TRANMENXIO IV

SCHEDULING STATUS

S4

HIGH ALERT FOR IV USE ONLY

1. Name of the medicine

TRANMENXIO IV

2. Qualitative and quantitative composition

Each 5 ml ampoule contains 500 mg Tranexamic acid.
Sugar free.
For a full list of excipients, see section 6.1.

3. Pharmaceutical Form

Solution for injection/infusion.
Clear, colourless solution with pH of 6,5 - 8,0.

4. Clinical Particulars

4.1 Therapeutic indications

- Short term use in the treatment of hyphaema
- Hereditary angioedema

4.2 Posology and method of administration

Posology

Tranexamic acid is given by slow intravenous infusion/injection. Administration by injection is usually changed to oral administration after a few days.

Traumatic hyphaema:

1,0 to 1,5 g every 8 hours for six to seven days.

Hereditary angioedema:

Some patients are aware of the onset of illness; a suitable treatment for these patients is 1,0 - 1,5 g two to three times daily for some days. Other patients are treated continually at this dosage.

Special populations:

Renal impairment

For patients in renal failure, tranexamic acid should be given with caution because of the risk of accumulation.
Dosages should be reduced in patients with renal impairment. For patients with moderate to severe impaired renal function, the following dosages are recommended.

Serum creatinine (µmol/L)	Intravenous Dose
120 – 250	10 mg/kg body weight twice daily
250 – 500	10 mg/kg body weight daily
> 500	5 mg/kg body weight daily

Method of administration

Tranexamic acid solution for injection is administered intravenously by slow injection over a period of at least five minutes.

4.3 Contraindications

- Hypersensitivity to tranexamic acid or to any of the excipients.
- Acute venous or arterial thrombosis (see section 4.4).
- Fibrinolytic conditions following consumption coagulopathy except in those with predominant activation of the fibrinolytic system with acute severe bleeding (see section 4.4).
- History of convulsions.
- In cases of massive upper urinary tract haemorrhage, antifibrinolytics should be avoided to reduce the risk of ureteric obstruction.
- Patients with pronounced thrombotic tendency or colour vision disorder should not be given TRANMENXIO IV.
- Thrombophlebitis, impaired liver function and subarachnoid bleeding.

4.4 Special warnings and precautions for use

The indications and method of administration indicated above should be followed strictly:

- Intravenous injections or infusions should be given very slowly (maximum 1 ml per minute).
- TRANMENXIO IV should not be administered by the intramuscular route.
- TRANMENXIO IV must not be administered by intrathecal or intraventricular injection, or intracerebral application (due to a risk of cerebral oedema and convulsions.)

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 (IV.) 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, 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 medical practitioner must decide after consulting a specialist on the necessity for the long-term use of TRANMENXIO IV in each individual case.

Haemauria

In case of haematuria from the upper urinary tract, there is a risk for urethral obstruction.

Thromboembolic events

Before use of TRANMENXIO IV, 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 after consulting a medical practitioner experienced in haemostaseology and under strict medical supervision (see section 4.3).

TRANMENXIO IV should be administered with care in patients receiving oral contraceptives because of the increased risk of thrombosis (see section 4.5).

Disseminated intravascular coagulation

Patients with disseminated intravascular coagulation (DIC) should in most cases not be treated with TRANMENXIO IV (see section 4.3). If TRANMENXIO IV 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 itself modify the various elements in this profile. In such acute cases a single dose of 1 g tranexamic acid is frequently sufficient to control bleeding. Administration of TRANMENXIO IV in DIC should be considered only when appropriate haematological laboratory facilities and expertise are available.
TRANMENXIO IV should not be administered concomitantly with Factor IX Complex Concentrates or Anti-inhibitor Coagulant Concentrates, as the risk of thrombosis may be increased.

The safety of tranexamic acid has not been established in pregnancy.
Tranexamic acid passes into breast milk at a concentration of a hundredth of the corresponding serum levels. Caution should be exercised when TRANMENXIO IV is given to nursing women.
For patients in renal failure, tranexamic acid as in TRANMENXIO IV should be given with caution because of the risk of accumulation.
Patients with a previous history of thromboembolic disease should not be given TRANMENXIO IV unless simultaneous treatment with anticoagulants can be given. For patients who are to receive continuous treatment with TRANMENXIO IV for longer than several days, an ophthalmological examination is advisable (including visual acuity, colour vision, eye-grounds, field of vision), before commencing treatment, and at regular intervals during treatment.
Medicines with actions on haemostasis should be given with caution to patients on antifibrinolytic therapy. The potential for thrombus formation may be increased by oestrogens, for example, or the action of the antifibrinolytic antagonised by compounds such as the thrombolytics.

