SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

1.1 Brand Name : UNOTATION
1.2 Generic Name : Tranexamic Acid Injection BP
1.3 Strength : 100 mg/ ml
1.4 Pharmaceutical Form: Injection

2. QUALITY AND QUANTITATIVE COMPOSITION

Each ml contains:
Tranexamic Acid BP …. 100 mg
Water for Injections BP ……. q.s.

3. PHARMACEUTICAL FORM VISUAL DESCRIPTION:

Injection

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS:

Local fibrinolysis:
For short term use in prophylaxis and treatment in patients at high risk of per- and post-operative haemorrhage following:
a) Prostatectomy
b) Confiscation of the cervix
c) Surgical procedures and dental extractions in haemophiliacs

General fibrinolysis:
a) Haemorrhagic complications in association with thrombolytic therapy.
b) Haemorrhage associated with disseminated intravascular coagulation with predominant activation of the fibrinolytic system.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Route of administration: Slow Intravenous injection.
Local fibrinolysis:
The recommended standard dose is 5-10ml (500-1000mg) by slow intravenous injection (1 ml/min), three times daily. Following an initial intravenous injection, subsequent treatment may proceed by intravenous infusion. Following addition to a suitable diluent, TranexamicAcid Injection may be administered at a rate of 25-50 mg/kg body wt/day.
General fibrinolysis:
1) In disseminated intravascular coagulation with predominant activation of the fibrinolytic system, usually a single dose of 10ml (1 g) is sufficientto control bleeding.
2) Neutralisation of thrombolytic therapy; 1 0mg/kg body wt by slow intravenous injection.
Children:
In children, the dosage is in the region of 20 mg/kg/day. However, data on efficacy, posology and safety for these indications is limited.

4.3 CONTRAINDICATIONS

• Hypersensitivity to Tranexamic acid.
• History of venous or arterial thrombosis
• History of convulsions
• lntrathecal and intraventricular injection, intracerebral application (risk of cerebral oedema and convulsions)

4.4 SPECIAL WARNINGS AND 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.

• Due to the risk of cerebral oedema and convulsions, intrathecal or intraventricular injection and intracerebral application is contra-indicated. In patients with a history of convulsion, Tranexamic acid should not be administered.

• In case of haematuria of renal origin, there is a risk of mechanical anuria due to formation of a ureteral clot.

• In patients with renal insufficiency, because of the risk of accumulation. The dose should be reduced according to the following table:

Serum Creatinine	Dose iv	Dose Frequency
120-250 mcmol/I	10 mg/kg	Twice daily
250-500 mcmol/I	10 mg/kg	Every 24th hour
> 500 mcmol/I	5 mg/kg	Every 24th hour

In massive haematuria from the upper urinary tract (especially in haemophilia) since, in a few cases, ureteric obstruction has been reported.

• In patients with disseminated intravascular coagulation (DIC) treatment 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 and alpha-2 macroglobulin; normal plasma levels of P and Pcomplex; 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 itself modify the various elements in this profile. In such acute cases a single dose of 1g tranexamic acid is frequently sufficient to control bleeding.

The fibrinolytic activity in the blood will be reduced for about 4 hours if renal function is normal. Anticoagulation with heparin should be instigated in order to prevent further fibrin deposition. Administration of Tranexamic Acid Injection in DIC should be considered only when appropriate haematological laboratory facilities and expertise are available. Tranexamic Acid Injection must not be administered in DIC with predominant activation of the coagulation system.

• Before use of TXA, risk factors of thromboembolic disease should be investigated.

• Tranexamic acid should be administered with care in patients receiving oral contraceptives because of the increased risk of thrombosis.

4.5 INTERATION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTIONS

The solution for injection may be mixed with the following solutions: dextrose 5%, sodium chloride 0.9%, dextran 40 in 5% dextrose and dextran 40 in 0.9% sodium chloride.

Tranexamic Acid Solution for Injection may be mixed with Heparin.

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.

Breastfeeding:

Tranexamic acid passes into breast milk to a concentration of approximately one hundredth of the concentration in the maternal blood. Therefore, any antifibrinolytic effect in the infant is unlikely.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINE

Not applicable.

4.8 UNDESIRABLE EFFECTS

Very rare adverse events have been reported:
Gastro-intestinal disorders:
Digestive effects such as nausea, Vomiting and Diarrhea.
Cardio-vascular disorders:
Malaise with hypotension, with or without loss of consciousness arterial or venous thrombosis at any sites.
Nervous system disorders:
Dizziness, Convulsions.
General disorders:
Hypersensitivity reactions including anaphylaxis.

4.9 OVERDOSE

Symptoms may be nausea, vomiting, orthostatic symptoms and/ or hypotension.
Maintain a high fluid intake to promote renal excretion. Anticoagulant treatment should be considered.
There is a risk of thrombosis in predisposed individuals.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMICS PROPERTIES

Tranexamic Acid is an antifibrinolytic that competitively inhibits the activation of plasminogen to plasmin. Tranexamic Acid is a competitive inhibitor of plasminogen activation, and at much higher concentrations, a non-competitive inhibitor of plasmin, i.e., actions similar to aminocaproic acid. Tranexamic acid is about 10 times more potent in vitro than aminocaproic acid. Tranexamic Acid competitively inhibits activation of plasminogen (via binding to the kringle domain), thereby reducing conversion of plasminogen to plasmin (fibrinolysin), an enzyme that degrades fibrin clots, fibrinogen, and other plasma proteins, including the procoagulant factors V and VIII. Tranexamic Acid also directly inhibits plasmin activity, but higher doses are required than are needed to reduce plasmin formation.

5.2 PHARMACOKINETIC PROPERTIES

Absorption:
Peak plasma TXA concentration is obtained immediately after IV administration (500mg). Then concentration decreases until the 6th hour. Elimination half-life is about 3 hours.
Distribution:
TXA is delivered in the cell compartment and the cerebrospinal fluid with delay. The distribution volume is about 33% of the body mass.
Metabolism:
Only a small fraction of the drug is metabolized (less than 5%).
Elimination:
TXA 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). Plasma concentrations are increased in patients with renal insufficiency.

5.3 PRECLINICAL SAFETY DATA

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction. Epileptogenic activity has been observed in animals with intrathecal use of Tranexamic acid.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Water for Injections BP

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

24 Months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

This medicine does not require any special storage conditions.

6.5 NATURE AND CONTENTS OF CONTAINER

Tray of 5 x 5ml ampoules packed in Mono Carton along with Pack Insert.

6.6 SPECIAL PRECAUTION FOR DISPOSAL

Not Applicable.

7. MARKETING AUTHORIZATION HOLDER

Name	:	**UNOSOURCE PHARMA NIGERIA LIMITED**
Address	:	# 47 Babapomile Street, Onipetesi Estate, Mangoro-Lagos, Nigeria.
Phone	:	002348038540440
Fax	:	002348129126660

8. MARKETING AUTHORIZATION NUMBERS

Not Applicable.

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Not applicable

10. DATE OF REVISION OF THE TEXT

Not applicable

11. NAME AND ADDRESS OF THE MANUFACTURE

Name	:	**AKUMS DRUGS & PHARMACEUTICALS LTD.**
Address	:	2,3,4 & 5, Sector-8B, IIE, SIDCUL, Ranipur, Haridwar, 249403, Uttarakhand, India.
Phone	:	+91-1334-239220-224
Fax	:	+91-1334-239219
E-mail	:	works@akums.in