INTRAVENOUS N-ACETYLCYSTEINE

PACKAGE INSERT

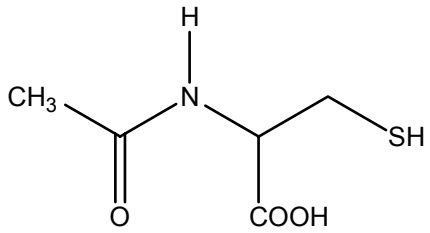
RX ONLY

PRESCRIBING INFORMATION

ACETADOTE®
(acetylcysteine) Injection
For Intravenous Use

DESCRIPTION

Acetylcysteine injection is an intravenous (I.V.) medication for the treatment of acetaminophen overdose. Acetylcysteine is the nonproprietary name for the N-acetyl derivative of the naturally occurring amino acid, L-cysteine (N-acetyl-L-cysteine, NAC). The compound is a white crystalline powder, which melts in the range of 104° to 110°C and has a very slight odor. The molecular formula of the compound is $C_5H_9NO_3S$, and its molecular weight is 163.2. Acetylcysteine has the following structural formula:



Acetadote is supplied as a sterile solution in vials containing 20% w/v (200 mg/mL) acetylcysteine. The pH of the solution ranges from 6.0 to 7.5. Acetadote contains the following inactive ingredients: 0.5 mg/mL disodium edetate, sodium hydroxide (used for pH adjustment), and Sterile Water for Injection, USP.

CLINICAL PHARMACOLOGY

Acetaminophen Overdose:
Acetaminophen is absorbed from the upper gastrointestinal tract with peak plasma levels occurring between 30 and 60 minutes after therapeutic doses and usually within 4 hours following an overdose. It is extensively metabolized in the liver to form principally the sulfate and glucoronide conjugates which are excreted in the urine. A small fraction of an ingested dose is metabolized in the liver by isozyme CYP2E1 of the cytochrome P-450 mixed function oxidase enzyme system to form a reactive, potentially toxic, intermediate metabolite. The toxic metabolite preferentially conjugates with hepatic glutathione to form nontoxic cysteine and mercapturic acid derivatives, which are then excreted by the kidney. Recommended therapeutic doses of acetaminophen are not believed to saturate the glucuronide and sulfate conjugation pathways and therefore are not expected to result in the formation of sufficient reactive metabolite to deplete glutathione stores. However, following ingestion of a large overdose, the glucuronide and sulfate conjugation pathways are saturated resulting in a larger fraction of the drug being metabolized via the cytochrome P-450 pathway and therefore, the amount of acetaminophen metabolized to the reactive intermediate increases. The increased formation of the reactive metabolite may deplete the hepatic stores of glutathione with subsequent binding of the metabolite to protein molecules within the hepatocyte resulting in cellular necrosis.

Acetylcysteine I.V. Treatment:
Acetylcysteine has been shown to reduce the extent of liver injury following acetaminophen overdose. It is most effective when given early, with benefit seen principally in patients treated within 8-10 hours of the overdose. Acetylcysteine likely protects the liver by maintaining or restoring the glutathione levels, or by acting as an alternate substrate for conjugation with, and thus detoxification of, the reactive metabolite.

PHARMACOKINETICS

Distribution:
The steady-state volume of distribution (Vd_{ss}) and the protein binding for acetylcysteine were reported to be 0.47 liter/kg and 83%, respectively.

Metabolism:
Acetylcysteine may form cysteine, disulfides, and conjugates in vivo (N, N'-diacetylcysteine, N-acetylcysteine-cysteine, N-acetylcysteine-glutathione, N-acetylcysteine-protein, etc). Based on published data, it was reported that after an oral dose of ^{35}S-acetylcysteine, about 22% of total radioactivity was excreted in urine after 24 hours. No metabolites were identified.

Elimination:
After a single intravenous dose of acetylcysteine, the plasma concentration of total acetylcysteine declined in a poly-exponential decay manner with a mean terminal half-life ($T_{1/2}$) of 5.6 hours. The mean clearance (CL) for acetylcysteine was reported to be 0.11 liter/hr/kg and renal CL constituted about 30% of total CL.

Special Populations:

Gender

Adequate information is not available to assess if there are differences in pharmacokinetics (PK) between males and females.

Pediatric

The mean elimination $T_{1/2}$ of acetylcysteine is longer in newborns (11hours) than in adults (5.6 hours). Pharmacokinetic information is not available in other age groups.

