Bosch

For Healthcare Professionals only

Antifibrinolytic Agent

Btrol® CAPSULES INJECTION

(Tranexamic Acid)

بٹرول کیپسولز / انجکشن

(ٹرانزیمک ایسڈ)

QUALITATIVE AND QUANTITATIVE COMPOSITION

Btrol 250mg Capsules:
Each capsule contains:
Tranexamic acid USP.....250mg
(Product Specs.: JP)

Btrol 500mg Capsules:
Each capsule contains:
Tranexamic acid USP.....500mg
(Product Specs.: JP)

Btrol 250mg/5mL Injection
Each ampoule contains:
Tranexamic acid USP…. 250mg
(Product Specs.: USP)

Btrol 500mg/5mL Injection
Each ampoule contains:
Tranexamic acid USP…. 500mg
(Product Specs.: USP)

PHARMACEUTICAL FORM
Capsules and Injection

CLINICAL PARTICULARS

Therapeutic indications
Tranexamic Acid is indicated for short-term use for hemorrhage or risk of hemorrhage in those with increased fibrinolysis or fibrinogenolysis.

Local fibrinolysis as occurs in the following conditions
Specific indications include:
- Hemorrhage caused by general or local fibrinolysis
- Menorrhagia and metrorrhagia
- Gastrointestinal bleeding
- Hemorrhagic urinary disorders, further to prostate surgery or surgical procedures affecting the urinary tract
- Ear Nose Throat surgery (adenoidectomy, tonsillectomy, dental extractions)
- Gynecological surgery or disorders of obstetric origin
- Thoracic and abdominal surgery and other major surgical intervention such as cardiovascular surgery
- Management of hemorrhage due to the administration of a fibrinolytic agent
- Epistaxis
- Conization of the cervix
- Traumatic hyphema
- Hereditary angioneurotic oedema
- Indicated in patients with hemophilia for short-term use (2 to 8 days) to reduce or prevent hemorrhage and reduce the need for replacement therapy during and following tooth extraction

Posology and Method of Administration

Posology

Oral

The usual adult dose of tranexamic acid is 750 to 2000mg per day, orally administered in 3 to 4 divided doses. The dosage may be increased or decreased as appropriate depending on age and symptoms or as directed by physician.
Adults: For prophylactic purposes, the average recommended daily doses, unless adapted on a case-by-case basis, are 0.5-1g orally. For the treatment of ongoing hemorrhagic manifestations, oral doses rise to 1-3g in divided doses.
Children: For prophylactic purposes, for every kilo of body weight they administer 5 to 10mg daily orally in divided doses. For therapeutic purposes, oral doses will be double (from 10 to 20mg/kg). However, data on efficacy, posology and safety for these indications are limited. The efficacy and safety of tranexamic acid in children undergoing heart surgery have not been fully established

Intravenous and Intramuscular Route

The usual adult dose of tranexamic acid is 250 to 500mg per day, divided into 1 to 2 doses, administered intravenously or intramuscularly. During and after surgery, administer a single intravenous injection of 500 to 1000mg, or intravenous drip infusion of 500 to 2500mg, as needed. The dosage may be increased or decreased as appropriate depending on age and symptoms.

For Tooth Extraction

Before Extraction: Administer 10mg/kg actual body weight of Tranexamic Acid in Sodium Chloride Injection intravenously with replacement therapy.
After Extraction: Administer 10mg/kg actual body weight 3-4 times daily for 2 to 8 days. Infuse no more than 10mL/minute to avoid hypotension.

Hepatic impairment

No dose adjustment is required in patient with hepatic impairment.

Pediatric Population

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

Elderly

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

Renal impairment

In renal insufficiency leading to a risk of accumulation, the use of tranexamic acid is contraindicated 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		Oral dose	Parenteral Dose	Administration
µmol/L	mg/10mL			
120 to 249	1.35 to 2.82	15mg/kg body weight	10mg/kg body weight	Every 12 hours
250 to 500	2.82 to 5.65	15mg/kg body weight	10mg/kg body weight	Every 24 hours
> 500	> 5.65	-	5mg/kg body weight	Every 24 hours

Method of administration

For IV

Administer slowly intravenously. If administered rapidly, nausea, chest discomfort, heart palpitations, and decreased blood pressure may occur in rare cases.

For IM

To avoid effects on tissues, nerves, etc., pay attention to the following points,

- Carefully administer the injection site, avoiding areas where nerves travel
- When injecting repeatedly, inject left and right alternately, etc. at the same site
- Special care with children
- In case of severe pain or seeing blood flowing backward when the needle is inserted

Contraindications

- Hypersensitivity to the active substance
- 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 cerebralo edema and convulsions)

Special warnings and precautions for use

The indications and method of administration indicated below should be followed strictly,

- Intravenous injections should be given very slowly. In case of hematuria of renal origin (especially in hemophilia), 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
- 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

Interaction with other medicinal products and other forms of interaction

Tranexamic Acid will counteract the thrombolytic effect of fibrinolytic preparations.

Fertility, Pregnancy and lactation

Women of childbearing potential have to use effective contraception during treatment.

Pregnancy

Tranexamic acid should be used during pregnancy only if the expected benefit justifies the potential risk.

