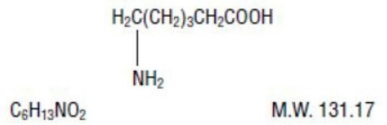
AMINOCAPROIC ACID - aminocaproic acid tablet
Edenbridge Pharmaceuticals LLC.

DESCRIPTION

Aminocaproic acid, USP is 6-
aminohexanoic acid, which acts as an inhibitor of fibrinolysis.

Its chemical structure is:



$C_6H_{13}NO_2$ M.W. 131.17

Aminocaproic acid is soluble in water, acid, and alkaline solutions; it
is sparingly soluble in methanol and practically insoluble in chloroform.

Each Aminocaproic Acid Tablet USP, for oral administration contains 500 mg of
aminocaproic acid and the following inactive ingredients: povidone,
crospovidone, stearic acid, and magnesium stearate.

FDA approved dissolution specification differs from the USP dissolution specification.

CLINICAL PHARMACOLOGY

The fibrinolysis-inhibitory effects of aminocaproic
acid appear to be exerted principally via inhibition of
plasminogen activators and to a lesser degree through antiplasmin activity.

In adults, oral absorption appears to be a zero-
order process with an absorption rate of 5.2 g/hr. The mean lag time in absorption is 10 minutes. After a single oral dose of 5 g, absorption was complete (F=1). Mean ± SD peak plasma concentrations (164 ± 28 mcg/mL) were reached within 1.2 ± 0.45 hours.

After oral administration, the apparent
volume of distribution was estimated to be 23.1 ± 6.6 L (mean ± SD). Correspondingly, the volume of distribution after intravenous administration has been reported to
be 30.0 ± 8.2 L. After prolonged administration, aminocaproic
acid has been found to distribute throughout
extravascular and intravascular compartments of the body, penetrating human red blood cells as well as other tissue cells.

Renal excretion is the primary route of elimination. Sixty-
five percent of the dose is recovered in the
urine as unchanged drug and 11% of the dose appears as the metabolite adipic acid. Renal clearance
(116 mL/min) approximates endogenous creatinine clearance. The total body clearance is 169 mL/min.
The terminal elimination half-life for aminocaproic acid is approximately 2 hours.

INDICATIONS & USAGE

Aminocaproic acid
is useful in enhancing hemostasis when fibrinolysis contributes to bleeding. In life-
threatening situations, transfusion of appropriate blood products and other emergency measures may be
required.

Fibrinolytic bleeding may frequently be associated with surgical complications following heart
surgery
(with or without cardiac bypass procedures) and portacaval shunt; hematological disorders such as
amegakaryocytic thrombocytopenia (accompanying aplastic anemia); acute and life-
threatening abruption
placentae; hepatic cirrhosis; and neoplastic disease such as carcinoma of the prostate, lung, stomach,
and cervix.

Urinary fibrinolysis, usually a normal physiological phenomenon, may contribute to excessive urinary
tract fibrinolytic bleeding associated with surgical hematuria (following prostatectomy and
nephrectomy) or nonsurgical hematuria (accompanying polycystic or neoplastic
diseases of the genitourinary system). (See **WARNINGS**.)

CONTRAINDICATIONS

Aminocaproic acid
should not be used when there is evidence of an active intravascular clotting process.

When there is uncertainty as to whether the cause of bleeding is primary
fibrinolysis or disseminated
intravascular coagulation (DIC), this distinction must be made before administering aminocaproic
acid.

The following tests can be applied to differentiate the two conditions:

- Platelet count is usually decreased in DIC but normal in primary fibrinolysis.
- Protamine paracoagulation test is positive in DIC; a precipitate forms when protamine sulfate is dropped into citrated plasma. The test is negative in the presence of primary fibrinolysis.
- The euglobulin clot lysis test is abnormal in primary fibrinolysis but normal in DIC
- Aminocaproic acid
  must not be used in the presence of DIC without concomitant heparin.

WARNINGS

In patients with upper urinary tract bleeding, aminocaproic acid
administration has been known to cause intrarenal
obstruction in the form of glomerular capillary thrombosis or clots in the renal pelvis and ureters. For
this reason, aminocaproic
acid should not be used in hematuria of upper urinary tract origin, unless the possible
benefits outweigh the risk.

