BECLOT – 500MG. INJECTION

Composition:
Each ml. contains:
Tranexamic Acid I.P. 100mg.

DESCRIPTION
Tranexamic acid is a synthetic analog of the amino acid lysine. It is used to treat or prevent excessive blood loss during surgery and in various medical conditions or disorders. It is an antifibrinolytic that competitively inhibits the activation of plasminogen to plasmin, by binding to specific sites of both plasminogen and plasmin, a molecule responsible for the degradation of fibrin, a protein that forms the framework of blood clots.

Chemical Name of Tranexamic Acid is trans-4-(aminomethyl)cyclohexanecarboxylic acid and empirical formula is C8H15NO2.
Tranexamic acid is a white crystalline powder. It is freely soluble in water and in glacial acetic acid and is very slightly soluble in ethanol and practically insoluble in ether.

CLINICAL PHARMACOLOGY
Mechanism of action:
Tranexamic acid is a potent antifibrinolytic drug occurring in two isomeric forms; the antifibrinolytic potency resides in the transisomeric form. The main action of Tranexamic Acid is blocking of the lysine-binding sites of the plasminogen molecule, which are of importance for the binding to fibrin. This prevents activation of plasminogen by plasminogen activator also absorbed to fibrin. Tranexamic Acid can be administered orally or intravenously and is excreted into the urine. It enters tissues and fluids in various concentrations and crosses the placenta. There is no evidence of a thrombogenic effect of Tranexamic Acid, but in accordance with its action, it prolongs dissolution of fibrin deposits already formed. Tranexamic Acid is a drug of high clinical value for the treatment of bleedings due to both systemic and local fibrinolysis.

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.

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.

INDICATIONS

Haemorrhage or risk of haemorrhage in increased fibrinolysis or fibrinogenolysis. Local fibrinolysis may occur in the following conditions:

- Prostatectomy and bladder surgery.
- Menorrhagia Epistaxis.
- Conisation of the cervix.
- Management of dental extraction in patients with coagulopathies.
- Ulcerative colitis Haematuria (Tranexamic acid therapy is not indicated in haematuria caused by diseases of the renal parenchyma.
- Gastrointestinal haemorrhage.
- General fibrinolysis as in prostatic and pancreatic cancer; after thoracic and other major surgery.
- In obstetrical complications such as abruptio placentae and post-partum haemorrhage.
- In leukaemia and liver diseases and in connection with thrombolytic therapy with streptokinase. Hereditary angioneurotic oedema.
- For the reduction of peri– and post-operative blood loss and the need for blood transfusion in adult patients undergoing cardiac surgery or total knee arthroplasty or total hip arthroplasty.
- For the reduction of peri- and post-operative blood loss and the need for blood transfusion in paediatric patients undergoing cardiac surgery.

CONTRAINDICATIONS

Beclot Injection is contraindicated:

- In patients with acquired defective color vision, since this prohibits measuring one endpoint that should be followed as a measure of toxicity.
- In patients with subarachnoid hemorrhage. Anecdotal experience indicates that cerebral edema and cerebral infarction may be caused by Beclot Injection in such patients.
- In patients with active intravascular clotting.
- In patients with hypersensitivity to tranexamic acid or any of the ingredients.

WARNING

Focal areas of retinal degeneration have developed in cats, dogs, and rats following oral or intravenous tranexamic acid at doses between 250 to 1600 mg/kg/day (6 to 40 times the recommended usual human dose) from 6 days to 1 year. The incidence of such lesions has varied from 25% to 100% of animals treated and was dose-related. At lower doses, some lesions have appeared to be reversible.

Limited data in cats and rabbits showed retinal changes in some animals with doses as low as 126 mg/kg/day (only about 3 times the recommended human dose) administered for several days to two weeks. No retinal changes have been reported or noted in eye examinations in patients treated with tranexamic acid for weeks to months in clinical trials.

For patients who are to be treated continually for longer than several days, an ophthalmological examination, including visual acuity, color vision, eye-ground, and visual fields, is advised, before commencing and at regular intervals during the course of treatment. Tranexamic acid should be discontinued if changes in examination results are found.

Convulsions have been reported in association with tranexamic acid treatment, particularly in patients receiving tranexamic acid during cardiovascular surgery and in patients inadvertently given tranexamic acid into the neuraxial system.

PRECAUTIONS
**General**
The dose of Beclot Injection should be reduced in patients with renal insufficiency because of the risk of accumulation.
Ureteral obstruction due to clot formation in patients with upper urinary tract bleeding has been reported in patients treated with Beclot Injection.
Venous and arterial thrombosis or thromboembolism has been reported in patients treated with Beclot Injection. In addition, cases of central retinal artery and central retinal vein obstruction have been reported.
Patients with a previous history of thromboembolic disease may be at increased risk for venous or arterial thrombosis.
Patients with disseminated intravascular coagulation (DIC), who require treatment with Beclot Injection, must be under strict supervision of a physician experienced in treating this disorder.
Tranexamic acid may cause dizziness and therefore may influence the ability to drive or use machines.

**Impairment of Fertility:**
Reproduction studies performed in mice, rats, and rabbits have not revealed any evidence of impaired fertility or adverse effects on the fetus due to tranexamic acid.

**Pregnancy (Category B):**
There are no adequate and well-controlled studies in pregnant women. However, tranexamic acid is known to pass the placenta and appears in cord blood at concentrations approximately equal to maternal concentration. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

**Nursing Mothers:**
Tranexamic acid is present in the mother's milk at a concentration of about a hundredth of the corresponding serum levels. Caution should be exercised when Beclot Injection is administered to a nursing woman.

