1.3 Product Information

Summary of Characteristics of the Product

1. Name of the Medicinal Product

TRENAXA 500 (Tranexamic Acid Tablets BP 500mg)

2. Qualitative and Quantitative Composition

Each film coated tablet contains

Tranexamic acid BP……500mg

3. Pharmaceutical Form

Coated Tablets.

4. Clinical Particulars

4.1 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:

a) Prostatectomy and bladder surgery

b) Menorrhagia

c) Epistaxis

d) Conisation of the cervix

e) Traumatic hyphaema

f) Management of dental extraction in haemophiliacs.

g) Hereditary angioneurotic oedema.

4.2 Posology and method of administration

Route of Administration:

Oral

Method of administration

Adults:

1.3 Product Information

Local Fibrinolysis: The recommended standard dose is 15-25mg/kg bodyweight (i.e. 2-3 tablets) two to three times daily. For the indications listed below the following doses may be used:

1a Prostatectomy: Prophylaxis and treatment of haemorrhage in high risk patients should commence per- or post-operatively with tranexamic acid injection; thereafter 2 tablets three to four times daily until macroscopic haematuria is no longer present.
1b Menorrhagia: Recommended dosage is 2 tablets 3 times daily as long as needed for up to 4 days. If very heavy menstrual bleeding, dosage may be increased. A total dose of 4g daily (8 tablets) should not be exceeded. Treatment with Tranexamic acid should not be initiated until menstrual bleeding has started.
1c Epistaxis: When repeated bleeding is anticipated oral therapy (2 tablets three times daily) should be administered for 7 days.
1d Cervix Conisation: 3 tablets three times daily.
1e Traumatic Hyphaema: 2-3 tablets 3 times daily. The dose is based on 25mg/kg three times a day.
2. Haemophilia: In the management of dental extractions 2-3 tablets every eight hours. The dose is based on 25mg/kg.
3. Hereditary angioneurotic oedema: Some patients are aware of the onset of illness; suitable treatment for these patients is intermittently 2-3 tablets two to three times daily for some days. Other patients are treated continuously at this dosage.

Children:

In children, for current approved indications as described in section 4.1, the dosage is in the region of 20 mg/kg/day. However, data on efficacy, posology and safety for these indications are limited.

Elderly:

No reduction in dosage is necessary unless there is evidence of renal failure (see guidelines below).
Renal Impairment

1.3 Product Information

By extrapolation from clearance data relating to the intravenous dosage form, the following reduction in the oral dosage is recommended for patients with mild to moderate renal insufficiency:

Serum Creatinine (μmol/l)	Oral Dose	Dose Frequency
120-249	15 mg/kg body weight	twice daily
250-500	15 mg/kg body weight	daily

4.4 Special warnings and precautions for use

Caution is advised in treating those with massive haematuria from the upper urinary tract, especially in haemophiliacs, as there have been some cases of ureteric obstruction.

Not to be used when disseminated intravascular coagulation is in progress.

The blood levels are increased in patients with renal insufficiency. Therefore a dose reduction is recommended.

In those patients requiring long term administration of tranexamic acid, such as those with hereditary angioneurotic oedema, regular eye examinations (e.g. visual acuity, slit lamp, intraocular pressure, visual fields) and liver function tests should be performed.

Patients who experience visual disturbance should be withdrawn from treatment.

Patients with irregular menstrual bleeding should not use tranexamic acid until the cause of irregular bleeding has been established. If menstrual bleeding is not adequately reduced by Tranexamic Acid Tablets, an alternative treatment should be considered.

Patients with a previous thromboembolic event and a family history of thromboembolic disease (patients with thrombophilia) should use Tranexamic Acid Tablets only if there is a strong medical indication and under strict medical supervision.

The use of tranexamic acid in cases of increased fibrinolysis due to disseminated intravascular coagulation is not recommended.

Clinical experience with Tranexamic Acid Tablets in menorrhagic children under 15 years of age is not available.

The indications and method of administration indicated above should be followed strictly:

• In case of haematuria of renal origin, there is a risk of mechanical anuria due to formation of a ureteral clot.

1.3 Product Information

• In renal insufficiency leading to a risk of accumulation, the dosage of tranexamic acid should be reduced according to the serum creatinine level.

