- Antiplasmin Agent -

TRANSAMIN® (Capsules)

CONTRAINDICATIONS (Transamin is contraindicated in the following patients.)
Patients receiving thrombin (see "Drug Interactions")

DESCRIPTION

1. Composition

Brand Name	Active ingredient	Inactive ingredients
Transamin (capsules)	Tranexamic Acid 250mg	Corn starch, colloidal silicon dioxide and magnesium stearate

2. Product description

Brand Name	Dosage Form	Color	Appearance		Identification code
			Size (mm)	Weight (mg)	
Transamin (capsules)	Capsule (No.2)	Cap: orange Body: yellow	17.7 (total length)	433	D605
Transamin (capsules)	Capsule (No.2)	Cap: white Body: white	17.7 (total length)	433	

INDICATIONS

- Abnormal bleeding and its symptoms in hemorrhagic diseases (purpura, aplastic anemia, cancer, leukemia etc.)
- Bloody sputum and hemoptysis in pulmonary tuberculosis
- Renal bleeding
- Genital bleeding
- Bleeding in prostatomegaly
- Abnormal bleeding during operation
- Menorrhagia (Heavy Menstrual Bleeding)

DOSAGE AND ADMINISTRATION

Usual oral dose for adult is 1-2 capsules 3 times a day. In menorrhagia (Heavy Menstrual Bleeding) indication, the recommended dose for adult is 1 gm (4 capsules) 3 times a day starting on the first day of period for days of heavy flow. Dosage of Transamin should be individualized in accordance with patient's age and clinical condition.

PRECAUTIONS

1. Careful Administration (Transamin should be administered with care in the following patients.)
   (1) Patients with thrombosis (e.g., cerebral thrombosis, myocardial infarction, or thrombophlebitis, etc.) and patients at risk of thrombosis
   [Transamin may stabilize thrombosis.]
   (2) Patients with consumption coagulopathy (Use comitantly with heparin, etc.)
   [Transamin may stabilize thrombosis.]
   (3) Postoperative, recumbent ridden patients and patients undergoing astriction
   [Venous thrombosis is likely to occur in these patients, and Transamin may stabilize thrombosis. Pulmonary embolism has been reported in association with resolution of recumbency or removal of astriction.]
   (4) Patients with renal failure
   [Blood concentration may increase.]
   (5) Patients with a history of hypersensitivity to any of the components of this product
2. Drug Interactions
   1) Contraindications for coadministration (Transamin should not be coadministered with the following drugs.)

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Thrombin	Coadministration may cause a thrombosis tendency.	Coadministration increases the tendency towards thrombosis due to the thrombogenic property of the product.

   2) Precautions for coadministration (Transamin should be administered with care when coadministered with the following drugs.)

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Hemocoagulase	Coadministration at high doses may cause a thrombosis tendency.	Due to the anti-plasmin action of the product, fibrin clots formed by hemocoagulase may persist in the blood stream for a relatively long period of time, which may resulting in a prolonged thrombotic state.
Batroxobin	Coadministration may cause thromboembolism	Transamin inhibits the decomposition of desA fibrin polymer produced by batroxobin.
Coagulation factor agents (eptacog-alfa, etc.)	Coagulation may be further activated at sites with enhanced local fibrinolysis, such as the oral cavity.	Coagulation factors exert hemostatic actions by activating the coagulation system, whereas tranexamic acid exerts hemostatic actions by inhibiting the fibinolytic system.

3. Adverse Reactions
   The most frequently observed adverse reactions reported in a total of 2,954 patients were anorexia 0.61% (18 events), nausea 0.41% (12 events), vomiting 0.20% (6 events), heartburn 0.17% (5 events), itching 0.07% (2 events), and rash 0.07% (2 events)
   (1) Clinically significant adverse reactions (frequency un-known [Note])
   Convulsion: Incidence of convulsion was reported in dialysis patients. Patients should be carefully moni-tored monitored, and appropriate measures, such as discontinuing treatment, should be taken if any abnormality is observed.
   (2) The following adverse reactions may occur. Patients should be carefully monitored, and appropriate measures, such as discontinuing treatment, should be taken if any abnormality is observed.

