THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR ISONIAZID 300 MG FILM COATED TABLETS

Version number 1.0
16 January, 2022

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1. Introduction

Mylan's Isoniazid 300 mg tablets is a generic medicine of Isoniazid tablet, 300 mg (Sandoz Inc. USA) contains isoniazid (antimycobacterial (J04AC01)). Isoniazid is highly active against Mycobacterium tuberculosis. It is bactericidal against actively dividing tubercle bacilli. It inhibits the synthesis of long-chain mycolic acids, which are unique constituents of mycobacterial cell wall. Mylan's Isoniazid 300 mg tablets is approved in Tanzania for use in adults, adolescents and children weighing over 21 kg.

1.1 Product details

Registration number	TAN 22 HM 0297
Brand name	N/A
Generic name, strength, and form	Each tablet contains 300 mg isoniazid
ATC classification	Isoniazid: antimycobacterial (J04AC01)
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Mylan Laboratories Limited Plot No. 564/A/22, Road No. 92, Jubilee Hills, Hyderabad, Telangana – 500 096, India
Local Technical Representative	Synermed Pharmaceuticals (Tanzania) Limited Plot No 31/32 Makaburini, Nyerere road, Dar-es-salaam,

1.2 Assessment procedure

The application for registration of Isoniazid 300 mg tablets was submitted on 07/10/2022. The product underwent abridged assessment. Assessment was completed in 2 (two) rounds of evaluation and the product was registered on 01 June 2023.

1.3 Information for users

Visual description of the finished product	White to off-white, round, biconvex, beveled edge tablet debossed with M on one side and IS1 on the other side
Primary packing material	HDPE bottle (with desiccant) HDPE bottle pack with desiccant comprising of round wide mouth white HDPE bottle with white opaque polypropylene screw cap with aluminium induction sealing liner wad. Pack sizes: 30 tablets HDPE bottle (without desiccant)

	HDPE bottle pack comprising of round wide mouth white HDPE bottle with white opaque polypropylene screw cap with aluminium induction sealing liner wad. Pack sizes: 30 tablets
Secondary packing materials	A printed carton box
Shelf-life and storage condition	24months, do not store above 30°C. Store in the original container. Store the tablets in blisters in the provided carton. Protect from light
Route of administration	Oral
Therapeutic indications	Isoniazid Tablets BP 300 mg is indicated for the treatment of tuberculosis, caused by Mycobacterium 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 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: Isoniazid

Composition: Each tablet contains 300 mg isoniazid

Pack size: 30's tablets

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

Storage conditions: Do not store above 30°C, Store in the original container. Store the tablets in blisters in the provided carton. Protect from light

Manufacturer address: physical address of release site

Unique identifier: Not applicable

Special warnings/precautions or instructions for use: See enclosed leaflet

The details of the primary pack include:

Brand name and strength: Isoniazid 300 mg tablets

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: Mylan Laboratories 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 quality of the API was submitted in form of WHO Prequalification proof.

General Information

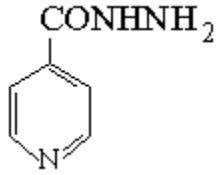
Isoniazid API is compendia in Ph.Int., Ph.Eur., and USP.

Molecular formula: $C_6H_7N_3O$

Chemical name:

Pyridine-4-carbohydrazide

Structure:



General properties

Isoniazid is a white or almost white, crystalline powder or colourless crystals. It is freely soluble in water, sparingly soluble in alcohol. Based on scientific principles the WHO Prequalification Team – Medicines (PQTm) has identified isoniazid (up to 300mg oral dose) as a BCS class 3 API. The API is thus BCS highly soluble.

Manufacture

Isoniazid API manufacturer is Second Pharma Co., Ltd, Hangzhou Gulf Fine Chemical Zone, Shangyu City, Zhejiang Province312369 P. R. China, DUNS NO: 527973171. The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by the WHO. 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

Specifications

The API specifications were set as per Ph. Eur. standards and ICHQ3A. The parameters monitored during quality control are: description (visual), solubility, identification (melting point, IR, and DSC), pH, appearance of solution, impurity E (HPLC), other related substances (HPLC), loss on drying, sulphated ash, assay (titrimetric), particle size of powders (sieve), manganese content, and residual solvents (GC). 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 24 months when packed in the original packing material when “Do not store above 30°C. Protect from light”.

