SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Tranexamic Acid 100mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each ampoule contains 500mg of tranexamic acid per 5ml (100mg/ml).
For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Solution for injection
Clear, colourless solution

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) conisation 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: by 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 (see Section 4.5), Tranexamic Acid Solution for 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 (1g) is sufficient to control bleeding.

2) Neutralisation of thrombolytic therapy; 10mg/kg body wt by slow intravenous injection.

**Children:**

In children, **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 is limited.

Injectable solution: The efficacy, posology and safety of Tranexamic acid in children undergoing cardiac surgery have not been fully established. Currently available data is limited and is described in section 5.1.

**Elderly patients:**

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

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**4.3 Contraindications**

Hypersensitivity to tranexamic acid or any of the other ingredients (see section 6.1)

History of venous or arterial thrombosis

History of convulsions

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

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**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 are 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:

<table>
<thead>
<tr>
<th>Serum Creatinine</th>
<th>Dose iv</th>
<th>Dose Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>120-250 mcmol/l</td>
<td>10 mg/kg</td>
<td>Twice daily</td>
</tr>
<tr>
<td>250-500 mcmol/l</td>
<td>10 mg/kg</td>
<td>Every 24th hour</td>
</tr>
<tr>
<td>&gt; 500 mcmol/l</td>
<td>5 mg/kg</td>
<td>Every 24th hour</td>
</tr>
</tbody>
</table>

• 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 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. 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 Solution for Injection in DIC should be considered only when appropriate haematological laboratory facilities and expertise are available. Tranexamic Acid Solution for 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 Interaction with other medicinal products and other forms of interaction
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 Fertility, 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.

Lactation:
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 machines

Not applicable.

4.8 Undesirable effects

Very rare adverse events have been reported:

• Gastro-intestinal disorders: digestive effects such as nausea, vomiting and diarrhoea.

• Cardio-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

• Nervous system disorders: dizziness; convulsions, particularly in case of misuse (see section 4.4 "Precautions and warnings")

• 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 Pharmacodynamic properties

Tranexamic acid is a competitive inhibitor of plasminogen activation, and at much higher concentrations, a noncompetitive inhibitor of plasmin, i.e., actions similar to aminocaproic acid. The antifibrinolytic activity of tranexamic acid is about 10 times more potent in vitro than aminocaproic acid.

Tranexamic acid binds more strongly than aminocaproic acid to both the strong and weak receptor sites of the plasminogen molecule in a ratio corresponding to the difference in potency between the compounds. Tranexamic acid in a concentration of 1 mg/mL does not aggregate platelets in vitro.

Tranexamic acid in concentrations up to 10 mg/mL blood has no influence on the platelet count, the coagulation time or various coagulation factors in whole blood or citrated blood from normal subjects. However, tranexamic acid in concentrations of 10 mg/mL and 1 mg/mL blood prolongs the thrombin time.

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.

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

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

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
3 years

6.4 Special precautions for storage
None

6.5 Nature and contents of container
Type I glass 5ml ampoules packed in outer cardboard carton.
Pack of 5 ampoules.

6.6 Special precautions for disposal
None.

7 MARKETING AUTHORISATION HOLDER
Mercury Pharmaceuticals Ltd,
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85 King William Street,
London EC4N 7BL, UK

8 MARKETING AUTHORISATION NUMBER(S)
PL 12762/0477

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
16/05/2013

10 DATE OF REVISION OF THE TEXT

21/03/2014