- serum creatinine between120 and 250 μmol/l,: TXA iv 10 mg/kg twice daily.
- serum creatinine between 250 and 500 μmol/l: TXA iv 10 mg/kg once daily (every 24 hours).
- serum creatinine > 500 μmol/l, TXA iv 10 mg/kg every other day (every 48 hours).

• Before use of TXA, risk factors of thromboembolic disease should be investigated.

• Tranexamic acid should be administered with care in patients receiving oral contraceptives because of the increased risk of thrombosis

4.5 Interaction with other medicinal products and other forms of interaction

Tranexamic Acid will counteract the thrombolytic effect of fibrinolytic preparations.

4.6 Pregnancy and lactation:

Pregnancy: There is no evidence from animal studies that tranexamic acid has any teratogenic effect, however, the usual caution with use of drugs in pregnancy should be observed.

Tranexamic acid crosses the placenta.

Lactation: Tranexamic acid passes into breast milk to a concentration of approximately one hundredth of the concentration in the maternal blood. An antifibrinolytic effect in the infant is unlikely**.**

4.7 Effects on ability to drive and use machines

Tranexamic Acid has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse events are listed below by system organ class and frequency.

Frequencies are defined as: very common (=1/l0), common (=1/100 to <1/10), uncommon (=1/1000 to <1/100), rare (=1/10,000 to <1/1000) and very rare (<1/10,000), not known (cannot be estimated from the available data).

Immune system disorders

Very rare: Hypersensitivity reactions including anaphylaxis

Nervous System Disorders

Very rare: convulsions, particularly in case of misuse

Eye disorders

Rare: Colour vision disturbances, retinal vein/artery occlusion

Vascular disorders

Rare: Thromboembolic events

Very rare: Arterial or venous thrombosis at any sites. Malaise with hypotension, with or without loss of consciousness (generally following a too fast intravenous injection, exceptionally after oral administration).

Gastro-intestinal disorders

Very rare: Digestive effects such as nausea, vomiting and diarrhoea.

Skin and subcutaneous tissue disorders

Rare: Allergic skin reactions

4.9 Overdose

No cases of overdosage have been reported. Symptoms may be nausea, vomiting, orthostatic symptoms and/or hypotension. Initiate vomiting, then stomach lavage, and charcoal therapy. Maintain a high fluid intake to promote renal excretion. There is a risk of thrombosis in predisposed individuals. Anticoagulant treatment should be considered.

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifibrinolytics**.**

ATC code: **B02AA02**

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.

5.2 Pharmacokinetic properties

Absorption

Peak plasma Tranexamic acid concentration is obtained immediately after intravenous administration (500mg). Then concentration decreases until the 6th hour. Elimination half-life is about 3 hours.

Distribution

Tranexamic acid administered parenterally is distributed in a two compartment model. Tranexamic acid is delivered in the cell compartment and the cerebrospinal fluid with delay. The distribution volume is about 33% of the body mass.

Tranexamic acid crosses the placenta, and may reach one hundredth of the serum peak concentration in the milk of lactating women.

Elimination

Tranexamic acid is excreted in urine as unchanged compound. 90% of the administered dose is excreted by the kidney in the twelve first hours after administration (glomerular excretion without tubular reabsorption).

Following oral administration, 1.13% and 39% of the administered dose were recovered after 3 and 24 hours respectively.

Plasma concentrations are increased in patients with renal insufficiency.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

6. Pharmaceutical Particulars

6.1 List of Excipients

Microcrystalline cellulose BP (PH101), Povidone BP, Purified water, Microcrystalline cellulose BP (PH302), Croscarmellose sodium BP, Colloidal anhydrous silica BP, Purified talc BP, Magnesium Stearate BP, Hypromellose BP, Dichloromethane BP, Isopropyl alcohol, Titanium dioxide BP, Propylene glycol BP, Diethyl phthalate BP.

1.3 Product Information

6.2 Incompatibilities: None

6.3 Shelf life: 24 months.

6.4 Special precautions for storage

Store below 30°C in a dry place. Protect from light.

6.5 Nature and contents of container

Alu/Alu Strip pack of 10 Tablets. such 1 strip is packed in a carton along with package insert.

6.6 Instructions for use and handling

Keep out of reach of children.

7. Supplier

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8. WHO Reference Number (Prequalification Programme)

9. Date of first Prequalification/ last renewal

10. Date of Revision of the Text: