TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR METAPROL (METOPROLOL TARTRATE 50 MG) FILM COATED TABLETS

Version number 0.1

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1. Introduction

Metaprol is a generic medicine of metoprolol tartrate. Metaprol is an antihypertensive medicine belonging to dihydropyridine group. Metaprol exerts is activity by blocking beta-receptor sites hence decreasing the blood pressure. Metaprol is approved in Tanzania for use in <adults, children, elderly etc>.

1.1 Product details

Registration number	TAN 21 HM 0121
Brand name	Metaprol
Generic name, strength and form	Metaprolol Tartrate 50 mg Tablets
ATC classification	C07AB02
Distribution category	POM
Country of origin	India
Associated product	Nil
Marketing Authorization Holder	Lincoln Pharmaceuticals Limited Trimul Estate, Khatraj, Taluka: Kalol, District: Gandhinagar Gujarat, India.
Local Technical Representative	Heko Pharmacy Ltd, P. O. Box 2657, Plot No.32/57, Sikukuu/Tandamti Street, Kariakoo, Dar es Salaam

1.2 Assessment procedure

The application for registration of Metaprol was submitted on 05.03.2019. The product underwent full assessment. Assessment was completed in three (3) rounds of evaluation. Metaprol was registered on 29/03/2021.

1.3 Information for users

Visual description of the finished product	White to off white coloured, round shaped, biconvex, plain on both sides, film coated tablets
Primary packing material	Alu/PVDC blister pack of 5x10's
Secondary packing materials	Carton box
Shelf-life and storage condition	Shelf life, Store below 30^0C
Route of administration	Oral
Therapeutic indications	Indicated for management of hypertension (alone or in Combination with other Hypertensive agents), angina Pectoris, Cardiac arrhythmias especially; Supraventricular tachyarrhythmias, Migraine prophylaxis, adjunct to treatment of Hyperthyroidism, long term Prophylaxis after recovery from acute myocardial infarction

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:
Composition: Metaprolol Tartrate 50 mg Tablets, Contains lactose
Pack size: Alu/PVDC blister pack of 5x10's in a carton box
Manufacturing details: batch number, manufacturing date, expiry date
Storage conditions: store below 30^0C. Protect from light.
Manufacturer address: Lincoln Pharmaceuticals Limited, Trimul Estate, Khatraj, Tal. Kalol, Dist. Gandhinagar, Gujarat, India

Unique identifier: barcode

Special warnings/precautions or instructions for use: Keep the medicine out of reach of children

The details of the primary pack include:
Brand name and strength: Metaprol 50 mg
Manufacturing details: batch number, manufacturing date, expiry date
Name of manufacturer: Lincoln Pharmaceuticals 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.

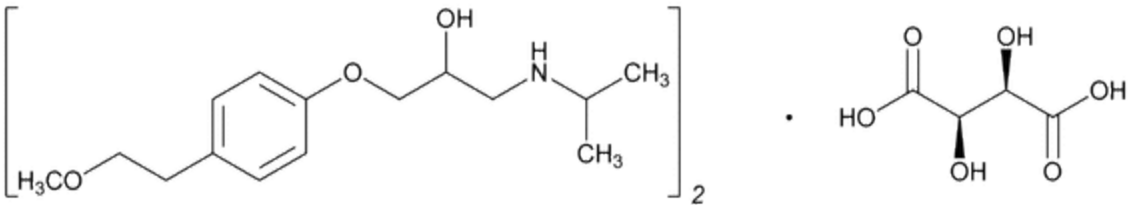
3. Scientific discussion

Quality of Active Pharmaceutical Ingredient(s)

Information on quality of the API was submitted in form of full detail as per Compendia requirements.

General properties
Metoprolol API is compendia in USP/BP.
Molecular formula: $(C_{15}H_{25}NO_3)_2.C_4H_6O_6$
Chemical name: 2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]-, (±)-, [R-(R*,R*)]-2,3-dihydroxy butanedioate (2:1) (salt);

Structure:



Manufacture

The API manufacturing site, IPCA Laboratories Limited, Village – Sejavta, Ratlam (Madhya Pradesh), Gujarat, India was noted to comply with WHO GMP requirements. Metoprolol 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/BP standards and ICHQ3A. The parameters monitored during quality control are: description, solubility, identification, specification rotation, pH, loss on drying, residue on ignition, related substances, residual solvents and assay. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of metoprolol API is 60 months when packed in Double white LDPE poly bags in FIBRE/ HMHDPE container and stored between 15-30°C.

Quality of the Finished Pharmaceutical Product

Formulation

Metaprolol is a White to off white coloured, round shaped, biconvex, plain on both sides, film coated tablets in ALU/PVDC blister pack then in a carton box. Metaprolol contains Metoprolol tartrate API and other ingredients listed here after; lactose monohydrate, microcrystalline cellulose, sodium starch glycolate (Type-A), sodium lauryl sulfate, povidone (P.V.P.K-30), croscarmellose sodium, purified talc, colloidal anhydrous silica (aerosil), magnesium stearate, colour white SC-SP-3180 (spraycel), isopropyl alcohol (IPA), dichloromethane (methylene dichloride) and purified water. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, Edition 7th 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 Lincoln Pharmaceuticals Limited, Trimul Estate, Khatraj, Tal. Kalol, Dist. Gandhinagar, Gujarat, India. The compliance of the site to TMDA GMP standards was confirmed through site inspection on 19th October, 2018.

Specifications

The FPP is compendia in BP/USP. The manufacturer controls the quality of the finished product as per reference monograph (BP/USP) and ICHQ3B requirements. The parameters monitored during quality control are: description, identification, average weight, uniformity of dosage units, diameter, thickness, disintegration, dissolution, assay, related substances and microbial limits. 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/65% ± 5% RH for 24 months and 40° ± 2°C/75% ± 5% RH for 6 months. Based on the stability data presented, the approved shelf-life is 24 months when stored in Alu/PVDC blister pack at 30°C.

In case of biowaiver

The biowaiver was approved based on BCS classification.

Metaprol fulfilled the criteria for waiving an in-vivo bioequivalence study as per relevant TMDA guidance. Dissolution profiles of Metaprol 50 mg Tablet was compared to Lopressor Tablets 50 mg. Less than 85% of the labelled amount of metoptolol had dissolved in all three media. Therefore, necessitating calculation of similarity factor f2, which was noted to be above 50.

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. Metaprol 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 label