SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Medsamic 100 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL contains: tranexamic acid 100 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection. Clear, colourless solution, pH 6.5 to 8.0.
After dilution, solution is clear and colourless
Compatible with:

- 0.9% NaCl
- Ringer's solution
- Glucose 5%
- Dextran 40
- Dextran 70

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- Bleeding tendencies in which systemic hyperfibrinolysis is considered to be involved (leukemia, aplastic anemia, purpura etc., abnormal bleeding during or after operation)
- Abnormal bleeding in which local hyperfibrinolysis is considered to be involved (pulmonary hemorrhage, epistaxis, vaginal hemorrhage, renal hemorrhage, abnormal bleeding during or after prostate surgery)
- Symptoms, such as erythema, swelling or pruritus in the following diseases: Eczema or similar conditions, urticaria, drug eruptions or toxicoderma
- Symptoms, such as pharyngalgia, redness, hyperemia or swelling in the following diseases: Tonsillitis, pharyngolaryngitis
- Pain in the oral cavity or mucosal aphtha in cases of stomatitis

4.2. Posology and method of administration

Posology

The usual daily adult dosage for intravenous injection is 250 to 500mg of tranexamic acid in one or two divided doses. During or after surgery, 500 to 1,000mg intravenously or 500 to 2,500mg by intravenous drip infusion are administered each time as required.
Medsamic Solution for 100mg/ml Injection: The usual daily adult dosage for intravenous injection is 2.5 to 5mL of tranexamic acid in one or two divided doses. During or after surgery, 5 to 10mL intravenously or 5 to 25mL by intravenous drip infusion are administered each time as required.
The dosage should be adjusted to individuals according to the patient's age and conditions.

This product is not for IM use.

Method of administration

Route of administration – strictly limited to slow intravenous injection.

4.3. Contraindications

- Hypersensitivity to the active substance or to any of its 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)
- Severe renal impairment (risk of accumulation)
- History of convulsions
- Intrathecal 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.

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 solution for injection, 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 solution for injection in each individual case.

Haematuria

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

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

Tranexamic acid 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 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 1g 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 theoretical risk of increased thrombus-formation potential, such as with oestrogens. Alternatively, the antifibrinolytic action of the drug may be antagonised with thrombolytic drugs.

4.6. Fertility, pregnancy and lactation

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

Pregnancy:
There is insufficient clinical data on the use of tranexamic acid in pregnant women. As a result, although studies in animals do not indicate teratogenic effects, as precaution for use, tranexamic acid is not recommended during the first trimester of pregnancy. Limited clinical use of tranexamic acid in different clinical haemorrhagic settings during the second and third trimesters did not identify deleterious effect for the foetus. Tranexamic acid should be used throughout pregnancy only if the expected benefit justifies the potential risk.

Breastfeeding:
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 fertility.

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 know (cannot be estimated from the available data).

MedDRA System Organ Class	*Frequency*	*Undesirable Effects*
Skin and subcutaneous tissue disorders	Uncommon	Dermatitis allergic
Gastrointestinal disorders	Common	Diarrhoea Vomiting Nausea
Nervous system disorders	Not known	Convulsions particularly in case of misuse (refer to 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
Immune system disorders	Not known	Hypersensitivity reactions including anaphylaxis

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: Antihemorrhagics, Antifibrinolytics
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 liters.
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 urineas 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.

Special populations
Plasma concentrations increase in patients with renal failure.
No specific PK study has been conducted in children.

6. PHARMACEUTICAL PARTICULARS
6.1. List of excipients
Water for injection

6.2. Incompatibilities
Solution for injection of tranexamic acid should not be added to blood for transfusion or to injections containing penicillin.

6.3. Shelf life
3 years

6.4. Special precautions for storage
Store below 30°C in the original package. Keep ampoule in the outer carton.
Do not refrigerate or freeze.

Storage conditions after dilution:
After first opening: the solution for injection/infusion is for single use only. Unused solution must be discarded.
Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C.
From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.5. Nature and contents of container
Clear glass type I ampoules of 5ml capacity. Boxes of 10 ampoules × 5 ml.

6.6. Special precautions for disposal and other handling
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MANUFACTURER
Medochemie Ltd (Ampoule Injectable Facility)
48, Iapetou Street, Agios Athanassios Industrial Area, 4101 Agios Athanassios, Limassol-Cyprus

8. PRODUCT REGISTRATION HOLDER
Komedic Sdn Bhd
4, Jalan PJS 11/14, Bandar Sunway, 46150 Petaling Jaya, Selangor, Malaysia

9. MARKETING AUTHORISATION NUMBER
[To be completed nationally]

10. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
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10/03/2023

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