THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR TRENAXA 500 (TRANEXAMIC ACID 500MG) FILM COATED TABLETS

Version number 1.0
21 August 2023

TMDA Headquarters, Plot No. 56/1, Block E, Kisasa B Centre, Hombolo Road, P. O. Box 1253, Dodoma – Tanzania, Telephone: +255 (26) 2961989/2061990/+255 (22) 2450512/2450751/2452108, Email: info@tmda.og.tz, Website: **www.tmda.go.tz**

Toll free: 0800110084

1. Introduction

TRENAXA 500 tablets is a generic medicinal version of “Cyklokapron 500 mg tablets” by Meda manufacturing GMBH contains Tranexamic acid 500 mg per each tablet. Tranexamic acid is an antifibrinolytic compound which is a potent competitive inhibitor of the activation of plasminogen to plasmin. At much higher concentrations it is a non-competitive inhibitor of plasmin. The inhibitory effect of tranexamic acid in plasminogen activation by urokinase has been reported to be 6-100 times and by streptokinase 6-40 times greater than that of aminocaproic acid. The antifibrinolytic activity of tranexamic acid is approximately ten times greater than that of aminocaproic acid. TRENAXA 500 tablets is approved in Tanzania for use in adults and children.

1.1 Product details

Registration number	TAN 23 H 0279
Brand name	TRENAXA 500
Generic name, strength, and form	Each film coated tablet contains: Tranexamic Acid 500 mg
ATC classification	B02AA02 – Antifibrinolytic agent (Antihemorrhagic)
Distribution category	POM
Country of origin	India
Associated product	N/A
Marketing Authorization Holder	Macleods Pharmaceuticals Limited 304, Atlanta Arcade, Marol Church road, Andheri (East) - India
Local Technical Representative	RK Pharmacetical(Tz) Limited plot no326, Dar es Salaam,

1.2 Assessment procedure

The application for registration of TRENAXA 500 was submitted in 22/01/2020. The product underwent full 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 circular shaped, biconvex, film coated tablets having break line on one side and plain surface on other side
Primary packing material	Aluminium laminated with LDPE strip
Secondary packing materials	A printed carton box
Shelf-life and storage condition	36 months, Do not above 30°C. Protect from moisture
Route of administration	Oral
Therapeutic indications	Tranexamic Acid 500mg Tablets are indicated for short term use for haemorrhage or risk of haemorrhage in those with increased fibrinolysis or fibrinogenolysis. Local fibrinolysis as occurs in the following conditions:

	1. a) Prostatectomy and bladder surgery b) Menorrhagia c) Epistaxis d) Conisation of the cervix e) Traumatic hyphaema 2. Management of dental extraction in haemophiliacs. 3. Hereditary angioneurotic oedema.

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: TRENAXA 500

Composition: Each film coated tablet contains: Tranexamic Acid 500 mg

Pack size: 5x6 tablets

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

Storage conditions: Do not above 30°C. Protect from moisture

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: TRENAXA 500

Manufacturing details: batch number, manufacturing date and expiry date

Name of manufacturer: Macleods Pharmaceuticals 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.

Tranexamic Acid

General Information

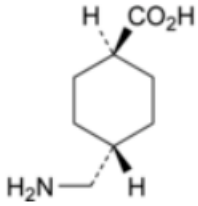
Tranexamic acid API is compendia in USP, Ph.Eur., and BP.

Molecular formula: $C_8H_{15}N0_2$

Chemical name:

trans-4-(Am inomethyl)cyclohexane carboxylic acid

Structure:



General properties

Tranexamic Acid is a white or almost white, crystalline powder and freely soluble in water and glacial acetic acid and practically insoluble in alcohol or acetone. Tranexamic acid has two isomers. It does not exist in any different crystalline form than provided by this active substance manufacturer.

Manufacture

Tranexamic Acid API manufacturer is Hunan Dongting Pharmaceutical Co., Ltd., No.16 Dongyan Road, Deshan, Changde, PC415001, Hunan Province, China. The manufacturing complies with GMP requirements as evidenced by the GMP certificate issued by the Hunan Medical Products Administration. Tranexamic Acid 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 by IR, pH, halides expressed as chlorides, related substances by HPLC, heavy metals, loss on drying, sulfated ash, assay. Compliance to these specifications were established via batch analysis data and stability studies.

Stability and container closure system

The re-test period of Tranexamic Acid API is 24 months when packed in transparent LDPE bag with storage condition 'Store in well-closed, airtight container at room temperature in inert atmosphere of (N2) and protect samples from light'.

