SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cyklokapron 500 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Tranexamic acid 500 mg as the active ingredient.

For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets.

White, oblong tablets, 8x18 mm, engraved CY with an arc above and below the lettering, for oral use.

4.1 Therapeutic indications

Short-term use for haemorrhage or risk of haemorrhage in increased fibrinolysis or fibrinogenolysis. Local fibrinolysis as occurs in the following conditions:

Prostatectomy and bladder surgery
Menorrhagia
Epistaxis
Conisation of the cervix
Traumatic hyphaema

Hereditary angioedema

Management of dental extraction in haemophiliacs

4.2 Posology and method of administration

Posology

1. Local fibrinolysis: The recommended standard dosage is 15-25 mg/kg bodyweight (i.e. 2-3 tablets) two to three times daily. For the indications listed below the following doses may be used:

1a. Prostatectomy: Prophylaxis and treatment of haemorrhage in high risk patients should commence pre- or post-operatively with Cyklokapron Injection; thereafter 2 tablets three to four times daily until macroscopic haematuria is no longer present.

1b. Menorrhagia: Recommended dosage is 2 tablets 3 times daily as long as needed for up to 4 days. If very heavy menstrual bleeding, dosage may be increased. A total dose of 4g daily (8 tablets) should not be exceeded. Treatment with Cyklokapron should not be initiated until menstrual bleeding has started.

1c. **Epistaxis**: Where recurrent bleeding is anticipated oral therapy (2 tablets three times daily) should be administered for 7 days.

1d. Conisation of the cervix: 3 tablets three times daily.

1e. Traumatic hyphaema: 2-3 tablets three times daily. The dose is based on 25 mg/kg three times a day.

2. Hereditary angioedema: Some patients are aware of the onset of the illness; suitable treatment for these patients is intermittently 2-3 tablets two to three times daily for some days. Other patients are treated continuously at this dosage.

3. Haemophilia: In the management of dental extractions 2-3 tablets every eight hours. The dose is based on 25 mg/kg.

***Renal insufficiency*:** By extrapolation from clearance data relating to the intravenous dosage form, the following reduction in the oral dosage is recommended for patients with mild to moderate renal insufficiency.

Serum Creatinine (µmol/l)	Dose tranexamic acid
120-249	15 mg/kg body weight twice daily
250-500	15 mg/kg body weight/day

Children's dosage: This should be calculated according to body weight at 25 mg/kg per dose. However, data on efficacy, posology and safety for these indications are limited.

Elderly patients: No reduction in dosage is necessary unless there is evidence of renal failure (see guidelines below).

<u>Method of administration</u>

Route of administration: Oral

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients listed in section 6.1.
Severe renal impairment because of risk of accumulation,
Active thromboembolic disease.
History of venous or arterial thrombosis
Fibrinolytic conditions following consumption coagulopathy
History of convulsions

4.4 Special warnings and precautions for use

In case of haematuria of renal origin (especially in haemophilia), 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.

In the long-term treatment of patients with hereditary angioedema, regular eye examinations (e.g. visual acuity, slit lamp, intraocular pressure, visual fields) and liver function tests should be performed.

Patients with irregular menstrual bleeding should not use Cyklokapron until the cause of irregular bleeding has been established. If menstrual bleeding is not adequately reduced by Cyklokapron, an alternative treatment should be considered.

Tranexamic acid should be administered with care in patients receiving oral contraceptives because of the increased risk of thrombosis.

Patients with a previous thromboembolic event and a family history of thromboembolic disease (patients with thrombophilia) should use Cyklokapron only if there is a strong medical indication and under strict medical supervision.

The blood levels are increased in patients with renal insufficiency. Therefore a dose reduction is recommended (see section 4.2).

The use of tranexamic acid in cases of increased fibrinolysis due to disseminated intravascular coagulation is not recommended.

Patients who experience visual disturbance should be withdrawn from treatment.

Clinical experience with Cyklokapron in menorrhagic children under 15 years of age is not available.

Cases of convulsions have been reported in association with tranexamic acid treatment. In cardiac surgery, most of the cases were reported following intravenous (i.v.) injection of tranexamic acid in high doses.

