AMINOCAPROIC ACID- aminocaproic acid tablet
AMINOCAPROIC ACID- aminocaproic acid syrup
Akorn Operating Company LLC

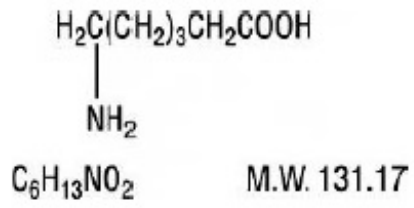
Aminocaproic Acid Tablets USP 500 mg, 1000 mg and Oral Solution 0.25 g/mL

Rx only

DESCRIPTION

Aminocaproic acid 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.

Aminocaproic acid oral solution for oral administration, contains 0.25 g/mL of aminocaproic acid with methylparaben 0.20%, propylparaben 0.05%, edetate disodium 0.30% as preservatives and the following inactive ingredients: sodium saccharin, sorbitol solution, citric acid anhydrous, natural and artificial raspberry flavor and an artificial bitterness modifier.

Each aminocaproic acid tablet for oral administration contains either 500 mg or 1000 mg of aminocaproic acid and the following inactive ingredients: povidone, crospovidone, stearic acid, and magnesium stearate.

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 AND 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 abruptio 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

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 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 clot of 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/Laboratory Test 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 injection, transient peak plasma concentrations of 4.6 mMol/L or 0.60 mg/mL have been obtained. The concentration of aminocaproic acid necessary 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

Pregnancy Category C.

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, vision decreased, 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.

OVERDOSAGE

A few cases of acute overdosage with aminocaproic acid administered intravenously have been reported. The effects have ranged from no reaction to transient hypotension to severe acute renal failure leading to death. One patient with a history of brain tumor and seizures experienced seizures after receiving an 8 gram bolus injection of aminocaproic acid. The single dose of aminocaproic acid causing symptoms of overdosage or considered to be life-threatening is unknown. Patients have tolerated doses as high as 100 grams while acute renal failure has been reported following a dose of 12 grams.

The intravenous and oral LD_{50} of aminocaproic acid were 3.0 and 12.0 g/kg respectively in the mouse and 3.2 and 16.4 g/kg respectively in the rat. An intravenous infusion dose of 2.3 g/kg was lethal in the dog. On intravenous administration, tonic-clonic convulsions were observed in dogs and mice.

No treatment for overdosage is known, although evidence exists that aminocaproic acid is removed by hemodialysis and may be removed by peritoneal dialysis. Pharmacokinetic studies have shown that total body clearance of aminocaproic acid is markedly decreased in patients with severe renal failure.

DOSAGE AND ADMINISTRATION

An identical dosage regimen may be followed by administering aminocaproic acid tablets or aminocaproic acid oral solution as follows:

For the treatment of acute bleeding syndromes due to elevated fibrinolytic activity, it is suggested that 5 aminocaproic acid 1000 mg tablets or 10 aminocaproic acid 500 mg tablets (5 g) or 20 milliliters of aminocaproic acid oral solution (5 g) be administered during the first hour of treatment, followed by a continuing rate of 1 aminocaproic acid 1000 mg tablet or 2 aminocaproic acid 500 mg tablets (1 g) or 5 milliliters of aminocaproic acid oral solution (1.25 g) per hour. This method of treatment would ordinarily be continued for about 8 hours or until the bleeding has been controlled.

HOW SUPPLIED

Aminocaproic Acid Oral Solution USP, 0.25 g/mL

Each mL of raspberry-flavored oral solution contains 0.25 g/ mL of aminocaproic acid.

8 Fl. Oz. (237 mL) Bottle - NDC 17478-447-08

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]; Dispense in a tight container with a child-resistant closure. Do not Freeze.

Aminocaproic Acid Tablets USP, 500 mg

Each round, white tablet, engraved with XP on one side and scored on the other with A to the left of the score and 10 on the right, contains 500 mg of aminocaproic acid.

Bottle of 30 – NDC 17478-768-30

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]; Dispense in a tight container with a child-resistant closure. Do not Freeze.