Pregnant Women

In four pregnant women with acetaminophen toxicity, oral or I.V. acetylcysteine was administered at the time of delivery. Acetylcysteine was detected in the cord blood of 3 viable infants and in cardiac blood of a fourth infant, samples at autopsy.

Hepatic Impairment

In subjects with severe liver damage, i.e., cirrhosis due to alcohol (with Child-Pugh score of 7-13), or primary and/or secondary biliary cirrhosis (with Child-Pugh score of 5-7), mean $T_{1/2}$ increased by 80% while mean CL decreased by 30% compared to control group.

Renal Disease

Pharmacokinetic information is not available in patients with renal impairment.

Geriatric Patients

Adequate information on acetylcysteine PK in geriatric patients is not available.

Drug-Drug Interactions

No drug-drug interaction studies have been conducted.

CLINICAL STUDIES

Safety Study
A randomized, open-label, multi-center clinical study was conducted in Australia to compare the rates of anaphylactoid reactions between two rates of infusion for the I.V. acetylcysteine loading dose. One hundred nine subjects were randomized to a 15 minute infusion rate and seventy-one subjects were randomized to a 60 minute infusion rate. The loading dose was 150 mg/kg followed by a maintenance dose of 50 mg/kg over 4 hours and then 100 mg/kg over 16 hours. Of the 180 patients, 27% were male and 73% were female. Ages ranged from 15 to 83 years, with the mean age being 29.9 years ($\pm$13.0).

Within the first 2 hours following I.V. acetylcysteine administration, 17% developed an anaphylactoid reaction (18% in the 15-minute treatment group; 14% in the 60-minute treatment group). (See **Warnings**). A subgroup of 58 subjects (33 in the 15-minute treatment group; 25 in the 60-minute treatment group) was treated within 8 hours of acetaminophen ingestion. No hepatotoxicity occurred within this subgroup; however with 95% confidence, the true hepatotoxicity rates could range from 0% to 9% for the 15-minute treatment group and from 0% to 12% for the 60-minute treatment group.

Observational Study
An open-label, observational database contained information on 1749 patients who sought treatment for acetaminophen overdose over a 16-year period. Of the 1749 patients, 65% were female, 34% were male and <1% was transgender. Ages ranged from 2 months to 96 years, with 71.4% of the patients falling in the 16-40 year old age bracket. A total of 399 patients received acetylcysteine treatment. A post-hoc analysis identified 56 patients who (1) were at high or probable risk for hepatotoxicity (APAP >150 mg/L at the four hours line according to the Australian nomogram) and (2) had a liver function test. Of the 53 patients who were treated with I.V. acetylcysteine (300 mg/kg I.V. acetylcysteine administered over 20-21 hours) within 8 hours, two (4%) developed hepatotoxicity (AST or ALT>1000U/L). Twenty-one of 48 (44%) patients treated with acetylcysteine after 15 hours developed hepatotoxicity. The actual number of hepatotoxicity outcomes may be higher than what is reported here. For patients with multiple admissions for acetaminophen overdose, only the first overdose treated with I.V. acetylcysteine was examined. Hepatotoxicity may have occurred in subsequent admissions.

INDICATIONS AND USAGE

Acetadote, administered intravenously within 8 to 10 hours after ingestion of a potentially hepatotoxic quantity of acetaminophen, is indicated to prevent or lessen hepatic injury (see **Dosage and Administration** and **Acetaminophen Assays – Interpretation and Methodology** sections).

CONTRAINDICATIONS

Acetadote is contraindicated in patients with hypersensitivity or previous anaphylactoid reactions to acetylcysteine or any components in the preparation.

WARNINGS

Serious anaphylactoid reactions, including death in a patient with asthma, have been reported in patients administered acetylcysteine intravenously.

Acute flushing and erythema of the skin may occur in patients receiving acetylcysteine intravenously. These reactions usually occur 30 to 60 minutes after initiating the infusion and often resolve spontaneously despite continued infusion of acetylcysteine. Anaphylactoid reactions (defined as the occurrence of an acute hypersensitivity reaction during acetylcysteine administration including rash, hypotension, wheezing, and/or shortness of breath)

have been observed in patients receiving I.V. acetylcysteine for acetaminophen overdose and occurred soon after initiation of the infusion (see **Adverse Reactions** section). If a reaction to acetylcysteine involves more than simply flushing and erythema of the skin, it should be treated as an anaphylactoid reaction. This usually entails administering antihistaminic drugs as well as epinephrine in severe cases. In addition, the acetylcysteine infusion may be interrupted until treatment of the anaphylactoid symptoms has been initiated and then carefully restarted. If the anaphylactoid reaction returns upon reinitiation of treatment or increases in severity, intravenous acetylcysteine should be discontinued and alternative patient management should be considered.
For additional information, contact the American Association of Poison Control Centers (1-800-222-1222).