4.5 Interaction with other medicines and other forms of interaction

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

4.6 Fertility, pregnancy and lactation

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

Pregnancy

The safety of tranexamic acid has not been established in pregnancy.

Breast Feeding

Tranexamic acid is excreted in human milk. Therefore, breast-feeding is not recommended.

Tranexamic acid passes into breast milk at a concentration of a hundredth of the corresponding serum levels. Caution should be exercised when tranexamic acid is given to nursing women.

Fertility

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

4.7 Effects on ability to drive and use machines
No studies have been performed on the ability to drive and use machines.
TRANMENXIO IV can cause side effects, such as dizziness and vision problems, and can affect the ability to drive a vehicle and use machines. Caution is advised when driving a vehicle or operating machinery until the effects of TRANMENXIO IV are known.

4.8 Undesirable effects
Tabulated list of adverse reactions
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.

System organ class	Frequent	Less Frequent	Frequency not known (cannot be estimated from the available data)
Immune system disorders			- Hypersensitivity reactions including anaphylaxis
Nervous system disorders			Convulsions particularly in case of misuse (see sections 4.3 and 4.4) Dizziness
Eye disorders			Visual disturbances including impaired colour vision Retinal/artery occlusion
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
Gastrointestinal disorders	Diarrhoea Vomiting Nausea		
Skin and subcutaneous tissue disorders		Dermatitis allergic	

Cases of giddiness have been reported. Transient disturbance of colour vision may occur. Patients who experience disturbances of colour vision should be withdrawn from treatment.
Rapid intravenous injection may cause dizziness and/or hypotension.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reactions Reporting Form",** found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
Treatment:
Symptoms of overdosage: Dizziness, headache, nausea and vomiting, diarrhoea.
Faintness and hypotension may occur.
Treatment is symptomatic.
Maintain adequate diuresis (with fluids plus diuretics).

5. Pharmacological properties

5.1 Pharmacodynamic properties
Pharmacological Classification: 8.1 Coagulants, haemostatics
Pharmacotherapeutic group Antihaemorrhagics, antifibrinolytics, amino acids
ATC Code: B02AA02
Pharmacological 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 on fibrin is lower than the activity of free plasmin alone.
In vitro studies showed that high tranexamic dosages decreased the activity of complement.

5.2 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.

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 litres.
Tranexamic acid passes through the placenta. Following administration of an intravenous injection of 10 mg/kg to 12 pregnant women, the concentration of tranexamic acid in serum ranged 10-53 microgram/ml while that in cord blood ranged 4-31 microgram/ml. Tranexamic acid diffuses rapidly into joint fluid and the synovial membrane. Following administration of an intravenous injection of 10 mg/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.

Elimination
It is excreted mainly in the urine as unchanged medicine. 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. Elimination half-life of tranexamic acid is approximately 3 hours.

Other special populations
Plasma concentrations increase in patients with renal failure.
No specific pharmacokinetic study has been conducted in children.

5.3 Preclinical safety data
No non-clinical study was performed.

6. Pharmaceutical particulars
6.1 List of excipients
Water for injection.

6.2 Incompatibilities
This medicinal product should not be mixed with blood for transfusion or with solutions containing penicillin.

6.3 Shelf life
3 years.
After first opening: the solution for injection/infusion is for single use only. Unused solution must be discarded.

6.4 Special precautions for storage
Store at or below 25 °C.
Use immediately after opening. Discard any unused portion.

6.5 Nature and contents of container
5 ml type 1 clear glass ampoules, 5 such ampoules are placed in tray and packed in carton.

6.6 Special precautions for disposal and other handling
TRANMENXIO IV may be mixed with most solutions for infusion such as electrolyte solutions for injection, Dextrose for injection, carbohydrate solutions, aminosol for injection solutions and dextran for injection.
Heparin may be added to TRANMENXIO IV.
TRANMENXIO IV is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
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8. REGISTRATION NUMBER(S)
56/8.1/0497

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29 March 2022

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14 April 2025