shelf-life and storage condition	24 months Store below 30°C, Protect from light and moisture
Route of administration	Oral
Therapeutic indications	Auritz 10 are indicated for treatment Primary hypercholesterolaemia (type IIa including heterozygous familial hypercholesterolaemia) or mixed dyslipidaemia (type IIb) as an adjunct to diet when response to diet and other nonpharmacological 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

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 that is intended for long term use, the package insert contains both full prescribing information as per SmPC and simplified information for patients.

Container labels

The product label information is presented in English. Details in the secondary pack label include:

Brand name: Auritz 10

Composition: Each film-coated tablet contains 10 mg of rosuvastatin as rosuvastatin calcium
Pack size: 3 x 10's tablets
Manufacturing details: batch number, manufacturing date, expiry date
Storage conditions: Store below 30°C in its own pack
Manufacturer address: Inventia Healthcare Limited F1-F1/1-F75/1, Additional Ambernath M.I.D.C. Ambernath (East), Thane 421 506, Maharashtra state, India

Unique identifier: N/A
Special warnings/precautions or instructions for use: This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

The details of the primary pack include:
Brand name and strength: Auritz 20
Manufacturing details: batch number, manufacturing date, expiry date
Name of manufacturer: Inventia Healthcare Limited F1-F1/1-F75/1, Additional Ambernath M.I.D.C. Ambernath (East), Thane 421 506, Maharashtra state, India

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 Ingredient(s)

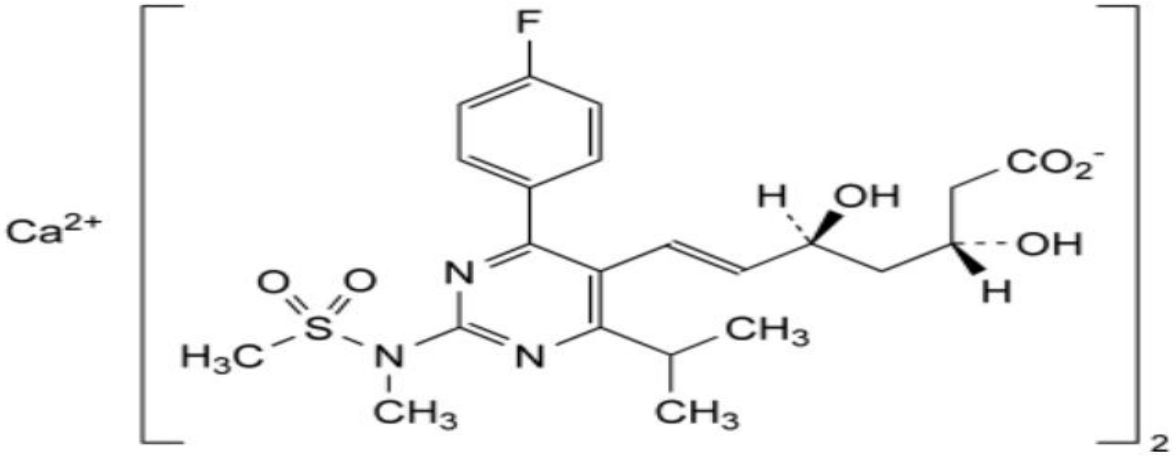
Information on quality of the API was submitted in form of full details.

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

Molecular formula: $C_{44}H_{54}CaF_2N_6O_{12}S_2$

Chemical names:
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:



Critical physico-chemical properties are:

The active substance rosuvastatin calcium is an established active substance described in the European Pharmacopoeia (Ph.Eur.)/USP. The active substance is a white to almost white powder. It is freely soluble in methylene chloride, slightly soluble in water and practically insoluble in anhydrous ethanol. Rosuvastatin calcium is an optically active molecule, having two stereogenic centres and hence 4 possible stereoisomers. The substance used is the 3R,5S isomer. The amorphous form is produced.

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

Manufacture

The API manufacturing sites, Hetero Drugs Limited; Unit-IX, Plot No.1, Hetero Infrastructure SEZ Ltd, N. Narasapuram (Village), Nakkapalli (Mandal), Visakhapatnam District-531 081, Andhra Pradesh, India and Dr. Reddy's Laboratories Limited, Chemical Technical Operations, Unit-V Peddadevulapalli, Tripuraram Mandal Nalgonda District, Telangana, India – 508 207, India were noted to comply with WHO GMP requirements as evidenced by the GMP certificates issued by ←----------->. 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 USP standards and ICH guidelines. The parameters monitored during quality control are: Appearance, solubility, Identification (IR), chemical test for Calcium, Water (by KF), Assay (HPLC), Enantiomeric purity (HPLC), related substances (HPLC), polymorphic, particle size distribution and residual solvents. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The stability results indicate that the active substance manufactured by the proposed supplier is stable and justify the proposed retest period of 60 months when stored in the proposed container.

Quality of the Finished Pharmaceutical Product

Formulation

Auritz 10 is presented as Pink, round, biconvex, coated tablets, debossed "062" on one sideand plain on other side.

Auritz 20 contains Microcrystalline Cellulose PH-122 NF, Lactose Monohydrate (SD250) NF, Carboxymethyl cellulose Calcium NF, Magnesium stearate NF, Opadry Pink 03K54121 IH, Purified water USP/Ph. Eur. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, Edition 8^{th} in terms of function and quantities. Ingredient, lactose is of safety concern therefore appropriate warnings were included in the product label.

