1.3Product Information
1.3.1 SPC, Labeling and Package Leaflet
SPC-Summary of Product Characteristics

1. Name of the Medicinal Product

AGNEXA TABLET 500MG

2. Qualitative and Quantitative Composition

Each film coated tablet contains:
Tranexamic Acid BP ……...500 mg
Excipient …….. q.s.
Colour: Tartrazine

3. Pharmaceutical Form

Oral Tablets (Film coated Tablets)

Route of Administration: Oral

4. Clinical particulars
4.1 Therapeutic indications

Tranexamic Acid is indicated for short term use for haemorrhage or risk of haemorrhage in those with increased fibrinolysis or fibrinogenolysis.

1. Local fibrinolysis as occurs in the following conditions:

a) Prostatectomy and bladder surgery

b) Menorrhagia

c) Epistaxis

d) Conisation of the cervix

e) Traumatic hyphaema

2. Management of dental extraction in haemophiliacs.

3. Hereditary angioneurotic oedema.

4.2 Posology and method of administration

Posology

Adults:

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

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

b. 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 tranexamic acid should not be initiated until menstrual bleeding has started.

c. Epistaxis: When repeated bleeding is anticipated oral therapy (2 tablets three times daily) should be administered for 7 days.

d. Cervix Conisation: 3 tablets three times daily

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

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

3. Hereditary angioneurotic oedema: Some patients are aware of the onset of 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.

Pediatric population:

This should be calculated according to bodyweight at 25mg/kg per dose at the adult dosing frequencies. However, data on efficacy, posology and safety for these indications are limited.

Elderly:

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

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)	**Oral Dose**	**Dose Frequency**
120-249	15 mg/kg body weight	twice daily
250-500	15 mg/kg body weight	daily

Method of administration: Oral Route

4.3 Contraindications

Hypersensitivity to the active substance

Severe renal failure 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 of mechanical anuria due to formation of a ureteral clot.

In the long-term treatment of patients with hereditary angioneurotic oedema, 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 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.

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 Tranexamic Acid 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.

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 Tranexamic Acid in menorrhagic children under 15 years of age is not available.

4.5 Interaction with other medicinal products and other forms of interaction
Tranexamic Acid will counteract the thrombolytic effect of fibrinolytic preparations.

4.6 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
Tranexamic Acid has no or negligible influence on the ability to drive and use machines

4.8 Undesirable effects
Adverse effects have been ranked under headings of frequency using the following convention:

Very common (≥ 1/10)
Common (≥1/100, <1/10)
Uncommon (≥1/1000, <1/100)
Rare (≥ 1/10,000, <1/1,000)
Very rare (<1/10,000) including isolated reports
Not known (cannot be estimated from the available data).

The following undesirable effects have been reported

Immune system disorders

Very rare: Hypersensitivity reactions including anaphylaxis

Gastrointestinal disorders

Very rare: Digestive effects such as nausea, vomiting and diarrhoea my occur but disappear when the dosage is reduced

Skin and subcutaneous tissue disorders

Rare: Allergic skin reactions.

Vascular disorders

Rare: thromboembolic events.

Very rare: Arterial or venous thrombosis at any sites

Eye disorders

Rare: impaired colour vision and other visual disturbances, retinal/artery occlusion

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 (www.mhra.gov.uk/yellowcard).

4.9 Overdose

Symptoms may be nausea, vomiting, orthostatic symptoms and/or hypotension. 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: antifibrinolytic agent.

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 6^{th} 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 crossed 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

Pregelatinized Starch BP
Microcrystalline Cellulose BP
Aerosil BP
PVPK 30 BP
Purified Water BP
Talcum BP
Magnesium Stearate BP
Croscarmelose Sodium BP
Microcrystalline Cellulose BP
Aerosil BP
Hydroxypropyl methyl cellulose BP
Titanium Dioxide BP
Talcum BP
Polyethylene Glycol BP (PEG-6000)
Iso propyl alcohol BP
Methylene Dichloride BP
Colour: Tartrazine Lake

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

3 years

6.4 Special precautions for Storage

Do not store above 30°C. Store in the original package.

6.5 Nature and contents of Container

Alu / Alu blister of 10 tablets such 10 blisters are packed in a carton along with insert.

Special precautions for disposal

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

7. REGISTRANT

ANNYGOD PHARMACEUTICAL COMPANY LTD, 28
UKWULU STREET, AWADA OBOSI, ANAMBRA STATE

8. MANUFACTURER

Merit Organics Ltd

Plot No 2104/2/A, G.I.D.C , Sarigam , Bhilad,
Dist- Valsad-396155, Gujarat , INDIA

9. DATE OF REVISION OF THE TEXT

Applicable once the registration is obtained.