SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cyklonova 500 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Tranexamic acid 500 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.
White, capsule shaped, scored, length 18 mm. The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Menorrhagia.

4.2 Posology and method of administration

Posology
Recommended dosage is as follows:

2-3 tablets (1-1.5 g) 3-4 times daily for 3-4 days. If very heavy menstrual bleeding, dosage may be increased up to 2 tablets (1 g) 6 times daily. Treatment with Cyklonova should not be initiated until menstrual bleeding has started.

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

Please refer to section 5.2.

Paediatric population
Clinical experience with Cyklonova in children or adolescents under 15 years of age is not available.

Method of administration
For oral use.

4.3 Contraindications

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

- Active thromboembolic disease such as deep vein thrombosis, pulmonary embolism and cerebral thrombosis.
- Severe renal failure because of risk of accumulation.
- History of convulsions
- Subarachnoid hemorrhage.

4.4 Special warnings and precautions for use

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

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

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

In haematuria from the upper urinary tract may the forming of clots, in rare cases, cause ureteric obstruction.

Convulsions
Convulsions have been reported in connection with tranexamic acid treatment, mostly after high dose intravenous injection of tranexamic acid.

4.5 Interaction with other medicinal products and other forms of interaction

Clinically relevant interactions have not been observed with tranexamic acid tablets.
Since no interaction studies have been performed concurrent treatment with anticoagulants should only be made under supervision of a doctor with expertise in coagulation disorders.

4.6 Fertility, pregnancy and lactation

Cyclonova is only intended for use in menorrhagia and should therefore not be used during pregnancy.

Pregnancy
Tranexamic acid crosses the placenta. Clinical experience in pregnant women is limited.
Animal studies do not indicate increased risk of harmful effects on the foetus.

Lactation
Tranexamic acid passes into breast milk but is unlikely to affect the infant at therapeutic doses.

Fertility
There are no available data of fertility.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness have been reported, which might influence the ability to drive and use machines.

4.8 Undesirable effects

The most common undesirable effects are dose dependent gastrointestinal disorders, which usually are mild and transient. Allergic skin reactions occur but are uncommon.

The frequency of undesirable effects is defined according to the following system:
Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000), Very rare (<1/10,000); Not known (cannot be estimated from the available data).

Frequency of undesirable effects:

Frequency Organ class	Common	Uncommon	Rare	Not known
Nervous system disorders	Headache, dizziness.			Convulsions (see section 4.3 and 4.4).
Eye disorders			Colour vision deficiency and other visual disturbances.	
Vascular disorders			Thrombo-embolism.	
Gastrointestinal disorders	Nausea, vomiting, diarrhoea, abdominal pain.			
Skin and subcutaneous tissue disorders		Allergic skin reactions.		

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 national reporting system listed in Appendix V.

4.9 Overdose

Symptoms of overdose
Nausea, diarrhoea, dizziness, headache. Orthostatic symptoms, hypotension, myopathy and convulsions may occur. There is a risk of thrombosis in predisposed individuals.

Treatment of overdose
If appropriate, initiate vomiting, gastric lavage and/or charcoal therapy, and initiate symptomatic treatment. Maintain adequate renal excretion. Anticoagulant treatment should be considered.

Toxicity
37 g to a 17 year old person caused a mild intoxication after gastric lavage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: fibrinolysis inhibitor, ATC code: B02AA02

Tranexamic acid inhibits the plasminogen activation i.e. the conversion of plasminogen to plasmin in the fibrinolytic system. The treatment of menorrhagia is symptomatic since the underlying patogenesis for menorrhagia is not affected.

5.2 Pharmacokinetic properties

The bioavailability is approximately 35 % in the dosage range 0,5-2 g and is not affected by simultaneous food intake.

Following a single dose C_{max} and urinary excretion increased linearly with doses between 0,5 g and 2,0 g. Following a single dose of 0,5 g C_{max} is approximately 5 microg/ml and after a dose of 2 g C_{max} is 15 microg/ml.

Therapeutic concentration in plasma is maintained up to 6 hours after an oral single dose of 2 g. Plasma protein binding (plasminogen) is approximately 3 % at therapeutic levels.

Plasma clearance is approximately 7 l/h. Halflife in plasma is approximately 2 hours after an intravenous single dose. Following repeated oral dosage the halflife is longer. The terminal halflife is about 3 hours.

Approximately 95 % of absorbed dose is excreted unchanged in urine. Two metabolites have been identified: a N-acetylated and a deaminated derivative.

Impaired renal function
Impaired renal function constitutes a risk of accumulation of tranexamic acid.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenicity, toxicity to reproduction. Retinal abnormalities has been observed in long term toxicity studies in dogs and cats: hyper-reflectivity, atrophy of photo receptor segments, peripheral retinal atrophy, atrophy of rod and cone cells. These ocular changes were dose related and occurred in high doses.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:
Microcrystalline cellulose
Povidone K90
Croscarmellose sodium
Colloidal anhydrous silica
Talc
Magnesium stearate

Coating:
Methacrylate polymer (Eudragit E100)
Titanium dioxide (E 171)
Talc
Magnesium stearate
Macrogol 8000
Vanillin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30˚C.

6.5 Nature and contents of container

Blister packs (PVC/aluminium).

Pack sizes: 18, 20, 30, 50, 60 and 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Alternova A/S
Energivej 15
5260 Odense S
Denmark

8. MARKETING AUTHORISATION NUMBER

22080

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

2006-06-09

10. DATE OF REVISION OF THE TEXT

2024-09-12