Quality of the Finished Pharmaceutical Product

Formulation

TRENAXA 500 is a white circular shaped, biconvex, film coated tablets having break line on one side and plain surface on other side

TRENAXA 500 contains the Tranexamic Acid, and other ingredients listed here after: microcrystalline cellulose, povidone, purified water, microcrystalline cellulose, croscarmellose sodium, colloidal anhydrous silica, purified talc, magnesium stearate, hypromellose, dichloromethane, isopropyl alcohol, titanium dioxide, purified talc, propylene glycol, diethyl phthalate. 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 Macleods Pharmaceuticals Limited, Plot 25-27, Survey No. 366, Premier Industrial Estate, Kachigam, Daman – 396210, (Phase-II), 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 of API and colourant, related substances, average weight, uniformity of dosage units (weight variation), disintegration time, loss on drying, dissolution, residual solvents, 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 Aluminium laminated with LDPE strip with storage condition 'Do not above 30°C. Protect from moisture'.

Safety and efficacy information

The biowaiver was approved based on BCS classification.

TRENAXA 500 fulfilled the criteria for waiving an in-vivo bioequivalence study as per relevant TMDA guidance. Dissolution profiles of Trenaxa 500 (Tranexamic Acid Tablets 500 mg) was compared to Cyklokapron 500 mg (Tranexamic acid Tablet 500 mg) of Meda manufacturing GMBH, Germany. At least 85% of the labelled amount of Tranexamic Acid had dissolved in all three media. Therefore, confirming similarity.

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. TRENAXA 500 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>.

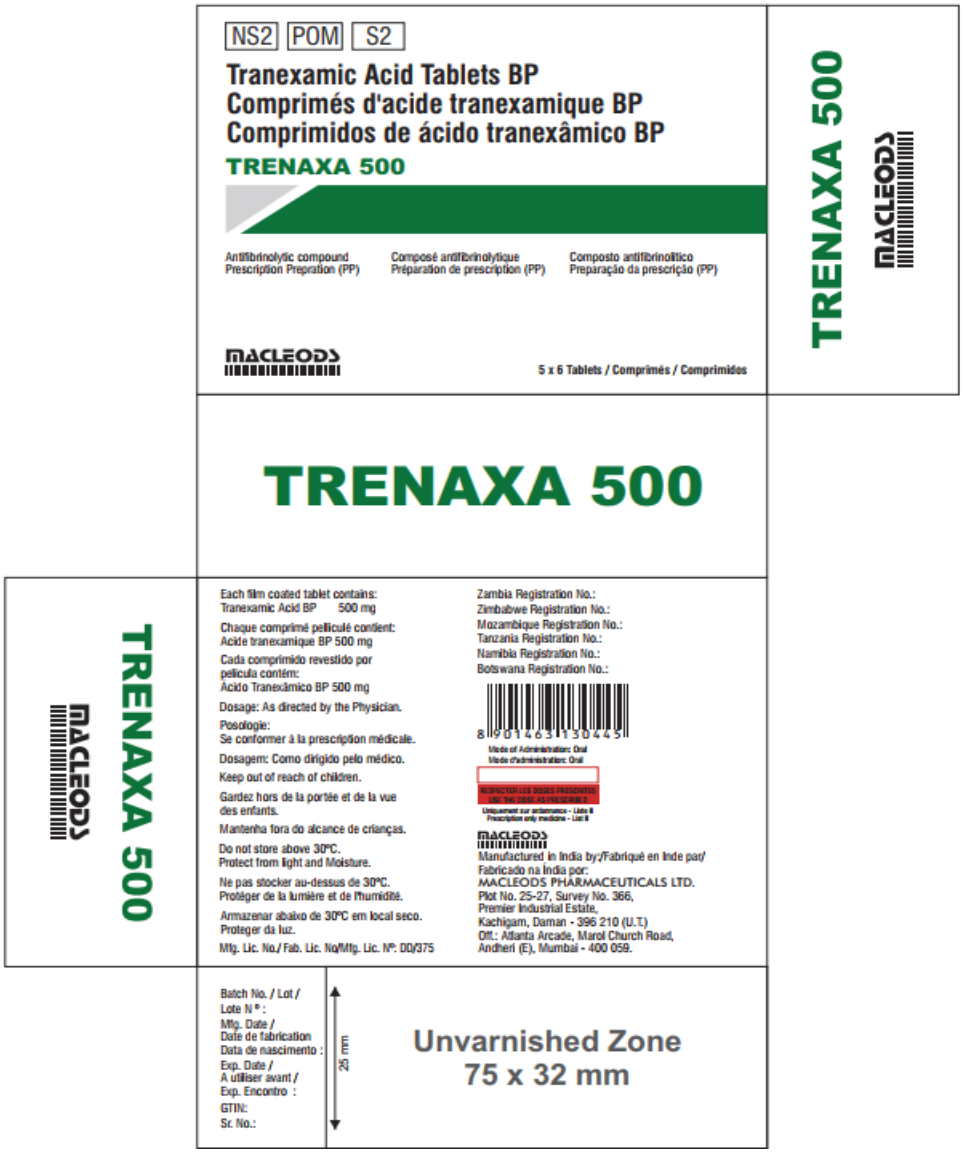
PART 5: CHANGE HISTORY

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