PRECAUTIONS

Acetadote should be used with caution in patients with asthma, or where there is a history of bronchospasm. The total volume administered should be adjusted for patients less than 40 kg and for those requiring fluid restriction. To avoid fluid overload, the volume of 5% dextrose should be reduced as needed (See DOSAGE AND ADMINISTRATION). If volume is not adjusted fluid overload can occur, potentially resulting in hyponatremia, seizure, and death.

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Long-term studies in animals have not been performed to evaluate the carcinogenic potential of acetylcysteine.

Acetylcysteine was not genotoxic in the Ames test or the in vivo mouse micronucleus test. It was, however, positive in the in vitro mouse lymphoma cell (L5178Y/TK+/-) forward mutation test.

Treatment of male rats with acetylcysteine at an oral dose of 250 mg/kg/day for 15 weeks (compared to the recommended total human intravenous dose of 300 mg/kg) did not affect the fertility or general reproductive performance.

Pregnancy: Teratogenic Effects: Pregnancy Category B

Teratology studies were performed in rats at oral doses up to 2000 mg/kg/day and in rabbits at oral doses up to 1000 mg/kg/day (compared to the recommended total human intravenous dose of 300 mg/kg) and revealed no evidence of impaired fertility or harm to the fetus due to acetylcysteine. There are, however no adequate and well-controlled studies in pregnant women. Because animal reproduction studies may not always be predictive of human response, this drug should be used during pregnancy only if clearly needed.

Pregnant Women

In four pregnant women with acetaminophen toxicity, oral or I.V. acetylcysteine was administered at the time of delivery. Acetylcysteine crossed the placenta and was measurable in newborn circulation and cord blood of three viable infants following delivery and in cardiac blood of a fourth infant at autopsy (22 weeks gestational age who died 3 hours after birth). No adverse sequelae developed in the three viable infants. All mothers recovered and none of the infants had evidence of acetaminophen poisoning.

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 acetylcysteine is administered to a nursing woman.

Pediatric Patients

No adverse effects were noted during I.V. infusion with acetylcysteine at a mean rate of 8.4 mg/kg/h for 24 hours to 10 preterm newborns ranging in gestational age from 25 to 31 weeks and in weight from 500 to 1380 grams in one

study (Study 1) or in 6 newborns ranging in gestational age from 26 to 30 weeks and in weight from 520 to 1335 grams infused with acetylcysteine at 0.1 to 1.3 mg/kg/h for 6 days (Study 2). Elimination of acetylcysteine was slower in these infants than in adults; mean elimination half-life was 11 hours (Study 1). There are no adequate and well-controlled studies in pediatric patients.

Geriatric Patients

The clinical studies do not provide a sufficient number of geriatric subjects to determine whether the elderly respond differently.

Drug Interactions

Drug stability and safety of acetylcysteine when mixed with other drugs have not been established.

ADVERSE REACTIONS

In the literature the most frequently reported adverse events attributed to I.V. acetylcysteine administration were rash, urticaria, and pruritus. The frequency of adverse events has been reported to be between 0.2% and 20.8%, and they most commonly occur during the initial loading dose of acetylcysteine.

The incidence of drug-related adverse events occurring within the first 2 hours following acetylcysteine administration reported in a randomized study (Infusion Rate Study) in patients with acetaminophen poisoning is presented in Table 5 by preferred term. In this study patients were randomized to a 15-minute or a 60-minute loading dose regimen.

