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MINISTRYOFHEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR ISONIAZID 300 MG TABLETS

Version number 1.0
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1. Introduction

Isoniazid is a generic medicine of Isonizaid tablets. Isoniazid is a an antimycobacterial medicine belonging to J04AC01 – Antimycobacterials, hydrazides group. Isoniazid exerts is activity by inhibiting the synthesis of long chain mycolic acids, which are unique constituents of mycobacterial cell wall. Isoniazid is approved in Tanzania for use in adults and children.

1.1 Product details

Registration number	TAN 20 HM 0238
Brand name	Isoniazid
Generic name, strength and form	Isoniazid 300 mg tablets
ATC classification	J04AC01 – Antimycobacterials, hydrazides
Distribution category	POM
Country of origin	india
Associated product	NA
Marketing Authorization Holder	Micro labs Limited, 31, Race Course Road, Bangalore, **India** **E-mail:** jainethesh@microlabs.in
Local Technical Representative	**Pyramid Pharma** Plot 46-48, Mikocheni Light Industrial Area, Opp. Coca Cola Kwanza, P.O. Box 16215, Dar es Salaam. Tanzania E-mail: aokore@pyramidpharma.com

1.2 Assessment procedure

The application for registration of Isoniazid was submitted on 17/04/2020. The product underwent abridged assessment. Assessment was completed in 1 round of evaluation. Isoniazid was registered on 09/07/2020.

1.3 Information for users

Visual description of the finished product	White to off- white, circular, beveled edge, uncoated tablets with break line on one surface
Primary packing material	Alu/PVC Blister
Secondary packing materials	In a conventional carton box
Shelf-life and storage condition	48 months Do not store above 30°C. Store tablets in blisters in the provided carton
Route of administration	Oral
Therapeutic indications	Isoniazid Tablets BP 100 mg is indicated for the

	treatment of tuberculosis caused byMycobacterium tuberculosis

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 simplified information for patients.

Container labels
The product label information is presented in English. Details in the secondary pack label include:
Brand name:
Composition: <generic name & strength, list of excipients (if applicable)>
Pack size: <primary & secondary pack>
Manufacturing details: <batch number, manufacturing date, expiry date>
Storage conditions: <state the condition as it appears on the label>
Manufacturer address: <physical address of release site>
Unique identifier: <state the unique identification used>
Special warnings/precautions or instructions for use: <include warnings or IFU if applicable>

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.

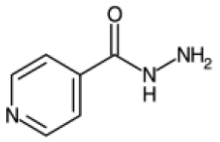
3. Scientific discussion

Quality of Active Pharmaceutical Ingredient(s)

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

General properties

Isoniazid API is compendia in USP and Ph.Eur.
Molecular formula: $C_6H_7N_3O$
Chemical name: 4-pyridine carboxylic acid hydrazide, ii) pyridine- 4-carboxyhydrazide, iii) pyridine-4-carbohydrazide and iii) pyridine--carboxylic acid hydrazide
Structure:



Critical physico-chemical properties of the API were freely soluble in water, sparingly soluble in alcohol, and very slightly soluble in ether.

Manufacture

The API manufacturing site, Amsal Chem Private Limited, A-1/ 401 -402-403, G.I.D.C. Area, Ankleshwar 393 002, Dist. Bharuch, Gujarat, India was noted to comply with WHO GMP requirements as evidenced by WHO prequalification. Isoniazid 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,solubility, identification, infrared absorption, pH, loss on drying, residue on ignition, assay, related substance, residual solvents, methyl alcohol, benzene, pyridine, particle size distribution, bulk density, melting range, metal impurities and impurity E. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Isoniazid API is 60 months when packed in Double polyethylene LDPE bag+Fibre / HDPE drum and stored at 30°C.

Quality of the Finished Pharmaceutical Product

Formulation

Isoniazid tablets is a white to off white, flat, circular, beveled edge, uncoated tablets with break line on one surface. Isoniazid tablets contains Isoniazid and other ingredients listed hereafter: lactose monohydrate, microcrystalline cellulose, colloidal silicon dioxide and hydrogenated castor oil. The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, Edition 8th in terms of function and quantities. Ingredient lactose monohydrate is of safety concern therefore appropriate warnings were included in the product label.

Manufacture

The finished product was manufactured at Micro Labs Limited (Unit -3), 92, Sipcot Industrial Complex, Hosur-635 126, Tamilnadu, India. The compliance of the site to TMDA GMP standards was confirmed through site inspection on 8th - 9th December 2016.

Specifications

The FPP is compendial in BP. The manufacturer controls the quality of the finished product as per BP,in-house and ICHQ3B requirements. The parameters monitored during quality control are: appearance, identification, average mass, uniformity of mass, dimensions (diameter,thickness), hardness, friability, disintegration time, dissolution , assay, microbial count, related substances, divisibility, water.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 30ºC ± 2ºC/75% ± 5% RH for 60 months and 40ºC ± 2ºC/75% ± 5% RH for 6 months. Based on the stability data presented, the approved shelf-life is 48 months when stored in Alu/PVC/EVOH/Aclar blister at below 30ºC .

Safety and efficacy information

Safety and efficacy of Isoniazid tablets was established through WHO prequalification procedure.

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. Isoniazid tablets 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