

TMDA/DMC/MRE/F/016

Rev #:02

THE UNITED REPUBLIC OF TANZANIA



MINISTRY OF HEALTH



TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

**PUBLIC ASSESSMENT REPORT FOR ALPHAMOX (AMOXICILLIN TRIHYDRATE  
287.50 MG USP EQUIVALENT TO AMOXICILLIN 250 MG) HARD GELATIN CAPSULES**

Version number 1.0  
21 August 2023

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Effective date: 03/10/2022

## 1. Introduction

ALPHAMOX is maroon colour cap & Yellow colour body size “2” hard gelatin capsule containing white to off white granular powder contains amoxicillin trihydrate equivalent to amoxicillin 250 mg per each capsule. Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes (often referred to as penicillin-binding proteins, PBPs) in the biosynthetic pathway of bactericidal peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death. ALPHAMOX is approved in Tanzania for use in adults and pediatric population.

### 1.1 Product details

Registration number	TAN 23 H 0248
Brand name	ALPHAMOX
Generic name, strength, and form	Each hard gelatin capsule contains: Amoxicillin Trihydrate equivalent to Amoxicillin 250 mg
ATC classification	J01CA04– penicillins with extended spectrum
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Salama Pharmaceuticals Limited, 13/19 Uhuru/Nyamwezi Street, Tanzania
Local Technical Representative	N/A

### 1.2 Assessment procedure

The application for registration of ALPHAMOX was submitted on 09/09/2022. 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	Maroon colour cap & Yellow colour□body size “2” hard gelatin capsule containing white to off white granular powder
Primary packing material	Alu/PVC blisters
Secondary packing materials	A printed carton box
Shelf-life and storage condition	36 months, do not above 30°C. Protect from light
Route of administration	Oral
Therapeutic indications	Amoxicillin is indicated for the treatment of the following infections in adults and children: ✓ <ul style="list-style-type: none"><li>• Acute bacterial sinusitis</li><li>• Acute streptococcal tonsillitis and pharyngitis</li><li>• Acute exacerbations of chronic bronchitis</li><li>• Community acquired pneumonia</li></ul>

	<ul style="list-style-type: none"><li>• Acute otitis media</li><li>• Acute cystitis</li><li>• Acute pyelonephritis</li><li>• Asymptomatic Bacteriuria in pregnancy</li><li>• Typhoid and paratyphoid fevers</li><li>• Dental abscess with spreading cellulitis</li><li>• Prosthetic joint infections</li><li>• Helicobacter pylori eradication</li><li>• Lyme disease</li></ul> <p>Amoxicillin is also indicated for the prophylaxis of endocarditis. Consideration should be given to official guidance on the appropriate use of antibacterial agents.</p>
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## 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: ALPHAMOX

Composition: Each hard gelatin capsule contains: Amoxicillin Trihydrate equivalent to Amoxicillin 250 mg

Pack size: 10x10 capsules

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

Storage conditions: Do not above 30°C. 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: ALPHAMOX

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: Scott-Edil Advance Research Laboratories & Education Ltd.

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.

#### Amoxicillin Trihydrate

##### General Information

Amoxicillin Trihydrate API is compendia in USP, Ph.Eur., and BP.

Molecular formula:  $C_{16}H_{19}N_3O_5S \cdot 3H_2O$

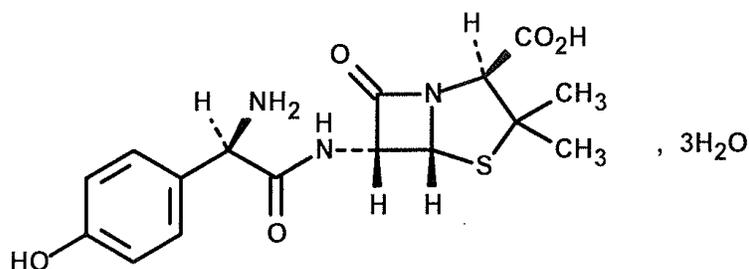
Chemical name:

4-Thia-1-azabicyclo[3.2.0]heptanes-2-carboxylic acid, 6-[[ amino-( 4 hydroxyphenyl)acetyl]amino]-3, 3-dimethyl-7-oxo, Trihydrate [2S-[2a, 5a, 6β (S\*)]]

Or

(2S,5R,6R)-6-[[ (2R)-2-Amino-2-(4-hydroxyphenyl) acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate

Structure:



## **General properties**

Amoxicillin Trihydrate is a white or almost white granulated powder, which is soluble in water, very slightly soluble in alcohol, practically insoluble in fatty oils. It dissolves in dilute acids and dilute solutions of alkali hydroxides.

