SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Tranexamic Acid 500 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 500 mg of tranexamicacid.

For the full list of excipients, see section6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

Off-white, capsule shaped, scored, film-coated tablets.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short-term use for haemorrhage or risk of haemorrhage in increased fibrinolysis or fibrinogenolysis. Local fibrinolysis as occurs in the following conditions:

- prostatectomy and bladder surgery
- menorrhagia
- epistaxis
- conisation of the cervix
- traumatic hyphaema
- hereditary angioneurotic oedema
- management of dental extraction in haemophiliacs.

4.2 Posology and method of administration

Posology

1. Local fibrinolysis: The recommended standard dosage is 15-25 mg/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 3times daily for up to 4 days. If very heavy menstrual bleeding, dosage may be increased.A total dose of 4g daily (8 tablets) daily should not be exceeded.Treatment withtranexamic acid should not be initiated until menstrual bleeding has started

1c. Epistaxis: Where recurrent bleeding is anticipated oral therapy (2 tablets three times daily) should be administered for 7 days.

1d. Conisation of the cervix: 3 tablets three times daily.

1e. Traumatic hyphaema: 2-3 tablets three times daily. The dose is based on 25 mg/kg three times a day.

2. Hereditary angioneurotic oedema: Some patients are aware of the onset of the 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.

3. Haemophilia: In the management of dental extractions 2-3 tablets every eight hours. The dose is based on 25 mg/kg.
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 (µmol/l)	Dose tranexamic acid
120-249	15 mg/kg body weight twice daily
250-500	15 mg/kg body weight / day

Children's dosage: This should be calculated according to body weight at 25 mg/kg per dose. However, data on efficacy, posology and safety for these indications are limited.

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

Method of administration
Oral

4.3 Contraindications

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

4.4 Special warnings and precautions for use

In case of haematuria of renal origin (especially in haemophilia), there is a risk of mechanical anuria due to formation of a ureteral clot.
In the long-term treatment of patients 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 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, an alternative treatment should be considered.

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

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

The blood levels are increased in patients with increased renal insufficiency.Therefore a dose reduction is recommended (see section 4.2).

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

Patients who experience visual disturbance should be withdrawn from treatment.

Clinical experience with tranexamic acid in menorrhagic children under 15 years of age is not available.

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

4.5 Interaction with other medicinal products and other forms of interaction

Tranexamic acidwill counteract the thrombolytic effect of fibrinolytic preparations.

4.6 Fertility, pregnancy and lactation

Pregnancy
Although there is no evidence from animal studies of a teratogenic effect, the usual caution with the 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 anduse 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 and <1/10)
- uncommon (≥ 1/1000 and <1/100)
- rare (≥ 1/10,000 and <1/1000) and
- very rare (<1/10,000) including isolated reports
- not known (cannot be estimated from the available data).

Immune system disorders
Very rare:hypersensitivity reactions including anaphylaxis.

Eye disorders
Rare: colour vision disturbances, retinal/artery occlusion.

Vascular disorders
Rare:thromboembolic events.
Very rare:arterial or venous thrombosis at any site.

Gastrointestinal disorders
Very rare:digestive effects such as nausea, vomiting, diarrhoea may occur but disappear when the dosage is reduced.

Skin and subcutaneous tissue disorders
Rare:allergic skin reactions have been reported.

Nervous system disorders
Frequency not known: Convulsions particularly in cases of misuse (refer to sections 4.3 and 4.4)

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 the national reporting system.

4.9 Overdose

Signs and symptoms may include 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

Pharmacotherapeutic group: Antihemorrhagics, Antifibrinolytics; ATC code: B02AA02

Tranexamic acid is an antifibrinolytic compoundwhichis 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

Core

Cellulose,microcrystalline
Povidone
Sodium starch glycolate (type A)
Silica, colloidal anhydrous
Magnesium stearate

Coating
Hypromellose
Macrogol 400
Titanium dioxide
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Store below 25ºC.Protected from light and moisture.

6.5 Nature and contents of container

PVC/Aluminium blisters. Pack-sizes of 20, 30, 100 and 1000 film-coated tablets.
PP containers with PE closure. Pack-sizes of 60 and 1000 film-coated tablets.

Not all pack-sizes may be marketed.

6.6Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Remedica Ltd
Aharnon Str., Limassol Industrial Estate,
3056 Limassol, Cyprus

8. MARKETING AUTHORISATION NUMBER(S)

06394/07608/NMR/2019

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorization: 25-07-2021

10. DATE OF REVISION OF THE TEXT

11/07/2023