Subendocardial hemorrhages have been observed in dogs given intravenous infusions of 0.2 times the
maximum human therapeutic dose of aminocaproic
acid and in monkeys given 8 times the maximum human therapeutic dose of aminocaproic
acid.

Fatty degeneration of the myocardium has been reported in dogs given intravenous doses of aminocaproic
acid
at 0.8 to 3.3 times the maximum human therapeutic dose and in monkeys given intravenous doses of aminocaproic
acid at 6 times the maximum human therapeutic dose.

Rarely, skeletal muscle weakness with necrosis of muscle fibers has been reported following
prolonged
administration. Clinical presentation may range from mild myalgias with weakness and fatigue to a severe proximal myopathy with rhabdomyolysis, myoglobinuria, and acute renal failure. Muscle
enzymes, especially creatine phosphokinase (CPK) are elevated. CPK levels should be monitored in patients on long-
term therapy. Aminocaproic acid
administration should be stopped if a rise in CPK is noted.

Resolution follows discontinuation of aminocaproic
acid; however, the syndrome may recur if aminocaproic acid is restarted.

The possibility of cardiac muscle damage should also be considered when skeletal myopathy occurs.

One case of cardiac and hepatic lesions observed in man has been reported. The patient received 2 g of
aminocaproic acid every 6 hours for a total dose of 26 g. Death was due to continued cerebrovascular
hemorrhage. Necrotic changes in the heart and liver were noted at autopsy.

PRECAUTIONS

GENERAL PRECAUTIONS

Aminocaproic acid inhibits both the action of plasminogen activators and to a
lesser degree, plasmin activity. The
drug should NOT be administered without a definite diagnosis and/or laboratory finding indicative of
hyperfibrinolysis (hyperplasminemia).1 Inhibition of fibrinolysis by aminocaproic acid may
theoretically result
in clotting or thrombosis. However, there is no definite evidence that administration
of aminocaproic acid has been responsible for the few reported cases of intravascular clotting which
followed this treatment. Rather, it
appears that such intravascular clotting was most likely due to the patient's preexisting clinical condition, e.g., the presence of DIC. It has been postulated that extravascular clots formed *in vivo* may not
undergo spontaneous lysis as do normal clots.

Reports have appeared in the literature of an increased incidence of certain neurological deficits such as hydrocephalus, cerebral ischemia, or cerebral vasospasm associated with the use of antifibrinolytic agents in the treatment of subarachnoid hemorrhage (SAH). All of these events have also been described as part of the natural course of SAH, or as a consequence of diagnostic procedures such as angiography. Drug relatedness remains unclear.

Aminocaproic acid should not be administered with Factor IX Complex concentrates or Anti-Inhibitor Coagulant concentrates, as the risk of thrombosis may be increased.

LABORATORY TESTS

The use of aminocaproic acid should be accompanied by tests designed to determine the amount of fibrinolysis present. There are presently available: (a) general tests such as those for the determination of the lysis of a clotof blood or plasma; and (b) more specific tests for the study of various phases of the fibrinolytic mechanisms. These latter tests include both semiquantitative and quantitative techniques for the determination of profibrinolysin, fibrinolysin, and antifibrinolysin.

DRUG INTERACTIONS

Prolongation of the template bleeding time has been reported during continuous intravenous infusion of aminocaproic acid at dosages exceeding 24 g/day. Platelet function studies in these patients have not demonstrated any significant platelet dysfunction. However, *in vitro* studies have shown that at high concentrations (7.4 mMol/L or 0.97 mg/mL and greater) aminocaproic acid inhibits ADP and collagen- induced platelet aggregation, the release of ATP and serotonin, and the binding of fibrinogen to the platelets in a concentration-response manner. Following a 10 g bolus of aminocaproic acid, transient peak plasma concentrations of 4.6 mMol/L or 0.60 mg/mL have been obtained. The concentration of aminocaproic acidnecessary to maintain inhibition of fibrinolysis is 0.99 mMol/L or 0.13 mg/mL. Administration of a 5 g bolus followed by 1 to 1.25 g/hr should achieve and sustain plasma levels of 0.13 mg/mL. Thus, concentrations which have been obtained *in vivo* clinically in patients with normal renal function are considerably lower than the *in vitro* concentrations found to induce abnormalities in platelet function tests. However, higher plasma concentrations of aminocaproic acid may occur in patients with severe renal failure.