## **Manufacture**

Amoxicillin Trihydrate API manufacturer is Aurobindo Pharma Limited, Sy. No. 1/22,2/1 to 5,6 to 8,61 to 69, Pydibhimavaram Village, Ranasathlam Mandal, Srikakulam District, Andhra Pradesh, India. The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by the Andhra Pradesh Drugs Control Administration. Amoxicillin Trihydrate is semi-synthetic product derived from a fermentation product. 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 (IR), related substance (HPLC), assay, appearance of solution, pH, N,N-Dimethylaniline, and water. Compliance to these specifications were established via batch analysis data and stability studies.

### Stability and container closure system

The re-test period of Amoxicillin Trihydrate API is 60 months when packed in low density polyethylene (LDPE) bag with storage condition 'Should be stored Below 25°C'.

## **Quality of the Finished Pharmaceutical Product**

### **Formulation**

ALPHAMOX is maroon colour cap & Yellow colour body size "2" hard gelatin capsule containing white to off white granular powder

ALPHAMOX contains the Amoxicillin Trihydrate and other ingredients listed here after: Sodium Starch Glycollate, Magnesium Stearate, Purified Talcum, Sodium Lauryl Sulphate, E.H.G Capsule Size "2" IH (cap: gelatin, sodium lauryl sulfate, purified water, brilliant blue, carmoisine, tartrazine, titanium di oxide and body: gelatin, sodium lauryl sulfate, purified water, brilliant blue, sunset yellow, tartrazine, titanium di oxide). The quantities of all ingredients are confirmed to be in line with the recommendations of Handbook of Pharmaceutical Excipients, 8<sup>th</sup> Edition in terms of function and quantities.

### **Manufacture**

The finished product manufacturers are Scott-Edil Advance Research Laboratories & Education Ltd., Hill Top Industrial Area, Bhatoli Kalan, Baddi-173205, (HP) 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 USP and ICH requirements. The parameters monitored during quality control are: Description, identification, uniformity of fill weight, average fill weight, disintegration, dissolution, assay, related substance, and microbial enumeration. 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 R.H. 75±5% for 36 months and 40±2°C R.H. 75±5% for 6 months. Based on the stability data presented, the approved shelf-life is 36 months when stored in Alu/PVC blisters with storage condition 'Do not above 30°C. Protect from light.'

## Safety and efficacy information

Safety and efficacy of ALPHAMOX was established through a bioequivalence trial.

BE trial report number TAB/SCO/AMOX-0522 was submitted.

Study title	An open label, randomized, two-treatment, two-period, two-sequence, single dose, crossover bioequivalence study comparing Amoxicillin capsules USP 500 mg containing Amoxicillin trihydrate equivalent to Amoxicillin 500 mg of Scott-Edil Advance Research Lab. & Edu. Limited, India with Amoxil (Amoxicillin) capsules containing Amoxicillin trihydrate equivalent to Amoxicillin 500 mg of Glaxo Wellcome Production Mayenne, France) in healthy, adult, human male subjects under fasting conditions.	
Study design	Comparative randomised, single dose, two-way cross over open label study under fasting condition	
Study site	TAAB Biostudy Services 77/2/1/B/I, Bade Raipur Road, Jadavpur, Kolkata-700032, India	
Study dates	Period I (dosing)	23 June 2022
	Period II (dosing)	28 June 2022 to 29 June 2022
	Validation and Analysis	Validation; 17 Jan 2015 to 18 March 2015  Analysis; 02 July 2022 to 09 July 2022
Primary objective	To investigate the bioequivalence of test product relative to reference product after a single oral dose administration of Amoxicillin to healthy adults under fasting conditions	