Quality of the Finished Pharmaceutical Product

Formulation

Isoniazid 300 mg tablets is a white to off-white, round, biconvex, beveled edge tablet debossed with M on one side and IS1 on the other side contains the Isoniazid and other ingredients listed here after: mannitol, microcrystalline cellulose, croscarmellose sodium, povidone, pregelatinized starch, colloidal anhydrous silica and stearic acid. 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 manufacturers are Mylan Laboratories Limited, Plot No. H-12 & H-13, MIDC, Waluj Industrial Area, Aurangabad. – 431136, Maharashtra State, India. The compliance of the sites to TMDA GMP standards was confirmed through site inspection on DD/MM/YYYY.

Specifications

The FPP is compendium. The manufacturer controls the quality of the finished product as per BP standards and ICH requirements. The parameters monitored during quality control are: description, identification tests by IR and UV, disintegration, dissolution, uniformity of dosage units by mass variations, loss on drying, assay, related substances and microbial counts. 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 HDPE bottles with and without desiccants with storage condition ‘Do not store above 30°C, Store in the original container. Store the tablets in blisters in the provided carton. Protect from light’.

Safety and efficacy information

The product is pre-qualified by WHO on 26 September, 2017with WHO reference TB285 and has active status. Manufacturing sites of both API and FPP as declared under this application were confirmed to be the same as the one indicated in the WHO pre-qualification list which can be accessed through //extranet.who.int/pqweb/medicine/41029.Hence this section was not evaluated since it was already done by WHO Prequalification Team – Medicines (PQTm).

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. Isoniazid 300 mg 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

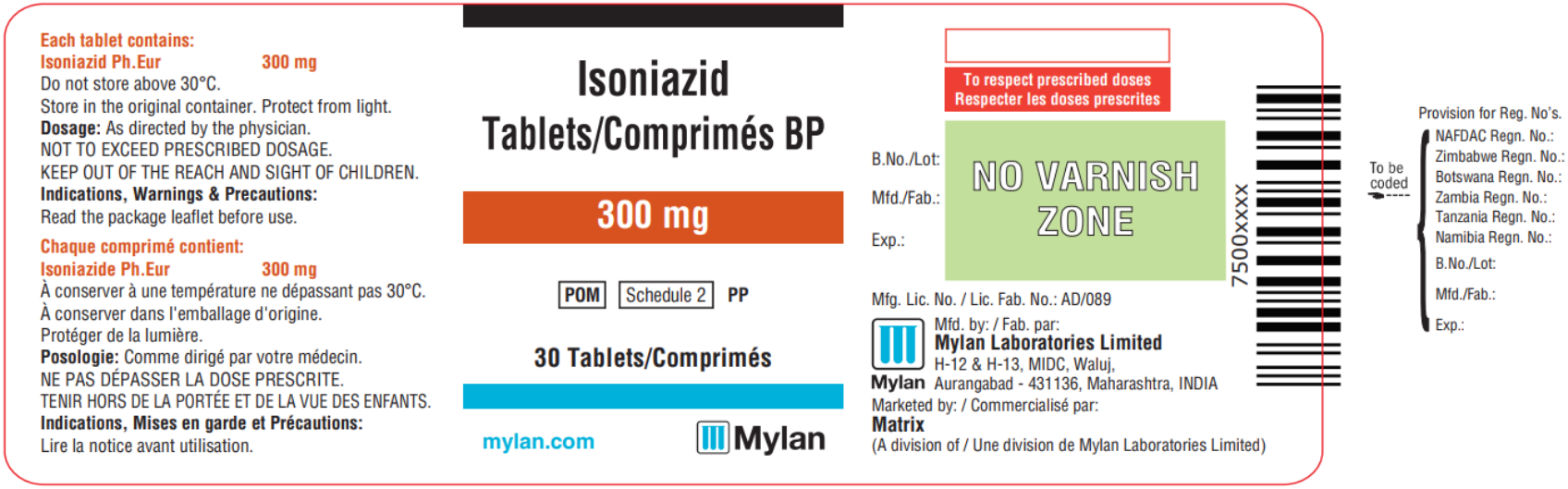
Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

