Proposed Professional Information for CYNEX 500 mg INJECTION

SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE

CYNEX 500 mg INJECTION, solution for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL ampoule contains 500 mg tranexamic acid.

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless liquid, free from visible particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short-term use for haemorrhage or risk of haemorrhage in increased

fibrinolysis or fibrinogenolysis. Local fibrinolysis occurs in the following conditions:

- Prostatectomy.
- Bladder surgery.

4.2 Posology and method of administration

Posology:

Haemorrhage or risk of haemorrhage in increased fibrinolysis or fibrinogenolysis:

Standard treatment of local fibrinolysis:

0,5 g (1 ampoule of 5 mL) to 1 g (2 ampoules of 5 mL) CYNEX 500 mg INJECTION by slow intravenous injection (IV) or infusion (= 1 mL/minute) two to three times daily, or alternatively suitable approved dosage forms of tranexamic acid (such as tablets) may be used.

Standard treatment of general fibrinolysis:

1,0 g (2 ampoules of 5 mL) CYNEX 500 mg INJECTION by slow intravenous injection or infusion (= 1 mL/minute) every 6 to 8 hours, equivalent to 15 mg/kg body weight (BW); or alternatively suitable approved dosage forms of tranexamic acid (such as tablets) may be used.

Prostatectomy and bladder surgery:

0,5 g (1 ampoule of 5 mL) to 1,0 g (2 ampoules of 5 mL) CYNEX 500 mg INJECTION by slow intravenous injection or infusion (1 mL/min), 2 – 3 times daily (the first injection being given during the operation)/ for the first three days after surgery, thereafter suitable approved dosage forms of tranexamic acid (such as tablets) may be used.

Special populations:

Renal impairment:

Intravenous dosages of CYNEX 500 mg INJECTION should be reduced in patients with renal impairment. For patients with moderate to severe impaired renal function, the following dosages based on serum creatinine concentration (SCC) are recommended:

- SCC 120 to 250 µmol/L: 10 mg/kg body weight twice a day.
- SCC 250 to 500 µmol/L: 10 mg/kg body weight daily.
- SCC > 500 µmol/L: 5 mg/kg body weight daily.

Paediatric population

Data on efficacy and safety in children are limited

Method of administration:

CYNEX 500 mg INJECTION is given by slow intravenous infusion/injection ver a period of at least five minutes. Administration by injection is usually changed to oral administration after a few days.

4.3 Contraindications

- Hypersensitivity to tranexamic acid or any of the inactive ingredients of CYNEX 500 mg INJECTION (listed in section 6.1).

- Pregnancy and lactation (see section 4.6).
- Avoid the use of CYNEX 500 mg INJECTION with medical conditions such as defective colour vision.
- In cases of massive haemorrhage of upper urinary tract origin.CYNEX 500 mg INJECTION should be avoided to reduce the risk of ureteric obstruction.
- Predisposition to or history of arterial or venous thromboembolism.
- Thrombophlebitis.
- Active intravascular clotting.
- Patients with hypercoagulopathies.
- Liver impairment.
- Subarachnoid haemorrhage.

4.4 Special warnings and precautions for use

For patients in renal failure, CYNEX 500 mg INJECTION should be given with caution because of the risk of accumulation (see section 4.2).

Rapid intravenous dosage may be associated with adverse effects. The indications and method of administration should be followed strictly (see section 4.2):

- Intravenous injections should be given very slowly.
- CYNEX 500 mg INJECTION should not be administered by the intramuscular route.

Patients with menorrhagia should not use CYNEX 500 mg INJECTION until the cause of the menorrhagia has been established.

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 CYNEX 500 mg INJECTION, the incidence of post-operative seizures was the same as that in untreated patients.

Visual disturbances:

An ophthalmological examination is advisable (including visual acuity, colour vision, eye-ground, field of vision) when CYNEX 500 mg INJECTION is used continuously in patients for several days, before commencing of treatment and at regular intervals during treatment. If ocular and visual disturbances (including disturbance of colour vision, visual impairment, blurred vision) occur, treatment with CYNEX 500 mg INJECTION should be stopped.

Haematuria:

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

Thromboembolic events:

Thrombotic complications (including cerebral thrombosis and central retina venous and arterial occlusion) have been reported in patients receiving tranexamic acid, usually as a consequence of its inappropriate use.

CYNEX 500 mg INJECTION should not be used in patients who suffer from or have a history of active intravascular clotting, due to the risk of thrombosis (unless simultaneous treatment with anticoagulants can be given).