Table 1 Incidence of Drug-Related Adverse Events Occurring Within the First 2 Hours Following Study Drug Administration by Preferred Term: CMAX Study

Treatment Group	15-min				60-min			
Number of Patients	n =109				n =71			
Cardiac disorders	5 (5%)				2 (3%)			
Severity:	*Unknown*	*Mild*	*Moderate*	*Severe*	*Unknown*	*Mild*	*Moderate*	*Severe*
Tachycardia NOS		4 (4%)	1 (1%)			2 (3%)		
Ear and labyrinth disorders	1 (1%)				0 (0%)			
Severity:	*Unknown*	*Mild*	*Moderate*	*Severe*	*Unknown*	*Mild*	*Moderate*	*Severe*
Ear pain			1 (1%)					
Gastrointestinal disorders	16 (15%)				7 (10%)			
Severity:	*Unknown*	*Mild*	*Moderate*	*Severe*	*Unknown*	*Mild*	*Moderate*	*Severe*
Nausea	1 (1%)		6 (6%)			1 (1%)	1 (1%)	
Vomiting NOS		2 (2%)	11 (10%)			2 (3%)	4 (6%)	
General disorders and administration site conditions	1 (1%)				1 (1%)			
Severity:	*Unknown*	*Mild*	*Moderate*	*Severe*	*Unknown*	*Mild*	*Moderate*	*Severe*
Chest tightness		1 (1%)						
Feeling hot						1 (1%)		
Immune system disorders	20 (18%)				10 (14%)			
Severity:	*Unknown*	*Mild*	*Moderate*	*Severe*	*Unknown*	*Mild*	*Moderate*	*Severe*
Anaphylactoid reaction	2 (2%)	6 (6%)	11 (10%)	1 (1%)		4 (6%)	5 (7%)	1 (1%)
Respiratory, thoracic and mediastinal disorders	2 (2%)				2 (3%)			
Severity:	*Unknown*	*Mild*	*Moderate*	*Severe*	*Unknown*	*Mild*	*Moderate*	*Severe*
Pharyngitis			1 (1%)					
Rhinorrhoea		1 (1%)						
Rhonchi						1 (1%)		
Throat tightness						1 (1%)		
Skin and subcutaneous tissue disorders	6 (6%)				5 (7%)			
Severity:	*Unknown*	*Mild*	*Moderate*	*Severe*	*Unknown*	*Mild*	*Moderate*	*Severe*
Pruritus		1 (1%)				2 (3%)		
Rash NOS		3 (3%)	2 (2%)			3 (4%)		
Vascular disorders	2 (2%)				3 (4%)			
Severity:	*Unknown*	*Mild*	*Moderate*	*Severe*	*Unknown*	*Mild*	*Moderate*	*Severe*
Flushing		1 (1%)	1 (1%)			2 (3%)	1 (1%)	

Adverse events summarized by the Rocky Mountain Poison and Drug Center from 76 published articles in which I.V. acetylcysteine was administered (acetaminophen overdose and other published uses) are listed with an incidence greater than 1% in Table 2. Charcoal, naloxone, and benzodiazepines were administered concomitantly in several of these studies.

Table 2 Adverse Events greater than 1% by Body System: Published Clinical Studies, Acetaminophen Overdose and Other Published Uses

Body System Classification	Adverse Event Occurrences	Distribution of All Adverse Events (%)	% Frequency in Patients with Safety Monitoring (N = 2040)
Body as a Whole & Combinations			
Urticaria	34	7.96	1.67
Vasodilatation and rash	30	7.03	1.47
Vasodilatation, rash, and pruritus	42	9.84	2.06
Cardiovascular System			
Hypotension	16	3.75	0.78
Syncope	13	3.04	0.64
Vasodilatation	28	6.56	1.37
Digestive System			
Dyspepsia	5	1.17	0.24
Nausea	43	10.07	2.11
Vomiting	15	3.51	0.74
Nervous System			
Abnormal thinking (Dysphoria)	8	1.87	0.39
Gait disturbances	5	1.17	0.24
Respiratory System			
Bronchospasm	25	5.85	1.23
Coughing	18	4.22	0.88
Dyspnea	11	2.58	0.54
Skin & Appendages			
Angioedema	33	7.73	1.62
Facial erythema	5	1.17	0.24
Palmar erythema	6	1.41	0.29
Pruritus	5	1.17	0.24
Pruritus and rash	7	1.64	0.34
Rash	21	4.92	1.03
Sweating	6	1.41	0.29
Special Senses			
Pain – Eye	11	2.58	0.54

Data on file: Systematic Analysis of Medical Literature Regarding Safety of I.V. N-acetylcysteine, Rocky Mountain Poison & Drug Center, Denver Health; 27 December 2001.