Lactation

Tranexamic acid is excreted in human milk. Therefore, breastfeeding is not recommended.

Fertility

There are no clinical data on the effects of tranexamic acid on human fertility.

Effects on ability to drive and use machines

Oral Tranexamic Acid has no or negligible influence on the ability to drive and use machines.

UNDESIRABLE EFFECTS

Adverse reactions reported are presented in table below. Adverse reactions are listed according to MedDRA primary system organ class. Within each system organ class, adverse reactions are ranked by frequency. Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness. Frequencies were defined as follows. Very common (≥ 1/10), Common (≥1/100, <1/10), Uncommon (≥1/1000, <1/100), Rare (≥ 1/10,000, <1/1,000), Very rare (<1/10,000) including isolated reports.

MedDRA System Organ Class	Frequency		Undesirable Effects
	Parenteral	Oral	
Immune system disorders	Not known	Very Rare	Hypersensitivity reactions including anaphylaxis
Nervous system disorders	Not known	-	Dizziness, convulsions particularly in case of misuse
Eye disorders	Not known	Rare	Visual disturbances including impaired color vision
Vascular disorders	Not known	-	Malaise with hypotension, with or without loss of consciousness (generally following a too fast intravenous injection, exceptionally after oral administration)
		Rare	Thromboembolic Events
		Very Rare	Arterial or venous thrombosis at any sites
Gastrointestinal disorders	Common	Very Rare	Diarrhea, Vomiting, Nausea
Skin and subcutaneous tissues disorders	Uncommon	Rare	Dermatitis allergic

Overdose

For Parenteral

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.

For Oral

Symptoms may be nausea, vomiting, orthostatic symptoms and/or hypotension. 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.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: Antihemorrhagics, Antifibrinolytics, Amino acids

ATC code: B02AA02.

Mechanism of action: 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

For Oral

When this drug was administered orally in a single dose to five healthy adult males, the pharmacokinetic parameters of tranexamic acid were as follows

Pharmacokinetic parameters of tranexamic acid after single oral administration				
Dose	Number of cases	C_{max} (µg/mL)	T_{max} (hr)	$t_{1/2}$ (hr)
500mg	5	5.5	2∼3	3.3

For IV

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. The distribution volume is about 33% of the body mass. Tranexamic acid crossed the placenta, and may reach one hundredth of the serum peak concentration in the milk of lactating women.

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 116mL/min). Excretion of tranexamic acid is about 90% within the first 24 hours after intravenous administration of 10mg/kg body weight. Half-life of tranexamic acid is approximately 3 hours. Following oral administration, 1.13% and 39% of the administered dose were recovered after 3 and 24 hours respectively.

Renal impairment

Plasma concentrations increase in patients with renal failure.

PHARMACEUTICAL PROPERTIES

Incompatibilities

This medicinal product must not be mixed with other medicinal products.

Shelf life

03 years

Special precautions for storage and instructions

For Capsules: Protect from heat, sunlight & moisture, store between 15°C-30°C.
For injection: Protect from heat and sunlight store at or below 25°C.
The expiration date refers to the product correctly stored at the required condition.
Keep out of the reach of children.
Precautions: Do not use if injection is leaking, solution is cloudy or contains undissolved particles.
To be sold on the prescription of a registered medical practitioner only.

Nature and contents of containers/ Presentation

Btrol 250mg Capsules: Blister pack of 10 capsules
Btrol 500mg Capsules: Blister pack of 10 capsules
Btrol 250mg/5mL Injection: 10x5mL & 5x5mL Ampoules
Btrol 500mg/5mL Injection: 10x5mL & 5x5mL Ampoules

REGISTRATION HOLDER / MARKETING AUTHORIZATION HOLDER

Head Office:

Bosch Pharmaceuticals (Pvt.) Ltd.,
8, Modern Society, Tipu Sultan Road, Karachi-Pakistan

Manufacturing site:

Bosch Pharmaceuticals (Pvt.) Ltd.,
Plot No. 221-223, Sector 23, Korangi Industrial area Karachi-Pakistan

REGISTRATION / MARKETING AUTHORIZATION NUMBERS

Btrol 250mg Capsules: 030226
Btrol 500mg Capsules: 030789
Btrol 250mg/5mL Injection: 030790
Btrol 500mg/5mL Injection: 030791

DATE FROM WHICH MARKETING IS AUTHORIZED/RENEWAL OF AUTHORIZATION

Btrol 250mg Capsules:31-05-2003/30-05-2023
Btrol 500mg Capsules: 09-08-2003/08-08-2023
Btrol 250mg/5mL Injection: 09-08-2003/08-08-2023
Btrol 500mg/5mL Injection: 09-08-2003/08-08-2023

DATE OF REVISION OF THE TEXT.

13-03-2024

ہدایات :

گیپسولز: 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۔

Manufactured by:
Bosch Pharmaceuticals (Pvt.) Ltd.
221-223, Sector 23, Korangi Industrial Area,
Karachi - Pakistan

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Btrol®

CAPSULES
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(Tranexamic Acid)

بٹرول

کیپسولز / انجکشن

(ٹرانزِیمک ایسڈ)

FIRST & ONLY CERTIFIED HALAAL

PHARMACEUTICAL COMPANY