Tranmax Injection 500mg

(Tranexamic Acid Injection BP)

Solution for Intravenous Injection

ٹران میکس انجکشن

(ٹرانزامک ایسڈ)

۵۰۰ ملی گرام

COMPOSITION: Each 5ml ampoule contains:
Tranexamic Acid BP ... 500mg. [BP Specs.]

INDICATIONS: Prevention and treatment of haemorrhages due to general or local fibrinolysis in adults and children from one year.
Specific indications include: Haemorrhage caused by general or local fibrinolysis such as: Menorrhagia and metrorrhagia, Gastrointestinal bleeding, Haemorrhagic urinary disorders, further to prostate surgery or surgical procedures affecting the urinary tract, Ear Nose Throat surgery (adenoidectomy, tonsillectomy, dental extractions), Gynaecological surgery or disorders of obstetric origin, Thoracic and abdominal surgery and other major surgical intervention such as cardiovascular surgery, Management of haemorrhage due to the administration of a fibrinolytic agent.

DOSAGE AND ADMINISTRATION:
Adults: Unless otherwise prescribed, the following doses are recommended:
1. Standard treatment of local fibrinolysis: 0.5g (1 ampoule of 5ml) to 1g (1 ampoule of 10ml or 2 ampoules of 5ml) Tranexamic Acid by slow intravenous injection (= 1ml/minute) two to three times daily.
2. Standard treatment of general fibrinolysis: 1g (1 ampoule of 10ml or 2 ampoules of 5ml) Tranexamic Acid by slow intravenous injection (= 1ml/minute) every 6 to 8 hours, equivalent to 15mg/kg Body weight.
Renal impairment: In renal insufficiency leading to a risk of accumulation, the use of Tranexamic Acid is contra-indicated in patient with severe renal impairment. For patient with mild to moderate renal impairment, the dosage of Tranexamic Acid should be reduced according to the serum creatinine level:

Serum creatinine		Dose IV	Administration
µmol/l	mg/10ml		
120 to 249	1.35 to 2.82	10mg/kg Body weight	Every 12 hours
250 to 500	2.82 to 5.65	10mg/kg Body weight	Every 24 hours
> 500	> 5.65	5mg/kg Body weight	Every 24 hours

Hepatic impairment: No dose adjustment is required in patient with hepatic impairment.
Elderly: No reduction in dosage is necessary unless there is evidence of renal failure.
Method of administration: The administration is strictly limited to slow intravenous injection.

OVERDOSE: No cases of overdosage have been reported. Signs and symptoms may include dizziness, headache, hypotension, and convulsions. It has been shown that convulsions tend to occur at higher frequency with increasing dose. Management of overdose should be supportive.

PRECAUTIONS FOR USE: The indications and method of administration indicated above should be followed strictly: Intravenous injections should be given very slowly, Tranexamic Acid should not be administered by the intramuscular route.
Convulsions: Cases of convulsions have been reported in association with Tranexamic Acid treatment. In coronary artery bypass graft (CABG) surgery, most of these cases were reported following intravenous (i.v.) injection of Tranexamic Acid in high doses. With the use of the recommended lower doses of Tranexamic Acid, the incidence of post-operative seizures was the same as that in untreated patients.
Visual disturbances: Attention should be paid to possible visual disturbances including visual impairment, vision blurred, impaired colour vision and if necessary the treatment should be discontinued. With continuous long-term use of Tranexamic Acid solution for injection, regular ophthalmologic examinations (eye examinations including visual acuity, colour vision, fundus, visual field etc.) are indicated. With pathological ophthalmic changes, particularly with diseases of the retina, the physician must decide after consulting a specialist on the necessity for the long-term use of Tranexamic Acid solution for injection in each individual case.
Haematuria: In case of haematuria from the upper urinary tract, there is a risk for urethral obstruction.
Thromboembolic events: Before use of Tranexamic Acid, risk factors of thromboembolic disease should be considered. In patients with a history of thromboembolic diseases or in those with increased incidence of thromboembolic events in their family history (patients with a high risk of thrombophilia), Tranexamic acid solution for injection should only be administered if there is a strong medical indication after consulting a physician experienced in hemostaseology and under strict medical supervision. Tranexamic Acid should be administered with care in patients receiving oral contraceptives because of the increased risk of thrombosis.
Disseminated intravascular coagulation: Patients with disseminated intravascular coagulation (DIC) should in most cases not be treated with Tranexamic Acid. If Tranexamic Acid is given it must be restricted to those in whom there is predominant activation of the fibrinolytic system with acute severe bleeding. Characteristically, the haematological profile approximates to the following: reduced euglobulin clot lysis time; prolonged prothrombin time; reduced plasma levels of fibrinogen, factors V and VIII, plasminogen fibrinolysin and alpha-2 macroglobulin; normal plasma levels of P and P complex; i.e. factors II (prothrombin), VIII and X; increased plasma levels of fibrinogen degradation products; a normal platelet count. The foregoing presumes that the underlying disease state does not of it self modify the various elements

Rev: 08-19/0

in this profile. In such acute cases a single dose of 1g Tranexamic Acid is frequently sufficient to control bleeding. Administration of Tranexamic Acid in DIC should be considered only when appropriate haematological laboratory facilities and expertise are available.