OVERDOSAGE

Single intravenous doses of acetylcysteine at 1000 mg/kg in mice, 2445 mg/kg in rats, 1500 mg/kg in guinea pigs, 1200 mg/kg in rabbits and 500 mg/kg in dogs were lethal. Symptoms of acute toxicity were ataxia, hypoactivity, labored respiration, cyanosis, loss of righting reflex and convulsions.

DOSAGE AND ADMINISTRATION

On admission for suspected acetaminophen overdose, a serum blood sample should be drawn at least 4 hours after ingestion to determine the acetaminophen level and will serve as a basis for determining the need for treatment with acetylcysteine. If the patient presents after 4 hours post-ingestion, the serum acetaminophen sample should be determined immediately.

Acetadote should be administered within 8 hours from acetaminophen ingestion for maximal protection against hepatic injury for patients whose serum acetaminophen levels fall above the "possible" toxicity line on the Rumack-Matthew nomogram (line connecting 150 mcg/mL at 4 hours with 50 mcg/mL at 12 hours; see **Acetaminophen Assays – Interpretation and Methodology** section). If the time of ingestion is unknown, or the serum acetaminophen level is not available, cannot be interpreted, or is not available within the 8 hour time interval from acetaminophen ingestion, Acetadote should be administered immediately if 24 hours or less have elapsed from the reported time of ingestion of an overdose of acetaminophen, regardless of the quantity reported to have been ingested.

The aspartate aminotransferase (AST, SGOT), alanine aminotranferase (ALT, SGPT), bilirubin, prothrombin time, creatinine, blood urea nitrogen (BUN), blood glucose, and electrolytes also should be determined in order to monitor hepatic and renal function and electrolyte and fluid balance.

NOTE: The critical ingestion-treatment interval for maximal protection against severe hepatic injury is between 0 – 8 hours. Efficacy diminishes progressively after 8 hours and treatment initiation between 15 and 24 hours post ingestion of acetaminophen yields limited efficacy. However, it does not appear to worsen the condition of patients and it should not be withheld, since the reported time of ingestion may not be correct.

The following procedures are recommended for I.V. administration**:**

Adults
Loading Dose: 150 mg/kg in 200 mL of 5% dextrose, infuse intravenously over 15 minutes.
Maintenance Dose: 50 mg/kg in 500 mL of 5% dextrose, infuse intravenously over 4 hours followed by 100 mg/kg in 1000 mL of 5% dextrose, infuse intravenously over 16 hours.

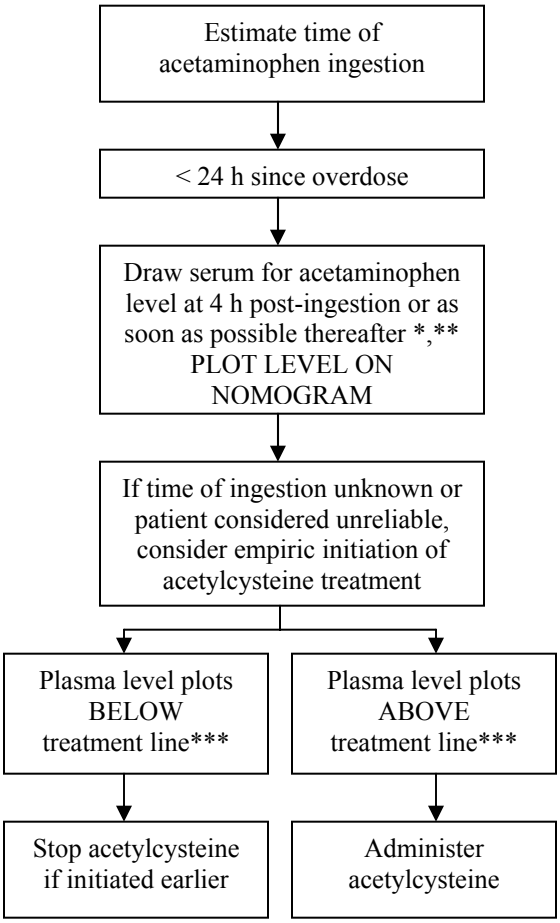
The total volume administered should be adjusted for patients less than 40 kg and for those requiring fluid restriction. To avoid fluid overload, the volume of 5% dextrose should be reduced proportionately as needed (See PRECAUTIONS).

Single-dose vial, preservative-free, discard unused portion. If vial was previously opened, do not use for I.V. administration.

