THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR LINEZOLID 600 MG FILM COATED TABLETS

Version number 1.0
21 August, 2023

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1. Introduction

Linezolid is a synthetic, antibacterial agent that belongs to a new class of antimicrobials, the oxazolidinones. It has in vitro activity against aerobic Gram-positive bacteria and anaerobic microorganisms. Linezolid selectively inhibits bacterial protein synthesis via a unique mechanism of action. Specifically, it binds to a site on the bacterial ribosome (23S of the 50S subunit) and prevents the formation of a functional 70S initiation complex which is an essential component of the translation process. Linezolid 600 mg film coated tablet is approved in Tanzania for use in adults only.

Product details

Registration number	TAN 23 HM 0244
Brand name	N/A
Generic name, strength, and form	Linezolid 600 mg
ATC classification	J01XX08, Antibacterials for systemic use, other antibacterials
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Lupin Limited 3rd Floor, Kalpataru Inspire, Off W.E Highway, Santacruz (East), Mumbai – 400055, India
Local Technical Representative	Talemwa Investment Consulting Company Limited Sinza Mori “A”, Ubungo, PO Box 31179, Dar Es Salaam,

1.1 Assessment procedure

The application for registration of Linezolid 600 mg film coated tablet was submitted in 08/04/2020. The product underwent abridged assessment. Assessment was completed in 2 (two) rounds of evaluation and the product was registered on 01/06/2023.

1.2 Information for users

Visual description of the finished product	White to off white coloured, oval shaped, bevealed edges, biconvex film coated tablets having score on one side and plain on other side
Primary packing material	Clear PVC/PVDC Blister pack and Clear PVC Blister pack
Secondary packing materials	Printed carton box
Shelf-life and storage condition	24 months, Do not above 30°C. Protect from moisture.
Route of administration	Oral

Therapeutic indications	Linezolid is indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the specific conditions listed below. Linezolid is not indicated for the treatment of Gram-negative infections. It is critical that specific Gram-negative therapy be initiated immediately if a concomitant Gram-negative pathogen is documented or suspected Pneumonia Nosocomial pneumonia caused by Staphylococcus aureus (methicillin-susceptible and resistant isolates) or Streptococcus pneumoniae Community-acquired pneumonia caused by Streptococcus pneumoniae, including cases with concurrent bacteremia, or Staphylococcus aureus (methicillin-susceptible isolates only) Skin and Skin Structure Infections Complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis, caused by Staphylococcus aureus (methicillin-susceptible and – resistant isolates), Streptococcus pyogenes, or Streptococcus agalactiae. Linezolid has not been studied in the treatment of decubitus ulcers Uncomplicated skin and skin structure infections caused by Staphylococcus aureus (methicillin susceptible isolates only) or Streptococcus pyogenes. Vancomycin-resistant Enterococcus faecium Infections Vancomycin-resistant Enterococcus faecium infections, including cases with concurrent bacteremia

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: N/A

Composition: Linezolid 600 mg

Pack size: 10x10 tablets

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

Storage conditions: Do not above 30°C. Protect from moisture.

Manufacturer address: physical address of release site

Unique identifier: Not applicable

Special warnings/precautions or instructions for use: The product contains lactose monohydrate

The details of the primary pack include:

Brand name and strength: N/A

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: Lupin Limited

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

Information on the quality of the API was submitted in form of WHO Prequalification proof.

General Information

Linezolid API is compendia in USP.

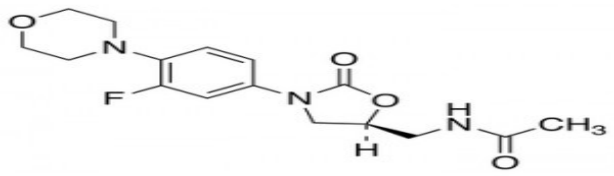
Molecular formula: $C_{16}H_{20}FN_3O_4$

Chemical name:

a. N-[[(5 S)-3-[3-Fluoro-4-(4-morpholinyl) phenyl]-2-oxo -5- oxazolidinyl]methyl] acetamide

b. (S)-N -[[3-[3-Fluoro-4-(4morpholinyl)phenyl]-2-oxo-5-oxazolidinyl] methyl]-acetamide.

Structure:



General properties

The active substance is a white to off-white crystalline powder, which is freely soluble in chloroform and sparingly soluble in methanol. The substance exhibits at least three polymorphic forms, and one chiral center. Linezolid has the S- configuration. the polymorph manufactured is Form-II.

Manufacture

Linezolid API manufacturer is SYMED LABS LIMITED (Unit -1), Block -A, Survey No.353, Domadugu (Village), Gummadidala (Mandal), Sanga Reddy (Dist). 502 313, Telangana, INDIA. The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by the WHO. Linezolid 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

Specifications

The API specifications were set as per USP, in-house standards and ICHQ3A. The parameters monitored during quality control are: description, solubility, identification by HPLC and IR, residue on ignition, related substances, water content, assay, residual solvents, enantiomeric impurity, polymorphism, and particle size. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The retest period of Linezolid API is 36 months when packed in original container with storage condition 'Do not store above 25°C, protect from moisture'

Quality of the Finished Pharmaceutical Product

Formulation

Linezolid 600 mg film coated tablet is a white to off-white colored, oval shaped, beveled edges, biconvex, film coated tablets, plain on both sides.