Film coat: Composition of Opadry Pink 03K54121 IH; Hypromellose, Titanium Dioxide, Triacetin and Red Iron Oxide

Manufacture

The finished product was manufactured at Inventia Healthcare Limited F1-F1/1-F75/1, Additional Ambernath M.I.D.C. Ambernath (East), Thane 421 506, Maharashtra state, India. The compliance of the site to TMDA GMP standards was confirmed through physical inspection on 25/01/2019

Specifications

The FPP is compendia in EP/USP. The manufacturer controls the quality of the finished product as per USP standards and ICH requirements. The parameters monitored during quality control are: appearance, identity (HPLC and UV spectrum and coloring agents), average mass and Uniformity of mass, Dissolution (By HPLC), degradation products (HPLC), assay (HPLC) and microbial purity. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on three (3) batches of the finished product stored at 30 ± 2°C & 75% ± 5% RH for 24 months and 40 ± 2°C & 75% ± 5% RH for 6 months. Based on available stability data, the proposed shelf-life of 24 months is acceptable.

Safety and efficacy information

The Bio-equivalence study was carried out on Auritz 40. Based on acceptable Bioequivalence study for Auritz 40, a bio-waiver is requested for Auritz 10.

The biowaiver was approved based on additional strength. In relation to the strength biowaiver, comparative dissolution studies have been provided for Auritz 10 strength and the Auritz 40 bio batch in pH 1.2, pH 4.5 acetate buffer and pH 6.8 phosphate buffer. The study demonstrated similarity of the dissolution profiles and thus from this point of view the biowaiver has been accepted.

4. Benefit-Risk Assessment and Conclusion

On basis ofthe 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 Auritz 10 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

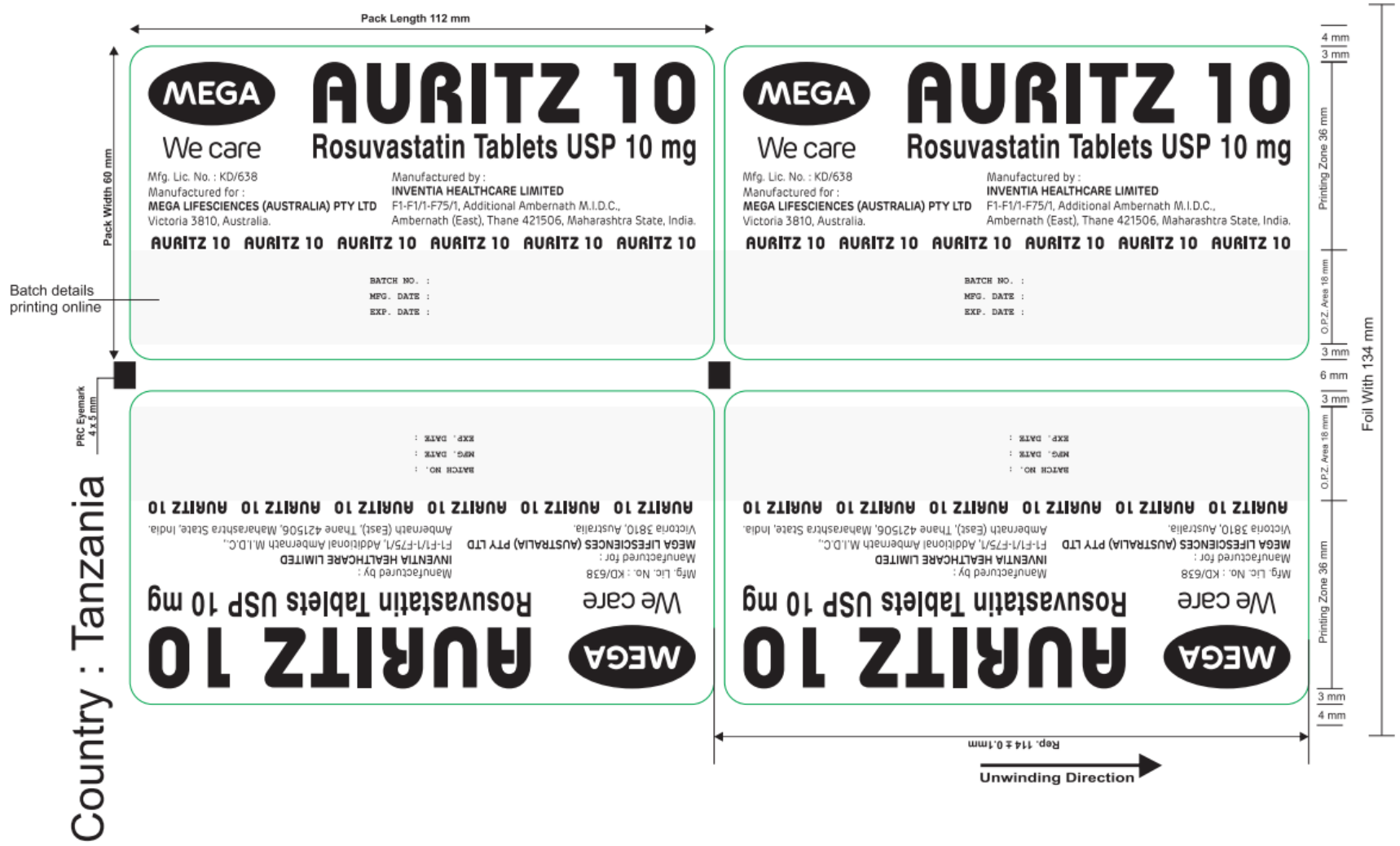
Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

PART 5: CHANGE HISTORY

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

Annex I: Mock up label

Primary artwork



Secondary artwork