Secondary objective	To monitor the safety and tolerability of a single dose of Amoxicillin 250 mg tablets when administered in 24 healthy adult human subjects under fasting condition	
Number of participants	Planned-41 subjects Enrolled-24 subjects Dosed-24 subjects Withdrawn - 00 subjects Bio-sample analyzed -24 subjects Pharmacokinetic and statistical data analyzed – 24 subjects	
Monitored parameters	Tmax, Cmax, AUC0→t, AUC0→∞, AUC% Extrapolation Kel and T1/2	
Investigational medicinal products	Test Product	Reference product
	Strength: 250 mg Batch number: BC065 Expiry date: 04/2025	Strength: 250 mg Batch number: DB2J Expiry date: 12/2022
Analytical method	High Pressure Liquid chromatography – MS/MS – detector (LC-MS/MS) method was used for the determination of plasma concentrations of analyte	
Statistical method	SAS® procedure	

Efficacy results are summarized as follows:

Obs. No.	Name	Geomean Ref	Geomean Test	MSE	Ratio	Power	Intra_cv	plower	pupper	p	BIO-EQUIV
1.	LnC <sub>max</sub>	6.421	6.146	0.019	95.708	99.891	14.014	89.315	102.558	0.288	Yes
2.	LnAUC <sub>0-t</sub>	33.830	31.330	0.047	92.611	92.362	22.003	83.148	103.151	0.234	Yes
3.	LnAUC <sub>0-inf</sub>	35.308	32.746	0.043	92.745	94.298	21.008	83.666	102.808	0.222	Yes

The acceptance limits of 80 – 125% are met by the AUC and Cmax values. Furthermore, the safety profile of the test product is similar to that of reference product. Therefore, Amoxicillin capsules USP 500 mg containing Amoxicillin trihydrate equivalent to Amoxicillin 500 mg of Scott-Edil Advance Research Lab. & Edu. Limited, India with Amoxil (Amoxicillin) capsules is equivalent and interchangeable with Amoxil (Amoxicillin) capsules containing Amoxicillin trihydrate equivalent to Amoxicillin 500 mg of Glaxo Wellcome Production Mayenne, France under acceptable in vivo experimental conditions.

#### 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. ALPHAMOX hard gelatin capsule 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;**

<p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p> <p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p> <p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p> <p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p>	<p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p> <p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p> <p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p> <p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p>	<p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p> <p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p> <p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p> <p><b>NEOMOX-250</b> Amoxicillin Capsules USP 250 mg Mfg. Lic. No.: MB/09/829 <b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddli, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p>
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Secondary pack label;

 <b>250</b> <b>NEOMOX</b>	<b>Size : 75x54x68mm</b>		
<b>NEOMOX</b> <b>250</b> Amoxicillin Capsules USP 250 mg 10x10 Capsules   	<p>Composition : Each hard gelatin capsule contains: Amoxicillin Trihydrate USP 250 mg eq. to Amoxicillin q.s. Excipients q.s. Approved colours used in empty capsule shells</p> <p>Dosage : As directed by the Physician</p> <p>Medicine : Keep out of reach of children.</p> <p>Store protected from light at a temperature not exceeding 30°C.</p> <p><b>PRESCRIPTION ONLY MEDICINE</b></p> 	<b>NEOMOX</b> <b>250</b> Amoxicillin Capsules USP 250 mg 10x10 Capsules   	<p>Mfg. Lic. No.: MB/09/829</p> <p>Batch No.:</p> <p>Mfg. date:</p> <p>Exp. Date:</p> <p><b>MANUFACTURED BY:</b> <b>Scott-Edil Advance Research Laboratories &amp; Education Ltd.</b> Hill Top Ind. Area Bhatoli Kalan, Baddi, Distt. Solan - 173205 (H.P.) INDIA (A WHO-GMP Certified Company)</p> <p><b>DISTRIBUTED BY :</b> <b>Salama Pharmaceuticals Ltd.</b>  Dar Es Salaam, Tanzania</p> <p><b>MANUFACTURED FOR:</b> <b>Alphaceuticals Limited</b> 97 High Street, Rickmansworth, Hertfordshire, WD3 1EF, United Kingdom</p>

Effective date: 03/10/2022