ADVERSE DRUG REACTIONS: The ADRs reported from clinical studies and post-marketing experience are listed below:
Skin and subcutaneous tissues disorders- Dermatitis allergic.
Gastrointestinal disorders- Diarrhoea, Vomiting, Nausea.
Nervous system disorders- Convulsions particularly in case of misuse.
Eye disorders- Visual disturbances including impaired colour vision Vascular disorders-Malaise with hypotension, with or without loss of consciousness (generally following a too fast intravenous injection, exceptionally after oral administration), Arterial or venous thrombosis at any sites.
Immune system disorders- Hypersensitivity reactions including anaphylaxis

DRUG INTERACTION: No interaction studies have been performed. Simultaneous treatment with anticoagulants must take place under the strict supervision of a physician experienced in this field. Medicinal products that act on haemostasis should be given with caution to patients treated with Tranexamic Acid. There is a theoretical risk of increased thrombus-formation potential, such as with oestrogens. Alternatively, the antifibrinolytic action of the drug may be antagonised with thrombolytic drugs.

PHARMACOLOGICAL PROPERTIES: Pharmacodynamics: Tranexamic Acid exerts an anti haemorrhagic activity by inhibiting the fibrinolytic properties of plasmin. A complex involving Tranexamic Acid, plasminogen is constituted; the Tranexamic Acid being linked to plasminogen when transformed into plasmin. The activity of the Tranexamic acid-plasmin complex on the activity on fibrin is lower than the activity of free plasmin alone. In vitro studies showed that high Tranexamic dosages decreased the activity of complement. **Paediatric population**: In children over one year old: Literature review identified 12 efficacy studies in paediatric cardiac surgery which have included 1073 children, 631 having received Tranexamic acid. Most of them were controlled versus placebo. Studied population was heterogenic in terms of age, surgery types, dosing schedules. Study results with Tranexamic Acid suggest reduced blood loss and reduced blood product requirements in paediatric cardiac surgery under cardiopulmonary bypass when there is a high risk of haemorrhage, especially in cyanotic patients or patients undergoing repeat surgery. The most adapted dosing schedule appeared to be: - first bolus of 10mg/kg after induction of anaesthesia and prior to skin incision, - continuous infusion of 10mg/kg/h or injection into the CPB (Cardiopulmonary Bypass) pump prime at a dose adapted on the CPB procedure, either according to patient weight with a 10mg/kg dose, either according to CPB pump prime volume, - last injection of 10mg/kg at the end of CPB. While studied in very few patients, the limited data suggest that continuous infusion is preferable, since it would maintain therapeutic plasma concentration throughout surgery. No specific dose-effect study or PK study has been conducted in children.

Pharmacokinetics: **Absorption**: Peak plasma concentrations of Tranexamic Acid are obtained rapidly after a short intravenous infusion after which plasma concentrations decline in a multi-exponential manner.
Distribution: The plasma protein binding of tranexamic acid is about 3% at therapeutic plasma levels and seems to be fully accounted for by its binding to plasminogen. Tranexamic acid does not bind to serum albumin. The initial volume of distribution is about 9 to 12 liters. Tranexamic Acid passes through the placenta. Following administration of an intravenous injection of 10mg/kg to 12 pregnant women, the concentration of Tranexamic Acid in serum ranged 10-53mg/mL while that in cord blood ranged 4-31mg/mL. Tranexamic Acid diffuses rapidly into joint fluid and the synovial membrane. Following administration of an intravenous injection of 10mg/kg to 17 patients undergoing knee surgery, concentrations in the joint fluids were similar to those seen in corresponding serum samples. The concentration of Tranexamic Acid in a number of other tissues is a fraction of that observed in the blood (breast milk, one hundredth; cerebrospinal fluid, one tenth; aqueous humor, one tenth). Tranexamic Acid has been detected in semen where it inhibits fibrinolytic activity but does not influence sperm migration. **Excretion**: It is excreted mainly in the urineas unchanged drug. Urinary excretion via glomerular filtration is the main route of elimination. Renal clearance is equal to plasma clearance (110 to 116mL/min). Excretion of Tranexamic Acid is about 90% within the first 24 hours after intravenous administration of 10mg/kg body weight.
Elimination: Half-life of Tranexamic Acid is approximately 3 hours.
Special populations: Plasma concentrations increase in patients with renal failure. No specific PK study has been conducted in children.

CONTRA-INDICATIONS: Hypersensitivity to the active substance or to any of the excipients. Acute venous or arterial thrombosis, Fibrinolytic conditions following consumption coagulopathy except in those with predominant activation of the fibrinolytic system with acute severe bleeding, Severe renal impairment (risk of accumulation), History of convulsions, Intrathecal and intraventricular injection, intracerebral application (risk of cerebral oedema and convulsions).

INSTRUCTIONS: Store below 30°C. Protect from heat and light. Keep out of the reach of children.

PRESENTATION: Tranmax Injection 500mg/5ml is available as Solution for Intravenous Injection in a pack of 5ml x 10 Ampoules.

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی اور روشنی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

PHARMA
Manufactured for: **Nabiqasim Industries (Pvt.) Ltd.**
17/24, Korangi Industrial Area, Karachi-Pakistan.
Manufactured by: **Surge Laboratories (Pvt.) Ltd.**
10th Km, Faisalabad Road, Bikhi, District Sheikhupura-Pakistan. Rev: 08-19/0