SCHEDULING STATUS

S4

PROPRIETARY NAME (AND DOSAGE FORM)

MORWAK (Tablets)

COMPOSITION

Each tablet contains 500 mg of tranexamic acid.

Other excipients include colloidal silicon dioxide,

croscarmellose sodium, magnesium stearate, microcrystalline cellulose, povidone and talc.

The film coating contains magnesium stearate, macrogol 8000, methacrylate polymers, talc and titanium dioxide (E171).

Sugar free.

PHARMACOLOGICAL CLASSIFICATION

A 8.1 Coagulants, haemostatics

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Tranexamic acid exerts an inhibitory effect on the activation of plasminogen in the fibrinolytic system, i.e. on the conversion of plasminogen to plasmin, in clinical conditions in which there is abnormal stimulation of the activation mechanism.

Pharmacokinetic properties

Absorption

Peak plasma tranexamic acid concentration is obtained immediately after intravenous administration (500 mg).The concentration then 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 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 to 12 litres.

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 first twelve 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.

Special populations

Plasma concentrations increase in patients with renal failure.

No specific pharmacokinetic study has been conducted in children.

INDICATIONS

1. Short term use in the treatment of hyphaema and in patients with established coagulopathies who are undergoing minor surgery.
2. Management of dental extraction in haemophiliacs.
3. Hereditary angioedema.
4. Menorrhagia.

CONTRAINDICATIONS

MORWAK is contraindicated in:

- patients who are hypersensitive to tranexamic acid or to any of the excipients of **MORWAK** (see COMPOSITION).
- history of acute venous or arterial thrombosis.
- patients who suffer from massive urinary tract haemorrhage.
- severe renal impairment because of risk of accumulation.
- active thromboembolic disease.
- fibrinolytic conditions following consumption coagulopathy except in those with predominant activation of the fibrinolytic system with acute severe bleeding.
- history of convulsions.

WARNINGS AND SPECIAL PRECAUTIONS

MORWAK is not recommended in patients suffering massive haematuria from the upper urinary tract (especially haemophilia) as ureteric obstruction has been reported occasionally (see CONTRAINDICATIONS).

Care should be taken:

- when prescribing **MORWAK** to patients with renal insufficiency because of the risk of accumulation (see CONTRAINDICATIONS);

- when disseminated intravascular coagulation is in progress;

Regular eye examination (e.g. visual acuity, slit lamp, intra-ocular pressure, visual fields) and liver function tests should be undertaken during long-term treatment of patients with hereditary angioedema.

Dosages should be reduced in patients with renal impairment. (See DOSAGE AND DIRECTIONS FOR USE).

Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

INTERACTIONS

Medicines with actions on haemostasis should be given with caution to patients on antifibrinolytic therapy such as **MORWAK**. The potential for thrombus formation may be increased by oestrogens, for example, or the action of the fibrinolytic antagonised by compounds such as the thrombolytic.

Concomitant chlorpromazine and tranexamic acid, as in **MORWAK**, therapy of subarachnoid haemorrhage has been reported to result in cerebral vasospasm and cerebral ischaemia, and possibly a reduction in cerebral blood flow.

It is not recommended to use **MORWAK** concomitantly with highly activated prothrombin products.

PREGNANCY AND LACTATION

The safety of **MORWAK** in pregnant and lactating women has not been established.

MORWAK passes into breast milk to a concentration of approximately one hundredth of the concentration in the maternal blood. Caution should be

exercised when **MORWAK** is given to lactating women.

DOSAGE AND DIRECTIONS FOR USE

MORWAK tablets are given orally.

Adults:

1. **Traumatic hyphaema**

1,0 to 1,5 g (two to three tablets) every eight hours for 6 to 7 days.

2. **Patients with established coagulopathies undergoing minor surgery**

   Conisation of the cervix: 1,0 to 1,5 g (two to three tablets) every eight to twelve hours for 12 days post-operatively.

3. **Dental operations/extractions**

   25 mg/kg orally two hours before the operation. Factor VIII and Factor IX should be given as well as tranexamic acid. After the operation 25 mg/kg **MORWAK** is given three to four times a day for 6 to 8 days.

4. **Hereditary angioedema**

   Some patients are aware of the illness; a suitable treatment of these patients is 1,0 to 1,5 g (two to three tablets) two to three times a day for a few days. Other patients are treated continually at this dosage.

5. **Menorrhagia**

Treatment with **MORWAK** should only be initiated after heavy bleeding has started. Two to three tablets should be given three to four times a day.

Elderly:

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

Impaired renal function:

Dosages should be reduced in patients with renal impairment. For patients with moderate to severe impaired renal function, the following dosages are recommended:

Serum clearance	**Oral dose**	**Dose frequency**
120 to 250 micromol/l	15 mg/kg	Twice daily
250 to 500 micromol/l	15 mg/kg	Once daily
> 500 micromol/l	7,5 mg/kg	Once daily

SIDE EFFECTS

Immune system disorders

Less frequent: Hypersensitivity reactions including anaphylaxis

Nervous System Disorders

Less frequent: Convulsions, particularly in case of misuse

Eye disorders

Less frequent: Visual disturbances including impaired colour vision, retinal vein/artery occlusion

Vascular disorders

Less frequent: Thromboembolic events, 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

Gastrointestinal disorders

Frequent: Nausea, vomiting, diarrhoea

Skin and subcutaneous tissue disorders

Less frequent: Allergic skin reactions

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Symptoms of overdose may be nausea, vomiting, orthostatic symptoms and/or hypotension. Initiate vomiting, then charcoal therapy. Maintain a high fluid intake to promote renal excretion.

IDENTIFICATION

White to off-white capsule shaped, film-coated tablet marked 'TA 500' on one face and with a central break line on the reverse side.

PRESENTATION

Blister packs composed of PVC covered by an aluminium foil lidding.

The blister packs are contained in an outer carton of 20 or 100 tablets.

STORAGE INSTRUCTIONS

Store at or below 25 °C in the original pack. Protect from moisture.

KEEP OUT OF THE REACH OF CHILDREN

REGISTRATION NUMBER

41/8.1/0742

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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