Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tranexamic acid 100 mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The active substance is tranexamic acid.

Each 5 ml of the solution contains 500 mg of tranexamic acid.
Each 10 ml of the solution contains 1000 mg of tranexamic acid.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Injection

A clear colourless solution, free from visible particulate matter.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Tranexamic acid is indicated in adults and children from one year in prevention and treatment of haemorrhages due to general or local fibrinolysis.

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.

4.2 Posology and method of administration

Posology

Adults

Unless otherwise prescribed, the following doses are recommended:

1. Standard treatment of local fibrinolysis:

0.5 g (1 ampoule of 5 mL) to 1 g (1 ampoule of 10 mL or 2 ampoules of 5 mL) tranexamic acid by slow intravenous injection (= 1 mL/minute) two to three times daily

2. Standard treatment of general fibrinolysis:

1 g (1 ampoule of 10 mL or 2 ampoules of 5 mL) tranexamic acid by slow intravenous injection (= 1 mL/minute) every 6 to 8 hours, equivalent to 15 mg/kg body weight BW

Renal impairment

For patients 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/10 ml		
120 to 249	1.35 to 2.82	10 mg/kg BW	Every 12 hours
250 to 500	2.82 to 5.65	10 mg/kg BW	Every 24 hours
> 500	> 5.65	5 mg/kg BW	Every 24 hours

Hepatic impairment

No dose adjustment is required in patient with hepatic impairment.

Paediatric Population:

In children from 1 year, for current approved indications as described in section 4.1, 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. Currently available data are limited and are described in section 5.1.

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.

TRANEXAMIC ACID MUST ONLY BE ADMINISTERED INTRAVENOUSLY and must not be administered intrathecally or epidurally (see sections 4.3 and 4.4).

IN ORDER TO REDUCE THE RISK OF FATAL MEDICATION ERRORS DUE TO INCORRECT ROUTE OF ADMINISTRATION OF TRANEXAMIC ACID, IT IS STRONGLY RECOMMENDED TO LABEL THE SYRINGES CONTAINING TRANEXAMIC ACID (see sections 4.3, 4.4 and 6.6).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

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

Intrathecal, epidural, intraventricular injection and intracerebral application (risk of cerebral oedema and convulsions and death)

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 must not be administered by the intramuscular route.

Risk of medication errors due to incorrect route of administration
Tranexamic acid is for intravenous use only. Intrathecal, epidural, intraventricular and intracerebral use of Tranexamic acid is contraindicated (see section 4.3). Serious adverse reactions including fatal events have been reported when tranexamic acid was inadvertently administered intrathecally. These include severe back, gluteal and lower limb pain, myoclonus and generalised seizures, and cardiac arrhythmias.
Care should be exercised to ensure the correct route of administration of Tranexamic acid. Healthcare professionals should be aware of the potential for confusion of Tranexamic acid with other injectables which could result in inadvertent intrathecal administration of Tranexamic acid. This includes in particular intrathecally administered injectables that may be used during the same procedure as tranexamic acid.
Syringes containing Tranexamic acid should be clearly labelled with the intravenous route of administration.

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 , 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 in each individual case.

Haematuria

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

If left untreated, urinary obstruction may lead to serious consequences such as renal insufficiency, urinary tract infection, hydronephrosis, and anuria. Therefore, close monitoring is recommended for those patients with haematuria or risk of haematuria from the upper urinary tract.

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 should only be administered if there is a strong medical indication after consulting a physician experienced in haemostaseology and under strict medical supervision (see section 4.3).

Tranexamic acid should be administered with care in patients using hormonal contraception 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 tranexamic acid (see section 4.3). 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 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 tranexamic acid in DIC should be considered only when appropriate haematological laboratory facilities and expertise are available.

4.5 Interaction with other medicinal products and other forms of 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 risk of increased thrombus-formation potential, during concomitant use with hormonal contraception. Alternatively, the antifibrinolytic action of the drug may be antagonised with thrombolytic drugs.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
Women of childbearing potential have to use effective contraception during treatment (see sections 4.4 and 4.5).

Pregnancy
Available data from published studies, case series and case reports with tranexamic acid use in pregnant women.
in the second and third trimester and at the time of delivery have not clarified whether there is a drug-associated risk of miscarriage or adverse maternal or foetal outcomes. There are cases of foetal structural abnormalities that resulted in death of the newborn following administration of tranexamic acid to the mother during conception or the first trimester of pregnancy however due to other confounding factors the risk of major birth defects with use of tranexamic acid during pregnancy is not clear.
Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).
Tranexamic acid passes through the placenta. The concentration in cord blood after an intravenous injection of 10 mg/kg to pregnant women is about 30 mg/L, as high as in the maternal blood.
There were 13 clinical studies that described foetal and/or neonatal functional issues such as low Apgar score, neonatal sepsis, cephalohematoma and 9 clinical
studies that discussed alterations to growth including low birth weight and preterm birth at 22-36 weeks of gestation in foetuses and infants exposed to tranexamic acid *in-utero* .
For decisions regarding the use of tranexamic acid during pregnancy, the potential risk of tranexamic acid administration on the foetus should always be considered along with the mother's clinical need for tranexamic acid; an accurate risk benefit evaluation should drive the treating physician's decision.

