SUMMARY OF PRODUCT CHARACTERISTICS

Pause-500 Tablets

(Tranexamic acid tablets BP 500 mg)

1. NAME OF THE MEDICINAL PRODUCT

Pause-500

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:

Tranexamic acid BP 500 mg

3. PHARMACEUTICAL FORM

Oral tablets

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

Route of administration: Oral.

Local fibrinolysis: The recommended standard dosage 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: 2 tablets three times daily as long as needed for up to 4 days. If very heavy bleeding, dosage may be increased. A total dose of 4g daily (8 tablets) should not be exceeded. Tranexamic acid therapy is initiated only after heavy 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) **Haemophilia**: In the management of dental extractions 2-3 tablets every eight hours. The dose is based on 25 mg/kg.

3) **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.

Children's dosage: This should be calculated according to body weight at 25 mg/kg per dose.

Elderly patients: No reduction in dosage is necessary unless there is evidence of renal failure.

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	15mg/kg bodyweight twice daily
250-500	15mg/kg bodyweight/day

4.3 Contraindications

- Hypersensitivity to the active substance or any 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 renal insufficiency. Therefore, a dose reduction is recommended (see section 4.2).

The use of tranexamic acid in cases of increased fibrinolysis due to 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 Tranexamic 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 acid will counteract the thrombolytic effect of fibrinolytic preparations.

4.6 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

No effects on the ability to drive or use machines have been observed.

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 sites

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

Nervous system disorders

Frequency not known: Convulsions particularly in cases of misuse.

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

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

Maize starch (USP)

Sodium starch glycolate (Type A) (BP)

Povidone (USP)

Colloidal silicon dioxide (USP)

Talc (USP)

Magnesium stearate (BP)

Isopropyl alcohol (BP)

Methylene chloride (USP)

Colour Opadry white OY-IN-58910 (In house)

Purified water (BP)

6.2 Incompatibilities

None of the In-active ingredients of the formulation have been known to exhibit incompatibility with the Active Ingredient.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store in a dry and dark place below 30^{o}C.

6.5 Nature and contents of container

10 tablets are packed in a VMCH coated Alu foil / PVC blister strip. 3 such blister strips are packed in a carton along with a package insert.

6.6 Instructions for use and handling

Store in a dry and dark place below 30^{o}C. . Keep away from the reach of children.

7. MARKETING AUTHORISATION HOLDER

Emcure Pharmaceuticals Ltd.

8. MARKETING AUTHORISATION NUMBER(S)

Shall be provided when available.

9. DATE OF AUTHORISATION/RENEWAL OF THE AUTHORISATION

Not Applicable.

10. DATE OF REVISION OF THE TEXT

Not Applicable.