THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR LOXAMOX (LEVOFLOXACIN (AS HEMIHYRDATE) 250MG/50ML) SOLUTION FOR INJECTION

Version number 1.0
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1. Introduction

Loxamox (250mg/50ml levofloxacin hemihydrate) solution for Injection is a generic medicine of Tavanic 5 mg/ml solution for infusion from sanofi aventis. Loxamox solution for Injection contains levofloxacin hemihydrate which is a synthetic antibacterial agent of the fluoroquinolone class; it is the S-enantiomer of the racemic drug substance ofloxacin. As a fluoroquinolone antibacterial agent, levofloxacin acts on the DNA-DNA-gyrase complex and topoisomerase IV. Loxamox solution for Injection is approved in Tanzania for use in adults only.

Product details

Registration number	TAN 23 HM 0237
Brand name	Loxamox
Generic name, strength, and form	Each ml contains 5 mg of levofloxacin as levofloxacin hemihydrate
ATC classification	Antibacterial for systemic use, fluoroquinolone. ATC code: J01MA12
Distribution category	POM
Country of origin	India
Associated product	Loxamox 500mg/100ml Solution for Infusion
Marketing Authorization Holder	MS Pharma Jordan King Abdulla (II) Bin Al-Hussein Industrial Estate Amman-Jordan
Local Technical Representative	Wide Spectrum (T) Limited P.O. Box: 90518 Dar Es Salaam

1.1 Assessment procedure

The application for registration of Loxamox was submitted on 05/09/2017. The product underwent full assessment. Assessment was completed in 3 (three) rounds of evaluation and the product was registered on 01/06/2023.

1.2 Information for users

Visual description of the finished product	Green yellowish clear solution
Primary packing material	Polyolefin bag and closed with a plug
Secondary packing materials	Printed carton box
Shelf-life and storage condition	24 months, Do not store above 30 °C
Route of administration	Intravenous
Therapeutic indications	Levofloxacin is indicated in combination with other tuberculosis medicines for the treatment of drug-resistant tuberculosiss due to Mycobacterium tuberculosis. It is also indicated as monotherapy for the prevention of multidrug-resistant tuberculosis in persons at risk.

	Treatment regimens should follow the most recent WHO treatment guidelines, supplemented by other authoritative guidelines

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: Loxamox

Composition: Each ml contains 5 mg of levofloxacin as levofloxacin hemihydrate

Pack size: 50 mL

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

Storage conditions: Do not above 30°C

Manufacturer address: physical address of release site

Unique identifier: Not applicable

Special warnings/precautions or instructions for use: Not applicable

The details of the primary pack include:

Brand name and strength: Loxamox

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: MS Pharma Jordan

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

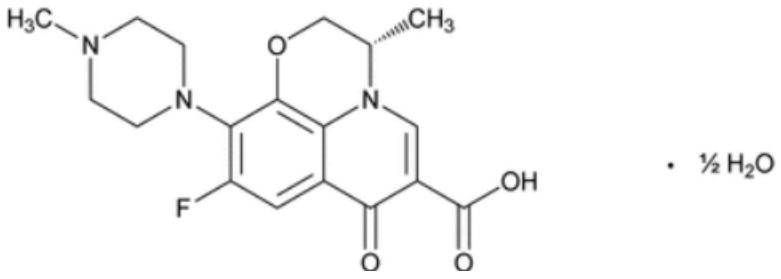
Levofloxacin hemihydrate API is compendia in USP, Ph.Eur., and BP.

Molecular formula: $C_{18}H_{20}FN_3O_4 \cdot ½H_2O$

Chemical name:

(S)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H- pyrido[1, 2,3-de]-1,4-benzoxazine-6- carboxylic acid, hemihydrate

Structure:



General properties

The active substance is yellowish crystalline powder freely soluble in acetic acid, slightly soluble in water, methanol and ethanol. The substance does not show polymorphism. The manufacturer consistently produces the same polymorphic form. Nonetheless, this is not considered important as the active substance is present in solution in the finished product. The active is present in the drug product dissolved in water, hence the polymorphic form and particle size distribution are not considered as critical quality aspects.

Manufacture

Levofloxacin hemihydrate API manufacturer is Shangyu Jingxin Pharmaceutical Co.,Ltd. No 31, Weisan Road,Zhejiang Hangzhou Bay, Shangyu Industrial area, Shangyu city,Zhejiang Province, P.R.China, 3122369, China. The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by the China Food and Drug Administration. Levofloxacin hemihydrate 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 ICHQ3A. The parameters monitored during quality control are: Description, identity by IR and HPLC, specific rotation, residue on ignition, organic impurities, heavy metals, optical rotation, water, 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 Levofloxacin hemihydrate API is 24 months when packed in original container with storage condition 'airtight container, protected from light,2-8 °C'.

Quality of the Finished Pharmaceutical Product

Formulation

Loxamox is a green yellowish clear solution.

Loxamox contains the Levofloxacin hemihydrate and other ingredients listed here after: sodium chloride, hydrochloric acid, water for injection. 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 MS Pharma Jordan, King Abdulla (II) Bin Al-Hussein Industrial Estate, Amman-Jordan. The compliance of the sites to TMDA GMP standards was confirmed through site inspection on DD/MM/YYYY.

Specifications

The FPP is non-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, identification, pH, extractable volume, particulate contamination, assay of API, related impurities, bacterial endotoxins, weight loss, and sterility. 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 Polyolefin bag and closed with a plug with storage condition 'Do not above 30°C'

Safety and efficacy information

Loxamox solution for Injection is a parenteral formulation and therefore fulfils the exemption mentioned in the part III: guidelines on therapeutic equivalence requirements, which states that a bioequivalence study is not required if the solutions for injection that contain the same active ingredients and excipients in the same concentrations as currently registered products and which are administered by the same route(s). The quantitative composition of Loxamox solution for Injection is entirely the same as the reference products in the market. Therefore, it may be considered as therapeutic equivalent, with the same efficacy/safety profile as known for the active substance of the reference medicinal product. The current product can be used instead of its reference product

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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. Loxamox 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;

Secondary pack label:

Effective date: 03/10/2022