Breast-feeding
Published literature reports the presence of tranexamic acid in human milk. There are limited data on the effects of tranexamic acid on the breast-fed child or the effects on milk production. The developmental and health benefits of breast-feeding should be considered along with the mother's clinical need for tranexamic acid and any potential adverse effects on the breast-fed child from tranexamic acid or from the underlying maternal condition.
Due to limited data, no final assessment can be established on the use of tranexamic acid during breast-feeding.

Fertility
There are no clinical data on the effects of tranexamic acid on fertility. In animal studies, tranexamic acid did not affect male or female fertility at clinically relevant doses (see section 5.3).

4.7 Effects on ability to drive and use machines

No studies have been performed on the ability to drive and use machines.

4.8 Undesirable effects

The ADRs reported from clinical studies and post-marketing experience are listed below according to system organ class.

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. Frequencies were defined as follows: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100), not known (cannot be estimated from the available data).

MedDRA System Organ Class	Frequency	Undesirable Effects
Immune system disorders	Not known	- Hypersensitivity reactions including anaphylaxis
Nervous system disorders	Not known	- Convulsions particularly in case of misuse (see sections 4.3 and 4.4)

Eye disorders	Not known	- Visual disturbances including impaired colour 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) - Arterial or venous thrombosis at any sites
Gastrointestinal disorders	Common	- Diarrhoea - Vomiting - Nausea
Skin and subcutaneous tissue disorders	Uncommon	- Dermatitis allergic
	Not known	-Fixed drug eruption
Renal and urinary disorders	Not known	-Acute renal cortical necrosis

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via
HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

No case of overdose has 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihaemorrhagics, Antifibrinolytics, Amino acids
ATC code: B02AA02

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 (CPB) where 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 10 mg/kg after induction of anaesthesia and prior to skin incision,
- continuous infusion of 10 mg/kg/h or injection into the CPB pump prime at a dose adapted on the CPB procedure, either according to a patient weight with a dose of 10 mg/kg dose, either according to CPB pump prime volume, last injection of 10 mg/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.

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 µg/mL while that in cord blood ranged 4-31 µg/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 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. 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

Carcinogenesis and mutagenesis
No evidence of carcinogenicity or mutagenicity was observed in conventional studies with tranexamic acid.

Reproductive toxicity
In reproductive toxicity studies (fertility and early embryonic development studies, embryo-foetal development studies, and pre and postnatal studies), tranexamic acid had no adverse effect on reproductive parameters of mice, rats and rabbits at clinically relevant doses.

General toxicology
Retinal toxicity has been observed in nonclinical studies with tranexamic acid. The observed toxicity was characterised by retinal atrophy commencing with changes to the retinal pigmented epithelium and progressing to retinal detachment in cats. The toxicity appeared to be dose-related, and changes were partially reversible at lower doses. Effects (some fully reversible) were seen in cats at clinically relevant doses, effects in dogs were only observed at multiples of the clinical dose. Studies suggest that the underlying mechanism may be related to a transient retinal ischemia at higher dose exposures, linked to the known sympathomimetic effect of high plasma levels of tranexamic acid. The clinical relevance of these findings is unknown.

Epileptogenic activity has been observed in animals with intrathecal use of tranexamic acid.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

Tranexamic acid solution for injection should not be added to blood for transfusion, or to injections containing penicillin.

6.3 Shelf life

2 years.

The product should be used immediately after opening.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Type I glass ampoules are packed in a tray pack or blister pack and further it is packed in a cardboard carton.

Pack sizes
1 x 5 ml
5 x 5 ml
10 x 5 ml
1 x 10 ml
5 x 10 ml
10 x 10 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Healthcare professionals are strongly advised to label the Tranexamic acid syringes during the withdrawal of the product from the ampoule for clear identification and proper route of administration, to help prevent inadvertent medication errors during administration to the patient.

The product is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Accord Healthcare Ireland Ltd.
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Euro Business Park
Little Island
Cork T45 K857
Ireland

8 MARKETING AUTHORISATION NUMBER

PA2315/178/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16th December 2016
Date of last renewal: 24th October 2021

10 DATE OF REVISION OF THE TEXT

April 2026