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MINISTRYOFHEALTH

TANZANIAMEDICINES ANDMEDICALDEVICESAUTHORITY

PUBLIC ASSESSMENT REPORT FOR LOSARZED 50 (LOSARTAN POTASSIUM 50 MG FILM COATED TABLETS)

Version number 1.0
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1. Introduction

Losarzed 50 is a generic medicine of Losartan film-coated tablets. Losarzed 50 is an antihypertensive medicine belonging to C09CA01- Angiotensin II antagonists group. Losarzed 50 exerts is activity by blocking angiotensin-II receptor (type AT1) found in many tissues (e.g. vascular smooth muscle, adrenal gland, kidneys and the heart) and elicits several important biological actions, including vasoconstriction and the release of aldosterone . Losarzed 50 is approved in Tanzania for use in adults, children and adolescents 6-18 years of age.

1.1 Product details

Registration number	TAN 20 HM 0195
Brand name	Losarzed 50
Generic name, strength and form	Losartan Potassium Tablets BP 50 mg
ATC classification	C09CA01- Angiotensin II antagonists
Distribution category	POM
Country of origin	India
Associated product	NA
Marketing Authorization Holder	Zota Health Care Limited, Ropar plot no 169, Sursez, GIDC, Sachin, Surat, Gujarat 394230 India. Telephone: 0261 233 1601 E-Mail: kamleshzota@zotahealthcare.com
Local Technical Representative	Moraf Pharmaceuticals Limited, Kipande street, Kariakoo, P.o. box 21323, Dar es salaam

1.2 Assessment procedure

The application for registration of Losarzed 50 was submitted on 13/02/2018. The product underwent full assessment. Assessment was completed in 5 rounds of evaluation. Losarzed 50 was registered on 25/07/2020.

1.3 Information for users

Visual description of the finished product	Blue colour, round standard biconvex film coated tablet, plain on both side
Primary packing material	Alu –ALU Blister of 10’s
Secondary packing materials	Blisters packed in a carton box along with a package insert
Shelf-life and storage condition	36 Months

	Store below 30ºC.Protect from moisture
Route of administration	Oral
Therapeutic indications	• Treatment of essential hypertension in adults and in children and adolescents 6-18 years of age. • Treatment of renal disease in adult patients with hypertension and type 2 diabetes mellitus with proteinuria ≥ 0.5 g/day as part of an antihypertensive treatment (see sections 4.3, 4.4, 4.5, and 5.1). • Treatment of chronic heart failure in adult patients, when treatment with Angiotensin converting enzyme (ACE) inhibitors is not considered suitable due to incompatibility, especially cough, or contraindication. Patients with heart failure who have been stabilised with an ACE inhibitor should not be switched to losartan. The patients should have a left ventricular ejection fraction ≤ 40% and should be clinically stable and on an established treatment regimen for chronic heart failure. • Reduction in the risk of stroke in adult hypertensive patients with left ventricular hypertrophy documented by ECG (see section 5.1 LIFE study, Race).

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 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: Losarzed 50

Composition: Losartan Potassium Tablets BP 50 mg

Pack size: 3 x 10’s

Manufacturing details: batch number, manufacturing date, expiry date

Storage conditions: Store below 30ºC
Manufacturer address: Zota Health Care Limted, Plot NO.169,Sursez,Near Sachin Railway Station,Sachin-394230, Surat,Gujarat State, India.
Unique identifier:
Special warnings/precautions or instructions for use: The product contains lactose

The details of the primary pack include:
Brand name and strength:
Manufacturing details: <batch number, manufacturing date, expiry date>
Name of manufacturer: <name only>

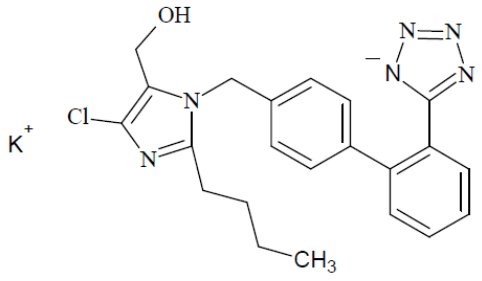
The content of the primary and secondary labels was aligned to the requirements of the Part V of the Compendium: Guidelines on Format and Content of Product Labels for Medicinal products. The label contains sufficient information for proper identification of the medicine and post marketing follow up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

3. Scientific discussion

Quality of Active Pharmaceutical Ingredient(s)

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

General properties
Losartan Potassium API is compendia in USP/BP.
Molecular formula: $C_{22}H_{22}ClKN_6O$
Chemical name: Potassium 5-[4'-[[2-butyl-4-chloro-5- (hydroxymethyl)-1H-imidazol-1-yl]methyl] biphenyl-2-yl]tetrazol-1-ide
Structure:



Critical physico-chemical properties of the API were freely soluble in water and in methanol, slightly soluble in acetonitrile, hygroscopic and exhibits polymorphism.

Manufacture
The API manufacturing site, Alembic Limited (API Plant – II) (Formerly Nirayu Pvt. Ltd.), Panelav, P.O. Tajpura, Taluka-Halol, District-Panchmahal,-389 350 Gujarat, India was noted to

comply with WHO GMP requirements as evidenced by the GMP certificate issued by Food and Drugs Control Administration. Losartan Potassium 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 BP/Ph.Eur standards and ICHQ3A. The parameters monitored during quality control are: appearance, solubility, identification, related substances, assay and residual solvents.Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Losartan Potassium API is 60 months when packed in translucent LPDE bags in in triple laminated bags kept in HDPE drums and stored at 25ºC ± 2ºC.

Quality of the Finished Pharmaceutical Product

Formulation

Losarzed 50 is a blue colour, round standard biconvex film-coated tablet, plain on both side

. Losarzed 50 contains Losartan Potassium and other ingredients listed hereafter:

Microcrystalline cellulose, Lactose, Colloidal Silicon Dioxide, Crospovidone, Magnesium Stearate, Colour Coat Brilliant Blue, Methylene Chloride and Isopropyl Alcohol. 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.

Manufacture

The finished product was manufactured at Zota Health Care Limited, Plot NO.169,Sursez,Near Sachin Railway Station,Sachin-394230, Surat,Gujarat State, India.
The compliance of the site to TMDA GMP standards was confirmed through site inspection on 14/05/2016.

Specifications

The FPP is compendia in BP. The manufacturer controls the quality of the finished product as per BP and in-house standards and ICHQ3B requirements. The parameters monitored during quality control are: appearance, weight uniformity, diameter, thickness, disintegration time, identification, related substances,microbial contamination and residual solvents . Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on 3 batches of the finished product stored at 30°C ± 2°C, 65 % ± 5 % for 36 months and 40°C ± 2°C, 75 % ± 5 % for 6 months. Based on the stability data presented, the approved shelf-life is 36 months when stored in Alu-Alu blister at below 30ºC.

Safety and efficacy information

Safety and efficacy of Losarzed 50 was established through biowaiver application.
Comparative dissolution report was submitted.

In case of biowaiver
The biowaiver was approved based on BCS classification.

Losarzed 50 fulfilled the criteriafor waiving an in-vivo bioequivalence study as per relevant TMDA guidance. Dissolution profiles of Losarzed 50 tablets was compared to COOZAR 50 mg Film-coated Tablets.At least > 85% of the labelled amount of Losartan had dissolved in all three media. Therefore, confirming similarity.

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. Losarzed 50 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