**Pediatric Use:**
The drug has had limited use in pediatric patients, principally in connection with tooth extraction. The limited data suggest that dosing instructions for adults can be used for pediatric patients needing Beclot Injection therapy.

**Geriatric Use:**
In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.
This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

**Renal Impairment**
The effect of renal impairment on the disposition of tranexamic acid has not been evaluated. Urinary excretion following a single intravenous injection of tranexamic acid declines as renal function decreases. Dose adjustment is needed in patients with renal impairment.

**Hepatic Impairment:**
The effect of hepatic impairment on the disposition of tranexamic acid has not been evaluated. One percent and 0.5 percent of an oral dose are excreted as a dicarboxylic acid and acetylated metabolite, respectively. Because only a small fraction of the drug is metabolized, no dose adjustment is needed in patients with hepatic impairment.

**DRUG INTERACTION**
No drug-drug interaction studies were conducted with tranexamic acid.
POSSIBLE OF SIDE EFFECTS

Gastrointestinal disturbances like nausea, vomiting, diarrhea may occur but disappear when the dosage is reduced. Allergic dermatitis, giddiness, and hypotension have been reported occasionally. Hypotension has been observed when intravenous injection is too rapid. To avoid this response, the solution should not be injected more rapidly than 1 ml per minute.

Thromboembolic events (e.g., deep vein thrombosis, pulmonary embolism, cerebral thrombosis, acute renal cortical necrosis, and central retinal artery and vein obstruction) have been rarely reported in patients receiving tranexamic acid for indications other than hemorrhage prevention in patients with hemophilia. Convulsion, chromatopsia, and visual impairment have also been reported. However, due to the spontaneous nature of the reporting of medical events and the lack of controls, the actual incidence and causal relationship of drug and event cannot be determined. Sudden severe headache, confusion, problems with vision, speech, or balance may be manifested. Chest pain, sudden cough, wheezing, rapid breathing, coughing up blood may occur.

DOSAGE

The doctor will decide the correct dose for a patient and how long they should take it.

**Usual adults dose:**

**Adult Cardiac Surgery**: After induction of anaesthesia and prior to skin incision, administer a pre-surgical loading dose of 15 mg/kg tranexamic acid, followed by infusion of 4.5 mg/kg/h for the duration of surgery. 0.6 mg/kg of this infusion dose may be added in the priming volume of the heartlung machine.

**Adult Total Knee Arthroplasty**: Administration of 15 mg/kg tranexamic acid prior to release of the tourniquet followed by repeat bolus injection of 15 mg/kg at 8 hourly intervals after the initial dose. The last bolus dose is to be administered 16 hours after the initial dose.

**Adult Total Hip Arthroplasty**: Administration of 15 mg/kg tranexamic acid immediately prior to skin incision, followed by a repeat bolus of 15 mg/kg at 8 hourly intervals after the initial dose. The last bolus dose is to be administered 16 hours after the initial dose.

**Treatment of Local Fibrinolysis**: The usual dose is 500-1000 mg (5-10 ml) three times a day. This will usually be given by a slow injection into the vein.

**Treatment of General Fibrinolysis**: The usual dose is 1000 mg (10 ml) every 6 to 8 hours, or up to 15 mg per kg of body weight.

**Use in Children**: The doctor will decide the right dose to administer a child patient and how long he or she should take it.

If Tranexamic Acid Solution for Injection is given to a child over one year old, the dose will be based on the child’s body weight.

**Use in Elderly**: No reduction in dose is necessary unless you have kidney problems.

**Use in Patients with Kidney Problems**: Patients having kidney problems the dose may be reduced. The doctor will decide what dose to be given to such type of patients based on a blood test.

**Use in Patients with liver problems**: No reduction in dose is necessary.

OVERDOSE AND TREATMENT

Cases of overdosage of Beclot Injection have been reported. Based on these reports, symptoms of overdosage may be gastrointestinal, e.g., nausea, vomiting, diarrhea; hypotensive, e.g., orthostatic symptoms; thromboembolic, e.g., arterial, venous, embolic; neurologic, e.g., visual impairment, convulsions, headache, mental status changes; myoclonus; and rash.

Although if there is experience overdose of tranexamic acid discontinuation of the medication is recommended.

For thromboembolic complications-Monitoring the patient carefully and administering appropriate therapy, depending on the location and size of the thrombus. Use of heparin or a thrombolytic agent may be considered in severe cases. However, these medications must be used with extreme caution, if at all, in patients receiving
tranexamic acid to prevent or treat hemorrhaging, because of the risk of uncontrollable hemorrhage being induced in such patients.

ROUT OF ADMINISTRATION
By slow intravenous injection.

PREPARATION OF DOSING FORM
Tranexamic acid injection may be mixed with intravenous infusion solutions, including solutions containing electrolytes, carbohydrates, amino acids, or dextran. Heparin may be added to the tranexamic acid injection, if necessary.

STABILITY
Intravenous infusion mixtures should be prepared the same day they are to be used.

INCOMPATIBILITY
Tranexamic acid should not be added to any solution containing penicillin or mixed with blood.

STORAGE
Store between 15 and 30°C.

PRESENTATION
Beclot Injection is presented 100mg./ml. in 5ml. ampoule. In a mono pack there are 5*5ml. clear ampoules.