THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR AXAMOL (2.5 MG/2.5ML SALBUTAMOL (AS SULPHATE)) NEBULIZER SOLUTION

Version number 1.0
21 August 2023

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1. Introduction

AXAMOL is a clear and colorless solution contains salbutamol sulphate equivalent to 2.5 mg/2.5 mL salbutamol. Salbutamol is a selective β2agonist providing short-acting (4-6 hour) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction. At therapeutic doses it acts on the β2adrenoceptors of bronchial muscle. With its fast onset of action, it is particularly suitable for the management and prevention of asthma attacks. AXAMOL is approved in Tanzania for use in adults and children over 4 years of age.

1.1 Product details

Registration number	TAN 23 H 0276
Brand name	AXAMOL
Generic name, strength, and form	Salbutamol sulphate equivalent to 2.5 mg/2.5 mL salbutamol.
ATC classification	R01A A07 – decongestants for topical use, sympathomimetics, plain
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Axa Parenterals Limited, Plot No 936, 937& 939 Vill. Kishanpur, Jamalpur, Roorkee-247667 Distt. Haridwar (Uttarakhand)-India.
Local Technical Representative	Skill Mix Consulting Group, Frame No. 34, CCM Office, Tabata Chama Street, Near Tusiime Secondary School, Dar-Es-Salaam.

1.2 Assessment procedure

The application for registration of AXAMOL was submitted in DD/MM/YYYY. The product underwent full assessment. Assessment was completed in 3 (three) rounds of evaluation and the product was registered on 01 June 2023.

1.3 Information for users

Visual description of the finished product	Clear and colorless solution
Primary packing material	LDPE bottle
Secondary packing materials	A printed carton box
Shelf-life and storage condition	24 months, Do not above 30°C. Protect from Light. Do not refrigerate or freeze.
Route of administration	Intranasal
Therapeutic indications	Salbutamol nebulizer solutions are indicated in adults, adolescents and children aged 4 to 11 years. For babies and children under 4 years of age Salbutamol is a selective β2-agonist providing short-acting (4-6 hour) bronchodilation with a fast

	onset (within 5 minutes) in reversible airways obstruction. Salbutamol nebulizer solutions are indicated for use in the routine management of chronic bronchospasm unresponsive to conventional therapy, and in the treatment of acute severe asthma.

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: AXAMOL

Composition: Each 2.5 mL Respules Contains Salbutamol Sulphate Eq. to Salbutamol 2.5 mg

Pack size: 1 bottle

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

Storage conditions: Do not above 30°C . Protect from Light. Do not refrigerate or freeze.

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: AXAMOL

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: Axa Parenterals 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 DMF.

Salbutamol Sulphate

General Information

Salbutamol Sulphate API is compendia in USP, Ph.Eur., and BP.

Molecular formula: $C_{16}H_{25}ClN_2$

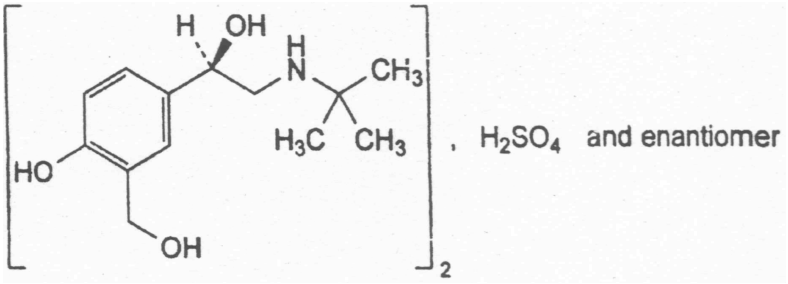
Chemical name:

Bis[(1RS)-2-[1,1-dimethylethyl) amino]-1-[4-hydroxy-3 (hydroxyl methyl) phenyl] ethanol] sulphate

1,3-Benzenedimethanol,α1 -1-[[(1,1-dimethylehtyl) amino] methyl]-4-hydroxy-, sulfate(2:1) (salt)

α1 –[(tert-Butylamino) methyl]-4-hydroxy-m-xylene, α,α'-diol sulfate (2:1) (salt)

Structure:



General properties

Salbutamol Sulphate is white to almost white crystalline powder freely soluble in water and practically insoluble or very slightly soluble in Ethanol (96%) and in Methylene Chloride.