Linezolid 600 mg film coated tablet contains the Linezolid and other ingredients listed here after: lactose monohydrate, polacrilin potassium, hypromellose, colloidal silica dioxide, magnesium stearate, hydroxy propyl methyl cellulose, polyethylene glycol, titanium dioxide, purified water. 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 Lupin Limited, EPIP, SIDCO Industrial Complex, Kartholi, Bari Brahmana, Jammu (J&K)- 181133, India. The compliance of the sites to TMDA GMP standards was confirmed through site inspection on DD/MM/YYYY.

Specifications

The FPP is compendia. The manufacturer controls the quality of the finished product as per in-house standards and ICH requirements. The parameters monitored during quality control are: description, identifications of the API (HPLC, UV) and colorant, average weight, disintegration, water content, uniformity of dosage units (by weight variation), dissolution (HPLC detection), degradation products (HPLC), assay (HPLC), tablet divisibility by average mass, and microbiological examination of non-sterile products. Compliance to the standard was established using batch analysis data and stability data.

Stability and container closure system

Stability studies were conducted on 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 24 months when stored in clear PVC/PVDC

blister pack or clear PVC blister pack with storage condition ‘Do not store above 30°C. Protect moisture’.

Safety and efficacy information

Lupin’s Linezolid 600 mg film coated tablet is already registered by WHO. Information on clinical data has been fully evaluated during the registration of the product (Refer: WHO pre-qualification reference Number TB350). In this context, re-assessment of this part is not considered as necessarily required.

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. Linezolid 600 mg film coated tablet 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

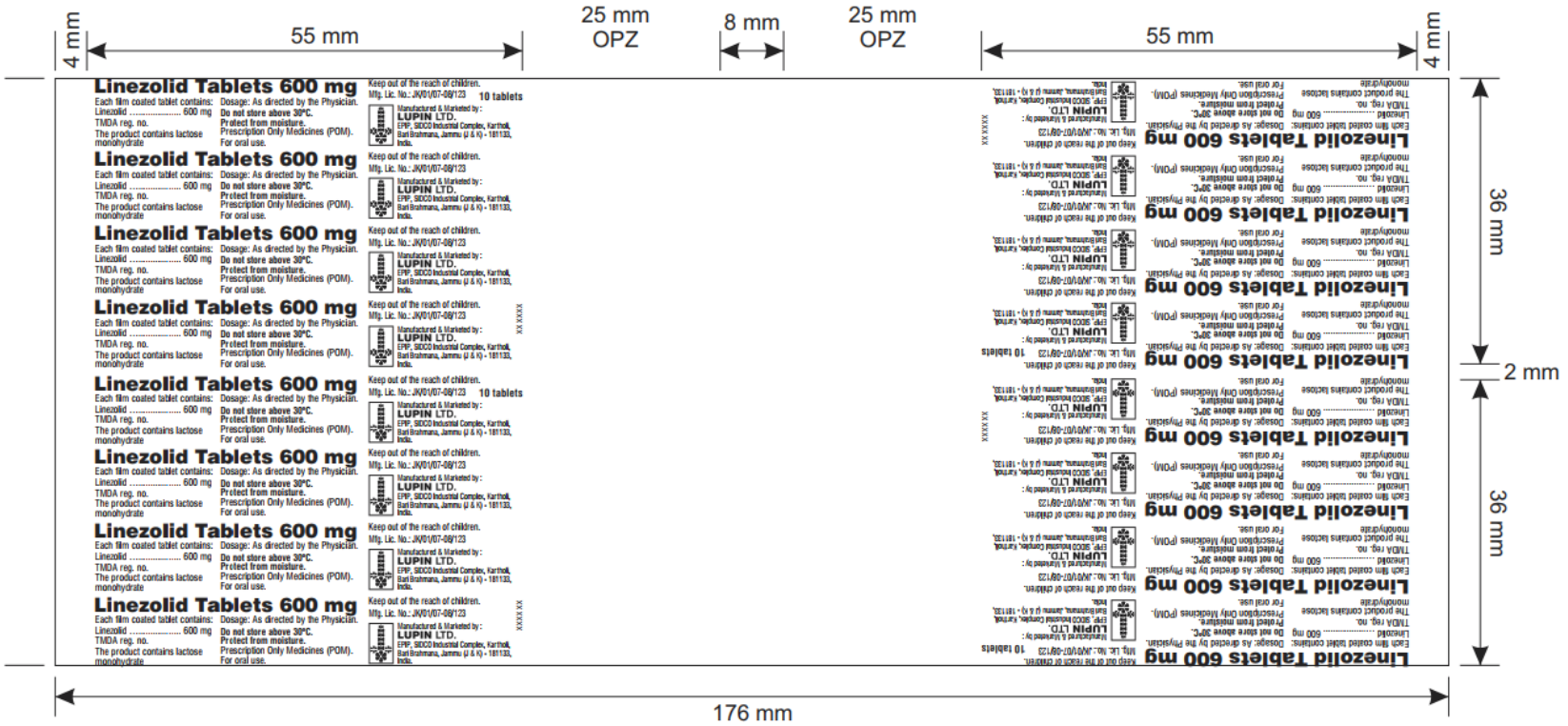
Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

