Bosch

For Medical Professional only

Antiplasminic Agent

Btrol® CAPSULES INJECTION

(Tranexamic Acid)

بٹرول کیپسولز / انجکشن

(ٹرانزیمک ایسڈ)

DESCRIPTION:
Tranexamic acid is trans-4-(aminomethyl)cyclohexanecarboxylic acid, an antifibrinolytic agent. Tranexamic acid is a white crystalline powder. Having Empirical formula $C_8H_{15}NO_2$ and Molecular weight: 157.2. Tranexamic Acid in Sodium Chloride Injection is a clear to colorless sterile, nonpyrogenic injectable solution for intravenous administration.

COMPOSITION:
Btrol 250mg Capsule:
Each Capsule Contains:
Tranexamic acid U.S.P. 250mg
(Product Specs.: J.P.)

Btrol 500mg Capsule:
Each Capsule Contains:
Tranexamic acid U.S.P. 500mg
(Product Specs.: J.P.)

Btrol 250mg/5ml Injection:
Each Ampoule Contains:
Tranexamic acid U.S.P. .... 250 mg
(Product Specs.: U.S.P.)

Btrol 500mg/5ml Injection:
Each Ampoule Contains:
Tranexamic acid U.S.P. .... 500 mg
(Product Specs.: U.S.P.)

CLINICAL PHARMACOLOGY:
Pharmacodynamic Properties:
Pharmacotherapeutic group: Antihemorrhagics, Antifibrinolytics, Aminoacids
ATC code: B02A A02

Mechanism of Action:
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 of fibrin is lower than the activity of free plasmin alone.

Pharmacokinetic Properties
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.
Tranexamic acid is absorbed from the gastrointestinal tract with peak plasma concentrations occurring after about 3 hours. Bioavailability is about 30% to 50%. Concomitant intake of food has no effect on the gastrointestinal absorption of the drug or on the peak plasma concentration following a dose of 2g.

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 10 mg/kg in pregnant women, the concentration of tranexamic acid in serum ranged 10-53 µg/mL while that in cord blood ranged 4-31 µg/mL. Tranexamic acid diffuses rapidly into joint fluid and the synovial membrane. 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.

Metabolism:
Only a small fraction of drug is metabolized. Possible routes of biotransformation are acetylation or deamination followed by oxidation or reduction.

Elimination:
It is excreted mainly in the urine as unchanged drug. Urinary excretion via glomerular filtration is the main route of elimination. Renal clearance is equal to plasma clearance (110 to 116 mL/min). Excretion of tranexamic acid is about 90% within the first 24 hours after intravenous administration of 10 mg/kg body weight. Half-life of tranexamic acid is approximately 3 hours.

SPECIFIC POPULATIONS
Renal Impairment:
Plasma concentrations increase in patients with renal failure.

THERAPEUTIC INDICATIONS:
BTROL (Tranexamic acid) is indicated for the treatment of:
- Hemorrhage or risk of hemorrhage in increased fibrinolysis or fibrinogenolysis.

Local fibrinolysis may occur in the following conditions:
- Prostatectomy and bladder surgery
- Menorrhagia
- Epistaxis
- Conization of the cervix
- Management of dental extraction in patients with coagulopathies
- Ulcerative colitis
- Hematuria
- Gastrointestinal hemorrhage

General fibrinolysis as in prostatic and pancreatic cancer; after thoracic and other major surgery;
- In obstetrical complications such as abruptio placentae and post-partum hemorrhage
- In leukemia 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 pediatrics patients undergoing cardiac surgery, or adult patients undergoing cardiac surgery or total knee arthroplasty or total hip arthroplasty.

DOSAGE AND ADMINISTRATION:

BTROL (Tranexamic acid) is given by mouth and by slow intravenous injection or continuous infusion. The recommended standard dose is 1000mg-1500mg orally or 500mg-1000mg by slow intravenous injection at a rate of 1mL/minute, two to three times daily.

General:

250-500mg/day IV or IM in 1-2 divided doses 500-1000mg each time IV or 500-2500mg by IV drip infusion as required during or after surgery.

Prostatectomy

500mg-1000mg by slow intravenous injection every eight hours (the first injection being given during the operation) for the first three days after surgery; thereafter 1000mg-1500mg orally three to four times daily until macroscopic hematuria is no longer present.

Menorrhagia

1000mg-1500mg orally three to four times daily for three to four days. BTROL (Tranexamic acid) therapy is initiated when bleeding has become profuse.

Epistaxis

1500mg orally three times daily for four to ten days. BTROL (Tranexamic acid) injection may be applied topically to the nasal mucosa of patients suffering from epistaxis. This can be done by soaking a gauze strip in the solution and then packing the nasal cavity.

Hematuria

1000mg-1500mg orally 2-3 times daily until macroscopic hematuria is no longer present.

Conization of the Cervix

1500mg orally 3 times a day for 12 to 14 days post-operatively.

Dental Surgery in Patients with Coagulopathies

Immediately before surgery, 10mg per kg body weight should be given intravenously. After surgery, 25mg per kg body weight are given orally three to four times daily for six to eight days. It may be necessary to administer coagulation factor concentrate.

General Fibrinolysis

1000mg by slow intravenous injection three to four times daily. With fibrinolysis in conjunction with diagnosed, increased intravascular coagulation, i.e., defibrillation syndrome, an anticoagulant such as heparin may be given with caution.

Hereditary Angioneurotic Oedema

1000mg-1500mg orally two to three times daily as intermittent or continuous treatment depending on whether the patient has prodromal symptoms or not.