Stability

1. Stability studies indicate that the reconstituted solution is stable for 24 hours at controlled room temperature.
2. Acetadote is not compatible with rubber and metals, particularly iron, copper and nickel.

Figure 1 Acetadote Treatment Flowchart



*Acetaminophen levels drawn less than 4 hours post-ingestion may be misleading.
**With the extended-release preparation, an acetaminophen level drawn less than 8 hours post-ingestion may be misleading. Draw a second level at 4 to 6 hours after the initial level. If either falls above the toxicity line, acetylcysteine treatment should be initiated.
***Acetylcysteine may be withheld until acetaminophen assay results are available as long as initiation of treatment is not delayed beyond 8 hours post-ingestion. If more than 8 hours post-ingestion, start acetylcysteine treatment immediately.

Renal Impairment

No data are available to determine if a dose adjustment in patients with moderate or severe renal impairment is required.

Hepatic Impairment

Although there was a threefold increase in acetylcysteine plasma concentrations in patients with hepatic cirrhosis, no data are available to determine if a dose adjustment in these patients is required. The published medical literature does not indicate that the dose of acetylcysteine in patients with hepatic impairment should be reduced.

Preparation of Acetadote (Acetylcysteine) for Intravenous Administration

Intravenous administration requires dilution with 5% dextrose (see **Dosage and Administration**).

Adults
Loading Dose: Dilute 150 mg/kg in 200 mL of 5% dextrose. First Maintenance Dose: 50 mg/kg in 500 mL of 5% dextrose. Second Maintenance Dose: 100 mg/kg in 1000 mL of 5% dextrose.

The total volume administered should be adjusted for patients less than 40 kg and for those requiring fluid restriction. To avoid fluid overload, the volume of 5% dextrose should be reduced proportionately as needed (See PRECAUTIONS).

Do not use previously opened vials for I.V. administration.

DOSAGE GUIDE AND PREPARATION

Table 3. Dosage Guide in Relation to Body Weight: Adult Patients

Body Weight		FIRST 150 mg/kg in 200 mL 5% Dextrose in 15 min	SECOND 50 mg/kg in 500mL 5% Dextrose in 4 hours	THIRD 100 mg/kg in 1000mL 5% Dextrose in 16 hours
(kg)	(lb)			
		Acetadote (mL)	Acetadote (mL)	Acetadote (mL)
100	220	75	25	50
90	198	67.5	22.5	45
80	176	60	20	40
70	154	52.5	17.5	35
60	132	45	15	30
50	110	37.5	12.5	25
40	88	30	10	20

ACETAMINOPHEN ASSAYS-INTERPRETATION AND METHODOLOGY

The acute ingestion of acetaminophen in quantities of 150 mg/kg or greater may result in hepatic toxicity. However, the reported history of the quantity of a drug ingested as an overdose is often inaccurate and is not a reliable guide to therapy of the overdose. **THEREFORE, PLASMA OR SERUM ACETAMINOPHEN CONCENTRATIONS, DETERMINED AS EARLY AS POSSIBLE, BUT NO SOONER THAN FOUR HOURS FOLLOWING AN ACUTE OVERDOSE, ARE ESSENTIAL IN ASSESSING THE POTENTIAL RISK OF HEPATOTOXICITY. IF AN ASSAY FOR ACETAMINOPHEN CANNOT BE OBTAINED, IT IS NECESSARY TO ASSUME THAT THE OVERDOSE IS POTENTIALLY TOXIC.**

Interpretation of Acetaminophen Assays

1. When results of the plasma acetaminophen assay are available, refer to the nomogram below to determine if plasma concentration is in the potentially toxic range. Values above the line connecting 200 mcg/mL at 4 hours with 50 mcg/mL at 12 hours (probable line) are associated with a probability of hepatic toxicity if an antidote is not administered.
2. If the predetoxification plasma level is above the line connecting 150 mcg/mL at 4 hours with 37.5 mcg/mL at 12 hours (possible line), continue with maintenance doses of acetylcysteine. It is better to err on the safe side and thus this line, defining possible toxicity, is plotted 25% below the line defining probable toxicity.
3. If the predetoxification plasma level is below the line connecting 150 mcg/mL at 4 hours with 37.5 mcg/mL at 12 hours (possible line), there is minimal risk of hepatic toxicity, and acetylcysteine treatment may be discontinued.

ESTIMATING POTENTIAL FOR HEPATOTOXICITY: The following depiction of the Rumack-Matthew nomogram (Figure 2) has been developed to estimate the probability that plasma levels in relation to intervals post ingestion will result in hepatotoxicity.