CARCINOGENESIS & MUTAGENESIS & IMPAIRMENT OF FERTILITY

Long-term studies in animals to evaluate the carcinogenic potential of aminocaproic acid and studies to evaluate its mutagenic potential have not been conducted. Dietary administration of an equivalent of the maximum human therapeutic dose of aminocaproic acid to rats of both sexes impaired fertility as evidenced by decreased implantations, litter sizes and number of pups born.

PREGNANCY

Animal reproduction studies have not been conducted with aminocaproic acid. It is also not known whether aminocaproic acid can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Aminocaproic acid should be given to a pregnant woman only if clearly needed.

NURSING MOTHERS

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when aminocaproic acid is administered to a nursing woman.

PEDIATRIC USE

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Aminocaproic acid is generally well tolerated. The following adverse experiences have been reported:

General: Edema, headache, malaise.

Hypersensitivity Reactions: Allergic and anaphylactoid reactions, anaphylaxis.

Cardiovascular: Bradycardia, hypotension, peripheral ischemia, thrombosis.

Gastrointestinal: Abdominal pain, diarrhea, nausea, vomiting.

Hematologic: Agranulocytosis, coagulation disorder, leukopenia, thrombocytopenia.

Musculoskeletal: CPK increased, muscle weakness, myalgia, myopathy (see **WARNINGS**), myositis, rhabdomyolysis.

Neurologic: Confusion, convulsions, delirium, dizziness, hallucinations, intracranial hypertension, stroke, syncope.

Respiratory: Dyspnea, nasal congestion, pulmonary embolism.

Skin: Pruritis, rash.

Special Senses: Tinnitus, visiondecreased, watery eyes.

Urogenital: BUN increased, renal failure. There have been some reports of dry ejaculation during the period of aminocaproic acid treatment. These have been reported to date only in hemophilia patients who received the drug after undergoing dental surgical procedures. However, this symptom resolved in all patients within 24 to 48 hours of completion of therapy.

To report SUSPECTED ADVERSE REACTIONS, contact Edenbridge Pharmaceuticals, LLC at 877-381-3336 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

A dosage regimen may be followed by administering Aminocaproic Acid Tablets as follows:

For the treatment of acute bleeding syndromes due to elevated fibrinolytic activity, it is suggested that 10 Aminocaproic Acid Tablets USP, 500 mg (5 g) be administered during the first hour of treatment, followed by a continuing rate of 2 Aminocaproic Acid Tablets USP, 500 mg (1 g) per hour. This method of treatment would ordinarily be continued for about 8 hours or until the bleeding situation has been controlled.

HOW SUPPLIED

Aminocaproic Acid Tablets USP, 500 mg

Each round, convex, white to off-white tablet scored on one side and imprinted with on the other side, contains 500 mg of Aminocaproic acid, USP.

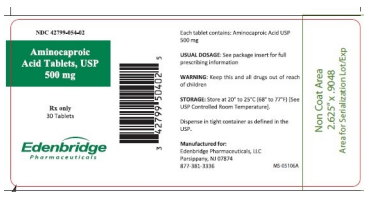
Bottle of 30 – NDC 42799 054 02

Store at 20°-25°C (68°-77°F)[see USP Controlled Room Temperature];Dispense in Tight Containers.

REFERENCES

1Stefanini M, Dameshek W:
The Hemorrhagic Disorders, Ed. 2, New York, Grune and Stratton; 1962:510-514.

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL



AMINOCAPROIC ACID
aminocaproic acid tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:42799-054
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
AMINOCAPROIC ACID (UNII: U6F3787206) (AMINOCAPROIC ACID - UNII:U6F3787206)	AMINOCAPROIC ACID	500 mg

Inactive Ingredients	
Ingredient Name	**Strength**
POVIDONE K30 (UNII: U725QWY32X)	

CROSPOVIDONE (UNII: 68401960MK)	
STEARIC ACID (UNII: 4ELV7Z65AP)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	

Product Characteristics

Color	WHITE	**Score**	2 pieces
Shape	ROUND	**Size**	13mm
Flavor		**Imprint Code**	D133
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:42799-054-02	30 in 1 BOTTLE; Type 0: Not a Combination Product	06/02/2021	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA212110	06/02/2021	

Labeler - Edenbridge Pharmaceuticals LLC. (948715060)

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