

Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

Nexamic 500mg Tablet

2. Qualitative and quantitative composition

Each Film-coated tablet contains 500mg Tranexamic Acid.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated Tablet.

White Coloured Circular Shaped Biconvex Film-coated Tablet having both sides plain.

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:

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.

4.2. Posology and method of administration

Posology

Adults

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 pre- 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.

Paediatric population

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.

Older patients

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

Renal insufficiency

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

Serum Creatinine ($\mu\text{mol/L}$)	Oral Dose	Dose Frequency
120-249	15 mg/kg body weight	twice daily
250-500	15 mg/kg body weight	daily

Method of administration

Oral.

4.3 Contraindications

- Hypersensitivity to the active substance or any of the excipients listed in section 6.1.
- Active thromboembolic disease.
- History of venous or arterial thrombosis.
- Fibrinolytic conditions following consumption coagulopathy.
- Severe renal impairment because of risk of accumulation.
- History of convulsions.

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 (see Section 4.2, Posology and Method of Administration).

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.
- 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 between 120 and 250 $\mu\text{mol/L}$: TXA iv 10 mg/kg twice daily.
 - serum creatinine between 250 and 500 $\mu\text{mol/L}$: TXA iv 10 mg/kg once daily (every 24 hours).
 - serum creatinine > 500 $\mu\text{mol/L}$, 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.

Cases of convulsions have been reported in association with tranexamic acid treatment. In cardiac surgery, most of these cases were reported following intravenous (IV) injection of tranexamic acid in high doses.

4.5 Interaction with other medicinal products and other forms of interaction

Tranexamic Acid will counteract the thrombolytic effect of fibrinolytic preparations.

4.6 Fertility, 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.

Breast-feeding

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 ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$) and 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, may occur but disappear when the dosage is reduced.

Skin and subcutaneous tissue disorders

Rare: Allergic skin reactions

Not known: fixed drug eruption

Renal and urinary disorders

Not known: Acute renal cortical necrosis

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Pharmacy and Poisons Board- Pharmacovigilance Electronic Reporting System (PvERS); <https://pv.pharmacyboardkenya.org> .

4.9 Overdose

No cases of overdosage have been reported. Symptoms may be nausea, vomiting, orthostatic symptoms and/or hypotension, dizziness, headache and convulsions. 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

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.

Tranexamic acid crosses the blood brain barrier.

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

Maize starch

Sodium starch glycolate

PVPK 30

Purified water

Purified talc

Magnesium stearate

Colloidal anhydrous silica

Sodium starch glycolate
Opadry 21K580031 White
Isopropyl alcohol
Dichloromethane

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store below 30°C.

6.5. Nature and contents of container

3x10 Alu/Alu Blister Tablets

6.6. Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorization Holder

Ravenbhel Healthcare Pvt Ltd.,
16-17, EPIP, SIDCO, Kartholi, Bari Brahmana,
Jammu, J&K-181133, INDIA.

8. Marketing Authorization Number(S)

H2022/CTD8084/15223

9. Date Of First Authorization/Renewal of the Authorization

2022 May 05

10. Date Of Revision of the Text

2022 May 05