The polymorphism is reported for this API. 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

Salbutamol Sulphate API manufacturer is Jayco Chemical Industries, Western Express Highway, Post Mira, Kashimira, District Thane- 401104. The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by the Food and Drug Administration of Maharashtra-, India. Salbutamol Sulphate 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 BP standards and ICHQ3A. The parameters monitored during quality control are: Description, solubility, identification, appearance of solution, optical rotation, acidity/alkalinity, related substances by HPLC, boron, loss on drying, sulfated ash, assay, additional test (residual solvents, microbial test, particle size). Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Salbutamol Sulphate API is 60 months when packed in double polythene bags with self-seals with storage condition 'Should be stored Below 30ºC'.

Quality of the Finished Pharmaceutical Product

Formulation

AXAMOL is a clear and colorless solution

AXAMOL contains the Salbutamol Sulphate, and other ingredients listed here after: sodium chloride, disodium edetate, sodium citrate, citric acid, water for injections. 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 Axa Parenterals Limited, Plot No 936, 937& 939, Vill. Kishanpur, Jamalpur, Roorkee-247667, Distt. Haridwar (Uttarakhand), 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 BP and ICH requirements. The parameters monitored during quality control are: Description, identification, pH, extractable volume, sterility, related substances, salbutamol ketone, and assay. 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 & RH: 75%RH± 5 % for 36 months and 40± 2°C & RH: 75% RH± 5 % for 6 months. Based on the stability data presented, the approved shelf-life is 36 months when stored in low density polyethylene bottle with storage condition 'Do not above 30°C. Protect from Light. Do not refrigerate or freeze'.

Safety and efficacy information

AXAMOL is a solution for nebulization formulation and therefore fulfils the exemption as the product is prepared as aqueous solution and containing the same active pharmaceutical ingredient in the same concentration as currently registered products and which are administered by the same route. The quantitative composition of AXAMOL 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

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. AXAMOL 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

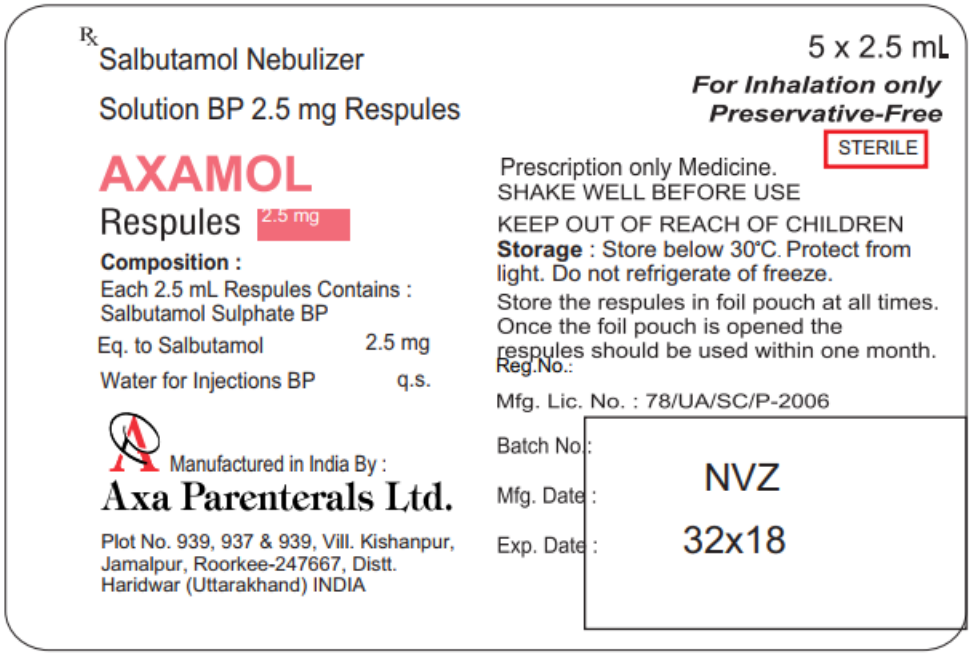
Application for renewal of registration was submitted on <DDMMYYYY>. The application was finalized in <number> rounds of evaluation. The product was confirmed to still be compliant to the standards of quality, safety and efficacy, hence registration was renewed on <DDMMYYYY>.

PART 5: CHANGE HISTORY

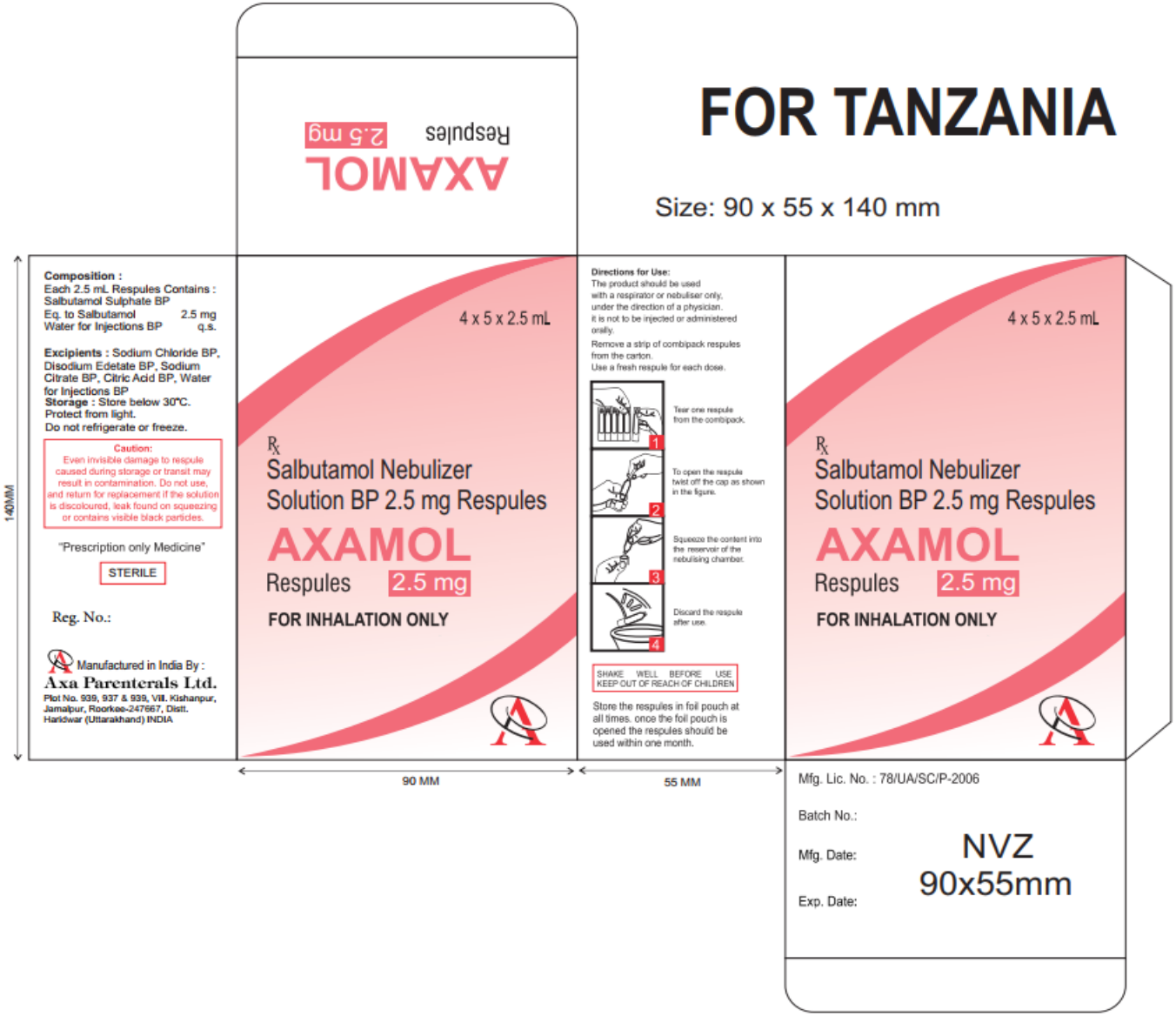
Version number	Date	Description of update	Section(s) Modified	Approval date

Annex I: Mock up labels;

Primary pack label;



Secondary pack label;



Effective date: 03/10/2022