Patients with Renal Impairment:

Following dosage should be followed

Serum creatinine (micromol/L)	eGFR (mL/min/1.73m^2)	Dose IV	Dose Orally	Dose frequency
120 - 249	60 - 89	10mg/kg	15mg/kg	twice daily
250 - 500	30 - 59	10mg/kg	15mg/kg	Daily
>500	< 29	5mg/kg	7.5mg/kg	Daily

Intravenous Administration

Adult Cardiac Surgery

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

Adult Total Knee Arthroplasty

Administration of 15mg/kg tranexamic acid prior to release of the tourniquet followed by repeat bolus injection of 15mg/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 15mg/kg tranexamic acid immediately prior to skin incision, followed by a repeat bolus of 15mg/kg at 8 hourly intervals after the initial dose. The last bolus dose is to be administered 16 hours after the initial dose.

Paediatric Population:

In children from 1 year, for current approved indications the dosage is in the region of 20 mg/kg/day. However, data on efficacy, posology and safety for these indications are limited.

The efficacy, posology and safety of tranexamic acid in children undergoing cardiac surgery have not been fully established.

Elderly:

No reduction in dosage is necessary unless there is evidence of renal failure. The administration is strictly limited to slow intravenous injection.

Method of Administration:

The administration is strictly limited to slow intravenous injection. For intravenous infusion, Btrol Injection may be mixed with most solutions for infusion such as electrolyte solutions, carbohydrate solutions, amino acid solutions, and Dextran solutions. Heparin may be added to Btrol Injection. Btrol Injection should NOT be mixed with blood. The drug is a synthetic amino acid and should NOT be mixed with solutions containing penicillin.

The mixture should be used immediately after preparation. If storage is necessary, the mixture should be stored at 2°C - 8°C for a maximum of 24 hours. Mixture not used within 24 hours of preparation, should be discarded.

CONTRAINDICATIONS:

Tranexamic acid is contraindicated in patients with:

- Known hypersensitivity to tranexamic acid or to any of the excipient of the product.
- Acute thromboembolic disease such as deep vein thrombosis, pulmonary embolism and cerebral 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). - Active intravascular clotting.
- History of convulsions.
- Intrathecal and intraventricular injection, intracerebral application (risk of cerebral edema and convulsions).
- Acquired disturbances of color vision. If disturbances of color vision arise during the course of treatment the administration of the preparation should be discontinued.
- Subarachnoid hemorrhage should not be given tranexamic acid as anecdotal experience indicates that cerebral edema and cerebral infarction may be caused in such cases.

WARNINGS AND PRECAUTIONS:

- Intravenous Injection of tranexamic acid should be given very slowly.
- Attention should be paid to possible visual disturbances including visual impairment, vision blurred, impaired color vision and if necessary the treatment should be discontinued. With continuous long-term use of tranexamic acid, regular ophthalmologic examinations (eye examinations including visual acuity, color vision, fundus, visual field etc.) are indicated.
- In case of haematuria from the upper urinary tract, there is a risk for urethral obstruction.
- 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 should only be administered if there is a strong medical indication and under strict medical supervision.
- Tranexamic acid should be administered with care in patients receiving oral contraceptives because of the increased risk of thrombosis.

- 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. Administration of tranexamic acid in DIC should be considered only when appropriate hematological laboratory facilities and expertise are available.
- Patients with irregular menstrual bleeding should not use tranexamic acid until the cause of the irregularity has been established.
- Convulsions have been reported in association of tranexamic acid treatment.

DRUG INTERACTIONS:
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.

ADVERSE EFFECTS:
Common: Diarrhea, Vomiting, Nausea
Uncommon: Dermatitis allergic
Not Known: Hypersensitivity reactions including anaphylaxis, Dizziness, convulsions particularly in case of misuse, Visual disturbances including impaired colour vision, 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.

USE IN PREGNANCY AND LACTATION:
Pregnancy:
There are no adequate and well-controlled studies in pregnant women. However, tranexamic acid is known to cross the placenta and appears in cord blood at concentrations approximately equal to maternal concentration. Therefore, tranexamic acid should be used during pregnancy only if clearly needed.

Lactation:
Tranexamic acid is secreted in the mother's milk at a concentration of about a hundredth of the corresponding serum levels but is not likely to influence the child at therapeutic doses.

OVERDOSE:
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.

SHELF LIFE:
3 Years

STORAGE AND INSTRUCTIONS:
Capsules: Protect from heat, sunlight & moisture, store between 15°C-30°C.
Injection: For intramuscular/ intravenous use only.
Protect from heat and sunlight store at or below 25°C.
Precautions: Do not use if injection is leaking, solution is cloudy or contains undissolved particles.
The expiration date refer to the product correctly stored at the required condition.
Keep out of the reach of children.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com
To be sold on prescription of a registered medical practitioner only.

PRESENTATION:
Btrol 250mg Capsules: .....1x10's in blister pack
Btrol 500mg Capsules: ..... 1x10's in blister pack
Btrol 250mg Injection:..... 5x5ml Ampoules
Btrol 500mg Injection:..... 5x5ml Ampoules

ہدایات :

کیپسولز: دھوپ، گرمی اور نمی سے محفوظ ۱۵۔۳۰ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان میں رکھیں۔
انجکشن: دھوپ اور گرمی سے محفوظ ۲۵ ڈگری سینٹی گریڈ یا اس سے کم درجہ حرارت پر رکھیں۔
بچوں کی پہنچ سے دور رکھیں۔
احتیاط: انجکشن لیک ہونے دھندلا ہونے یا اس میں کوئی غیر حل پزیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

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