PART 5: CHANGE HISTORY

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

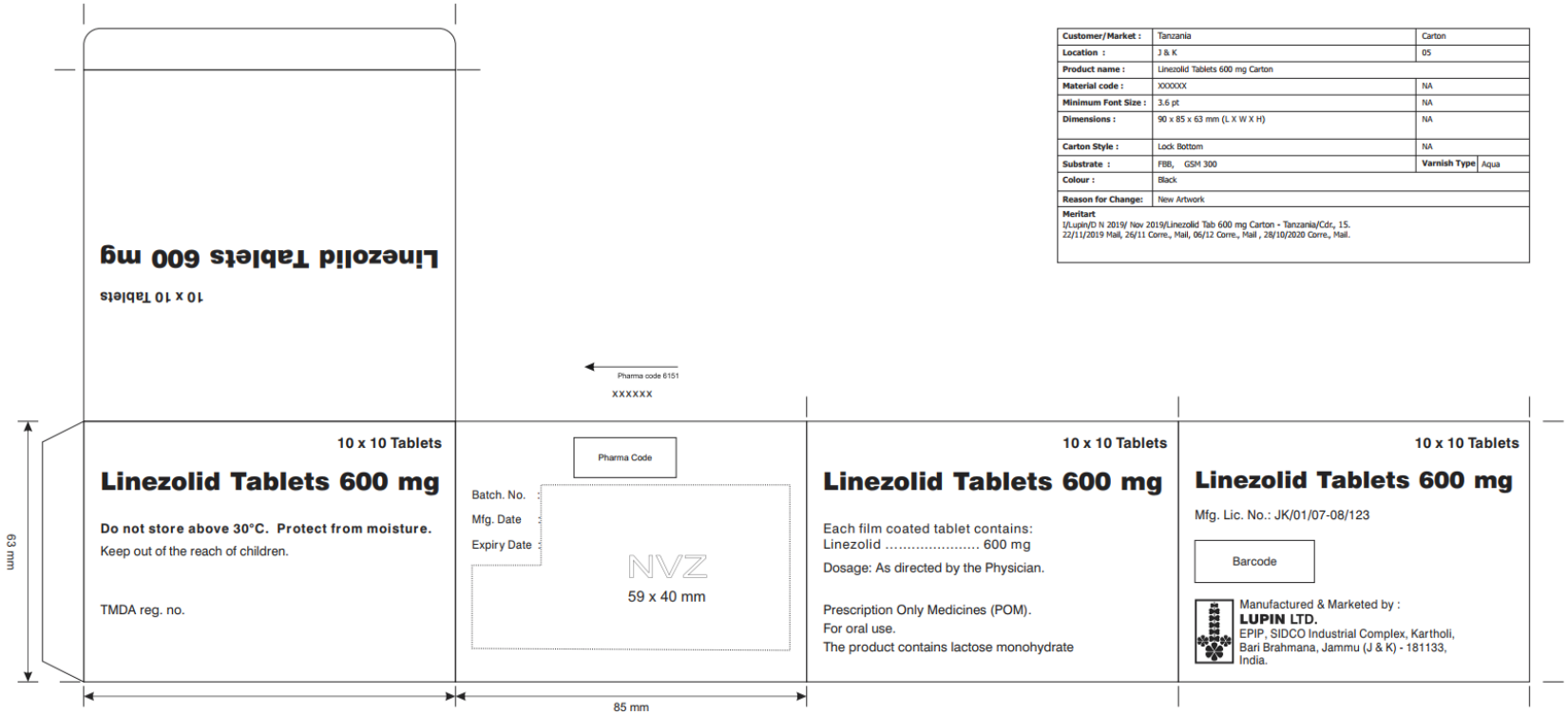
Annex I: Mock up labels;

Primary pack label;



Effective date: 03/10/2022

Secondary pack label:



Customer/Market :	Tanzania	Carton
Location :	J & K	05
Product name :	Linezolid Tablets 600 mg Carton	
Material code :	XXXXXX	NA
Minimum Font Size :	3.6 pt	NA
Dimensions :	90 x 85 x 63 mm (L X W X H)	NA
Carton Style :	Lock Bottom	NA
Substrate :	FBB, GSM 300	**Varnish Type** Aqua
Colour :	Black	
Reason for Change:	New Artwork	
Meritart I/Lupin/D N 2019/ Nov 2019/Linezolid Tab 600 mg Carton - Tanzania/Cdr., 15. 22/11/2019 Mail, 26/11 Corre., Mail, 06/12 Corre., Mail , 28/10/2020 Corre., Mail.		

Effective date: 03/10/2022