4.5 Interaction with other medicinal products and other forms of interaction

Cyklokapron will counteract the thrombolytic effect of fibrinolytic preparations.

4.6 Fertility, pregnancy and lactation

Pregnancy

Although there is no evidence from animal studies of a teratogenic effect, the usual caution with use of drugs in pregnancy should be observed.

Tranexamic acid crosses the placenta.

Breast-feeding

Tranexamic acid passes into breast milk to a concentration of approximately one hundredth of the concentration in the maternal blood. An antifibrinolytic effect in the infant is unlikely.

4.7 Effects on ability to drive and use machines

Cyklokapron has no or negligible influence on the ability to drive and use machines. Visual disturbances may occur following administration of tranexamic acid.

4.8 Undesirable effects

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/l0), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥ 1/10,000 and <1/1000) and very rare (<1/10,000) including isolated reports, not known (cannot be estimated from the available data).

Immune system disorders
Very rare: Hypersensitivity reactions including anaphylaxis

Renal and urinary disorders

Not known: Acute renal cortical necrosis

Eye disorders
Rare: Colour vision disturbances, retinal/artery occlusion

Vascular disorders
Rare: Thromboembolic events
Very rare: Arterial or venous thrombosis at any sites

Gastro-intestinal disorders
Very rare: Digestive effects such as nausea, vomiting and diarrhoea, may occur but disappear when the dosage is reduced.

Skin and subcutaneous tissue disorders
Rare: Allergic skin reactions
Not known: Fixed drug eruption

Nervous system disorders
Frequency not known: Convulsions particularly in cases of misuse (refer to sections 4.3 and 4.4)

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Signs and symptoms may include nausea, diarrhoea, vomiting, orthostatic symptoms and/or hypotension, dizziness, headache and convulsions. Initiate vomiting, then stomach lavage, and charcoal therapy. Maintain a high fluid intake to promote renal excretion. There is a risk of thrombosis in predisposed individuals. Anticoagulant treatment should be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihemorrhagics, Antifibrinolytics. ATC code: B02AA02

Tranexamic acid is an antifibrinolytic compound which is a potent competitive inhibitor of the activation of plasminogen to plasmin. At much higher concentrations it is a non-competitive inhibitor of plasmin. The inhibitory effect of tranexamic acid in plasminogen activation by urokinase has been reported to be 6-100 times and by streptokinase 6-40 times greater than that of

aminocaproic acid. The antifibrinolytic activity of tranexamic acid is approximately ten times greater than that of aminocaproic acid.

5.2 Pharmacokinetic properties

Absorption
Peak plasma Tranexamic acid concentration is obtained immediately after intravenous administration (500mg). Then concentration decreases until the 6th hour. Elimination half-life is about 3 hours.

Distribution
Tranexamic acid administered parenterally is distributed in a two compartment model. Tranexamic acid is delivered in the cell compartment and the cerebrospinal fluid with delay. The distribution volume is about 33% of the body mass.
Tranexamic acid crosses the placenta, and may reach one hundredth of the serum peak concentration in the milk of lactating women.

Elimination
Tranexamic acid 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).
Following oral administration, 1.13% and 39% of the administered dose were recovered after 3 and 24 hours respectively.
Plasma concentrations are increased in patients with renal insufficiency.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core

Microcrystalline cellulose;

Hydroxypropyl cellulose;

Talc;
Magnesium stearate;
Colloidal anhydrous silica;
Povidone.

Coating
Methacrylate polymers;
Titanium dioxide;
Talc;
Magnesium stearate;
Polyethylene glycol 8000;
Vanillin.

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 25°C (blister packs only).

6.5 Nature and contents of container

White, high density polyethylene container with white, medium-density polyethylene screw cap and a polyethylene tamper-proof membrane, containing 50 tablets.

Blister packs of PVC/PVDC with aluminium foil backing containing 60 tablets.

6.6 Special precautions for disposal

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Viatris Products Limited
20 Station Close
Potters Bar
Hertfordshire
EN6 1TL
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 46302/0123

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14th February 2005

10 DATE OF REVISION OF THE TEXT

07/05/2026