Medicines such as oestrogens may increase the potential for thrombus formation, while thrombolytics may antagonise the action of the antifibrinolytics. 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).

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, e.g. 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 1,0 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.

CYNEX 500 mg INJECTION contains sodium:

This medicine contains less than 1 mmol sodium (23 mg) per unit volume, that is to say essentially sodium free.

4.5 Interaction with other medicines and other forms of interaction

Medicines with actions on haemostasis should be given with caution to patients on antifibrinolytic therapy, including CYNEX 500 mg INJECTION. Thrombolytics may antagonise the action of CYNEX 500 mg INJECTION. Oestrogens may increase the potential for thrombus formation.

4.6 Fertility, pregnancy and lactation

Pregnancy:

CYNEX 500 mg INJECTION crosses the placenta. Safety in pregnancy has not been established. CYNEX 500 mg INJECTION should not be used during pregnancy (see section 4.3).

Breastfeeding:

CYNEX 500 mg INJECTION is excreted into breast milk and women using CYNEX 500 mg INJECTION should not breastfeed their infants (see section 4.3).

4.7 Effects on ability to drive and use machines

CYNEX 500 mg INJECTION may cause dizziness and may influence the ability to drive a vehicle or use machines.

4.8 Undesirable effects

Blood and lymphatic system disorders:

Less frequent: Hypotension (especially after rapid intravenous dosage).

Immune system disorders:

Less frequent: Hypersensitivity reactions (including anaphylaxis), skin rash.

Nervous system disorders:

Less frequent: Dizziness.

Frequency unknown: Convulsions, particularly in case of misuse (see sections 4.3 and 4.4).

Eye disorders:

Frequent: Ophthalmic disturbances (colour disturbances, blurred vision, retinopathy and visual impairment).

Cardiac disorders:

Frequent: Thromboembolic complications occur usually due to its inappropriate use.

Vascular disorders:

Frequency unknown: Malaise with hypotension, with or without loss of consciousness (generally following a too fast intravenous injection). Arterial or venous thrombosis at any sites.

Gastrointestinal disorders:

Frequent: Nausea, vomiting, diarrhoea.

Skin and subcutaneous tissue disorders:

Frequency unknown: Allergic dermatitis, allergic skin reactions.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of CYNEX 500 mg

INJECTION is important. It allows continued monitoring of the benefit/risk balance of CYNEX 500 mg INJECTION. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found SAHPRA website

4.9 Overdose

The following symptoms of overdosage may occur: dizziness, headache, nausea, vomiting, diarrhoea, fainting, convulsions and hypotension. It has been shown that convulsions tend to occur at higher frequency with increasing dose. Management of overdose should be supportive. Maintain adequate diuresis (with fluids plus diuretics).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 8.1 Coagulants, haemostatics.

Pharmacotherapeutic group: Antihemorrhagics, antifibrinolytics, amino acids.

ATC code: B02A A02.

Tranexamic acid exerts an inhibitory effect on the activation of plasminogen in the fibrinolytic system. It acts primarily by blocking the binding of plasminogen and plasmin to fibrin (direct inhibition of plasmin occurs only to a limited degree).

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. Tranexamic acid is absorbed and is excreted unchanged through the kidneys.

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 - 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 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.

Paediatric population

No specific pharmacokinetic study has been conducted in children.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid

Sodium hydroxide

Water for injection.

6.2 Incompatibilities

CYNEX 500 mg INJECTION is incompatible with benzylpenicillin.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 30 °C.

Protect from light. Do not refrigerate.

Keep the ampoules in the outer carton until required for use.

For single use only. Discard any unused portion.

6.5 Nature and contents of container

5 mL clear, colourless USP type-I OPC glass ampoule with a blue dot and three brown bands.

Pack size:

Five ampoules are packed into a plastic tray, which is packed in an outer carton.

6.6 Special precautions for disposal and other handling

CYNEX 500 mg INJECTION is compatible with electrolyte solutions (e.g. sodium chloride 0,9 %), carbohydrate solutions (e.g. dextrose 5 %), Aminosol and dextran solutions. Do not mix CYNEX 500 mg INJECTION with blood and infusion solutions containing penicillin. Heparin solutions may be added to CYNEX 500 mg INJECTION.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd

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Stormill, Ext. 1, Roodepoort

Johannesburg 1724

8. REGISTRATION NUMBER

43/8.1/0263

9. DATE OF FIRST AUTHORISATION

11 June 2018

10. DATE OF REVISION OF THE TEXT

28 October 2024

Namibia	NS2 23/8.1/0009
Botswana	S2 A2000097