PART 5: CHANGE HISTORY

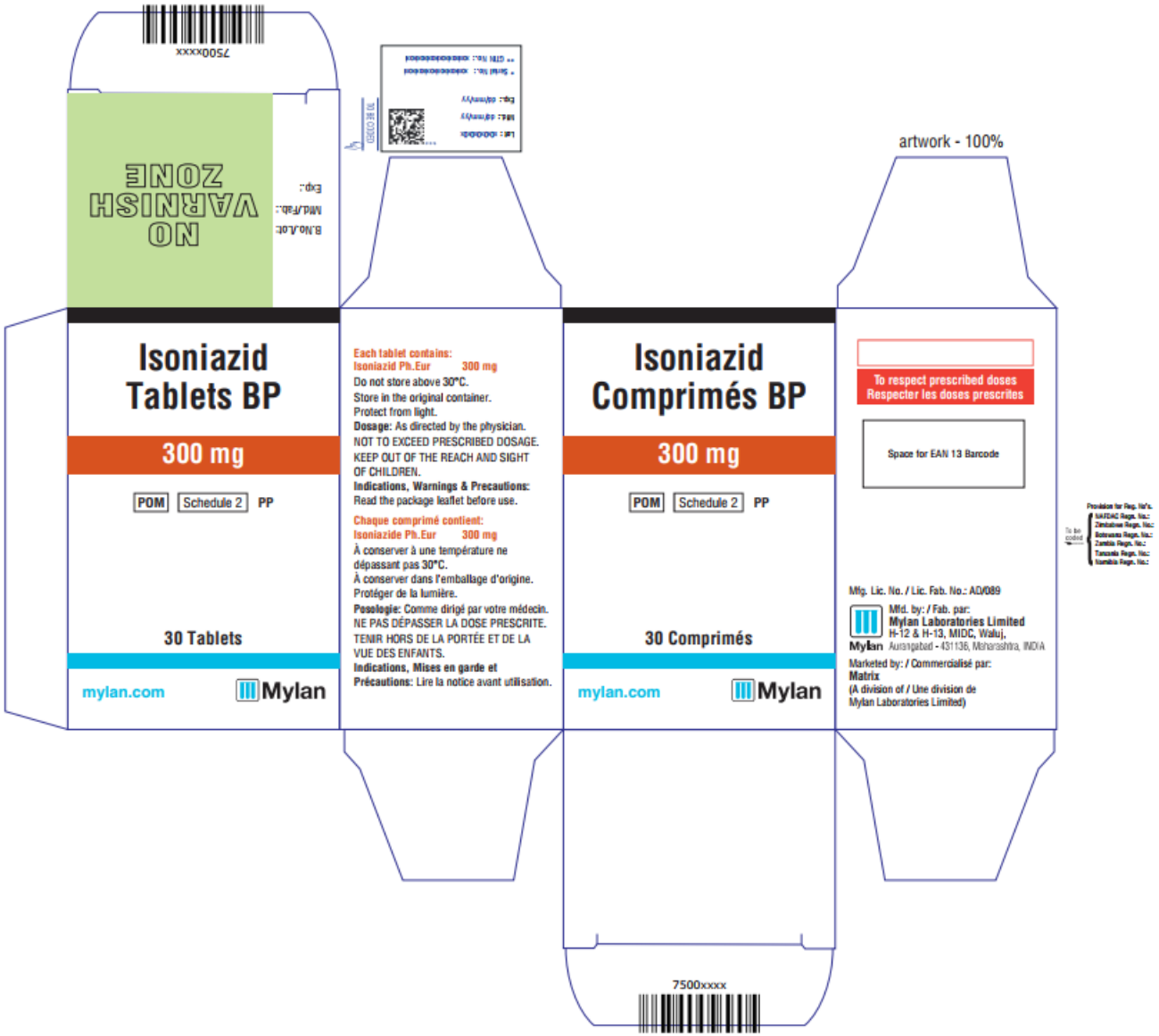
Version number	Date	Description of update	Section(s) Modified	Approval date

Annex I: Mock up labels;

Primary pack label;



Secondary pack label;



Effective date: 03/10/2022