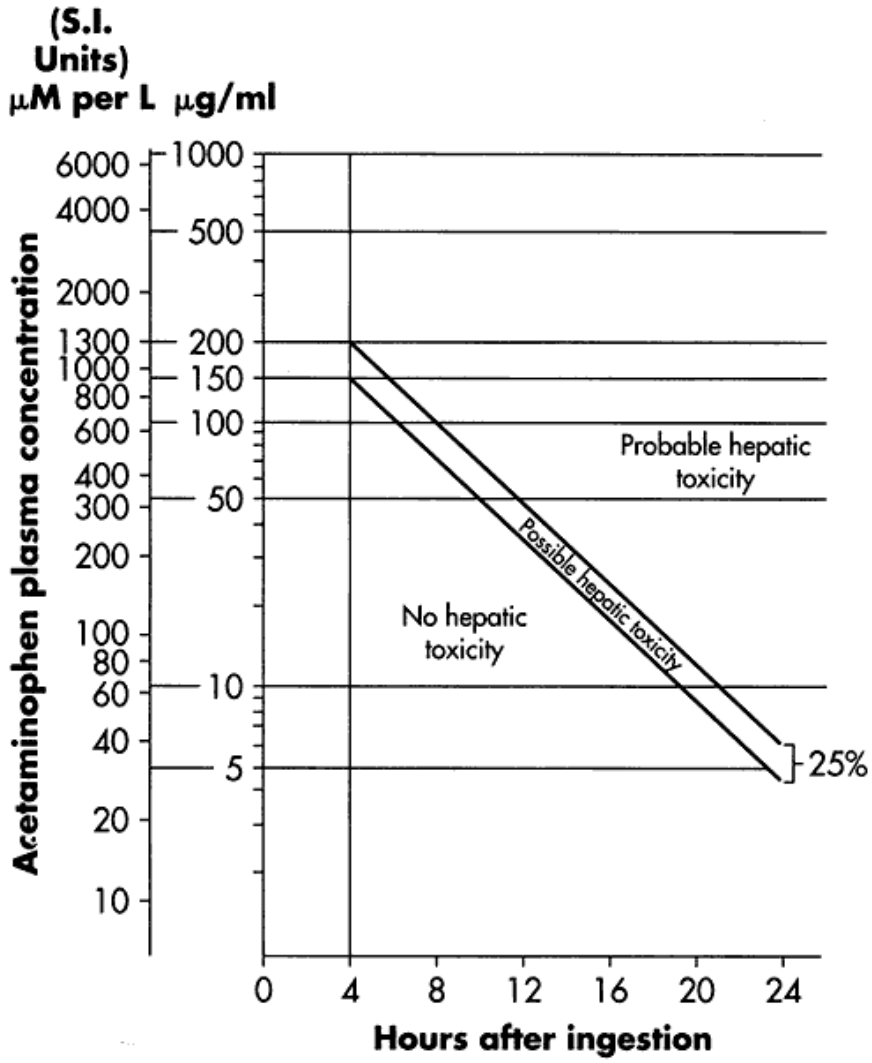


Figure 2 Rumack-Matthew Nomogram[19]: Plasma or Serum Acetaminophen Concentration vs. Time Post Acetaminophen Ingestion

Acetaminophen Assay Methodology

Suitable assay procedures for measuring acetaminophen levels in plasma are listed below. These methods detect only parent acetaminophen and not conjugated acetaminophen.

Selected Techniques (noninclusive)

HPLC:

Blair D and Rumack BH. *Clin Chem* 1977;23(4):743-5.

Howie D, Andriaenssens PI, and Prescott LF. *J Pharm Pharmacol*, 1977;29(4):235-7.

GC:

Prescott LF. *J Pharm Pharmacol*, 1971;23(10):807-8.

Colorimetric:

Glynn JP and Kendal SE. *Lancet*, 1975;1(May 17):1147-8.

HOW SUPPLIED

Acetadote (acetylcysteine) Injection is available as a 20% solution in 30 mL (200mg/mL) single dose glass vials. Acetadote is sterile and can be used for I.V. administration. It is available as follows:

NDC 66220-107-30 30 mL vials, carton of 4

Store unopened vials at controlled room temperature, 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

Manufactured for:
Cumberland Pharmaceuticals Inc.
Nashville, TN 37203