Aminocaproic Acid Tablets USP, 1000 mg

Each oblong, white tablet, engraved with XP on one side and scored on the other with A to the left of the score and 20 on the right, contains 1000 mg of aminocaproic acid.

Bottle of 30 – NDC 17478-769-30

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]; Dispense in a tight container with a child-resistant closure. Do not Freeze.

REFERENCE

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

Distributed by:
Akorn Operating Company LLC
Gurnee, IL 60031

Manufactured by:
Mikart, LLC

Atlanta, GA 30318

Code 909C00

Rev. 05/22

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

Bottle Label – 8 Fl. Oz. (236.5 mL)

NDC 17478-447-08

Aminocaproic Acid

Oral Solution, USP

0.25 grams/mL

Rx Only

8 Fl. Oz. (236.5 mL)

Akorn

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

Bottle Label – 500 mg Tablet

NDC 17478-768-30

Aminocaproic Acid

Tablets, USP

500 mg

Rx Only 30 Tablets

Akorn

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

Bottle Label – 1000 mg Tablet

NDC 17478-769-30

Aminocaproic Acid

Tablets, USP

1000 mg

Rx Only 30 Tablets

Akorn

AMINOCAPROIC ACID

aminocaproic acid tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:17478-768
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**
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POVIDONE K30 (UNII: U725QWY32X)	
STEARIC ACID (UNII: 4ELV7Z65AP)	
CROSPOVIDONE (UNII: 2S7830E561)	

Product Characteristics			
Color	WHITE (WHITE)	**Score**	2 pieces
Shape	ROUND (ROUND)	**Size**	13mm
Flavor		**Imprint Code**	XP;;A;;10
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:17478-768-30	30 in 1 BOTTLE; Type 0: Not a Combination Product	03/12/2019	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA015197	03/12/2019	

AMINOCAPROIC ACID

aminocaproic acid tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:17478-769
Route of Administration	ORAL		

Active Ingredient/Active Moiety		

Ingredient Name	Basis of Strength	Strength
AMINOCAPROIC ACID (UNII: U6F3787206) (AMINOCAPROIC ACID - UNII:U6F3787206)	AMINOCAPROIC ACID	1000 mg

Inactive Ingredients

Ingredient Name	Strength
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POVIDONE K30 (UNII: U725QWY32X)	
STEARIC ACID (UNII: 4ELV7Z65AP)	
CROSPOVIDONE (UNII: 2S7830E561)	

Product Characteristics

Color	WHITE (WHITE)	**Score**	2 pieces
Shape	OVAL (OBLONG)	**Size**	22mm
Flavor		**Imprint Code**	XP;;A;;20
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:17478-769-30	30 in 1 BOTTLE; Type 0: Not a Combination Product	03/12/2019	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA015197	03/12/2019	

AMINOCAPROIC ACID

aminocaproic acid syrup

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:17478-447
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMINOCAPROIC ACID (UNII: U6F3787206) (AMINOCAPROIC ACID - UNII:U6F3787206)	AMINOCAPROIC ACID	0.25 g in 1 mL

Inactive Ingredients

Ingredient Name	Strength
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
METHYLPARABEN (UNII: A2I8C7HI9T)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
PROPYLPARABEN (UNII: Z8IX2SC1OH)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
WATER (UNII: 059QF0KO0R)	
SACCHARIN SODIUM ANHYDROUS (UNII: I4807BK602)	
SORBITOL (UNII: 506T60A25R)	
RASPBERRY (UNII: 4N14V5R27W)	

Product Characteristics

Color		**Score**	
Shape		**Size**	
Flavor	RASPBERRY	**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:17478-447-08	236.5 mL in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	03/12/2019	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA015230	03/12/2019	

Labeler - Akorn Operating Company LLC (117693100)

Registrant - Akorn Operating Company LLC (117693100)

Establishment

Name	Address	ID/FEI	Business Operations
Mikart, Inc.		030034847	MANUFACTURE(17478-768, 17478-769, 17478-447)

Revised: 7/2022 Akorn Operating Company LLC