	0.1% to < 1%	< 0.1%
Hypersensitivity		Itching, rash, etc.
Gastrointestinal	Anorexia, nausea, vomiting, diarrhea, heartburn	
Other		Drowsiness

Note: The frequency of adverse reactions on the basis spontaneous reports is unknown

4. Use in the Elderly
   Since elderly patients often have reduced physiological function, careful supervision and measures such as reducing the dose are recommended.
5. Other Precautions
   Retinal degeneration has been reported with tranexamic acid in dogs after long-term, high-dose administration.
6. Use for pregnancy and lactation
   No safety information.
7. Overdosage
   No safety information.

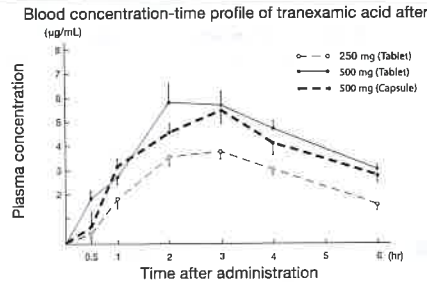
PHARMACOKINETICS

1. Blood concentration
   When a single dose of tranexamic acid was administered orally to healthy adults, the pharmacokinetic parameters were as shown below.

Pharmacokinetic parameters of tranexamic acid after a single oral dose (n=5)

Dose	250mg (Tablet)	500mg (Tablet)	500mg (Capsule)
T_{max} (hr)	2 to 3		
C_{max} (μg/mL)	3.9	6.0	5.5
$t_{1/2}$ (hr)	3.1	3.3	3.3

Blood concentration-time profile of tranexamic acid after a single oral dose



2. Distribution
   Reference information (animal study)
   When a single dose of ^{14}C-tranexamic acid was administered orally to rats, the concentration in most organs reached peak values as well as the blood concentration after 2 hours. Levels in kidney and liver were higher, and those of other organs were lower than that of the blood.
3. Metabolism and excretion
   When a single dose (250 mg or 500 mg) of tranexamic acid was administered orally to healthy adults, it was rapidly absorbed and about 40 to 70% of the administered dose was excreted as unchanged form in the urine within 24 hours.

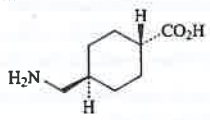
PHARMACOLOGY

In physiological and pathologic conditions, fibrinolysis affects enhancement of vascular permeability, and relevant to the development, progression and healing of hemorrhage induced by plasmin. Tranexamic acid inhibits the activity of plasmin, thereby exhibiting antihemorrhagic effects.

1. Antiplasmin action
   Tranexamic acid inhibits the binding of plasmin or plasminogen to fibrin by strongly binding to the lysine binding site (LBS) of fibrin, which is also the binding site for plasmin and plasminogen. Therefore, tranexamic acid strongly inhibits fibrinolysis induced by plasmin. In addition, in the presence of antiplasmins, such as α_2-macroglobulin in the plasma, the antifibrinolytic action of tranexamic acid is even further strengthened.
2. Hemostatic action
   When the blood level of plasmin is abnormally elevated, various phenomena occur, such as inhibition of platelet aggregation and decomposition of coagulation factors. Even a slight elevation in the blood level of plasmin specifically induces fibrinolysis. Tranexamic acid is considered to exhibit a hemostatic effect by inhibiting fibrinolysis in common types of hemorrhage.

PHYSICOCHEMISTRY

Nonproprietary name: Tranexamic Acid
Chemical name:
trans-4-(Aminomethyl) cyclohexanecarboxylic acid
Structural formula:



Molecular formula: $C_8H_{15}NO_2$
Molecular weight: 157.21
Description: Tranexamic acid occurs as white crystals or powder. It is freely soluble in water, and practically insoluble in ethanol (99.5).

PACKAGING

(orange-yellow) Bottle of 100, 500 capsules
(white) Bottle of 500 capsules

STORAGE AND HANDLING

Storage: Store below 30°C

Revised Date: July 2013

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Under licenced of: Daiichi Sankyo Co., Ltd. Tokyo, Japan

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