Acetylcysteine (NAC)

Brand names	Acetadote, generic
Medication error potential	Look-alike, sound-alike drug names. Acetylcysteine (NAC) may be confused with acetylcholine. Mucomyst may be confused with Mucinex.[1]
Contraindications and warnings	**Contraindications:** Hypersensitivity (i.e., anaphylactoid reaction) to acetylcysteine or any component of the formulation.[2] **Warnings:** Caution in patients with asthma or history of bronchospasm. Acute flushing and erythema can occur 30–60 minutes after initiation of the infusion, often with spontaneous resolution despite continued infusion.[2] Total volume administered should be adjusted for patients <40 kg and for those requiring fluid restriction.[2]
Infusion-related cautions	Anaphylactoid reactions and death have been reported.[2] (See the Comments section.)
Dosage	*Contact a poison center at 1-800-222-1222 to obtain information about the clinical management of acetaminophen overdoses.* **Acetaminophen overdose:** Refer to Monitoring in the Comments section. **21-hour, 3-dose regimen:** Infuse loading dose of 150 mg/kg over 60 minutes, followed by 50 mg/kg over 4 hours, then 100 mg/kg over 16 hours (for a full course consisting of 300 mg/kg administered IV over 21 hours).[2] One report suggests that standard acetaminophen overdose protocols may *not* be adequate in cases of massive acetaminophen ingestion.[3] **Modified dosing regimens:** Several studies have reported alternative NAC dosing regimens. Each reported a loading dose of 150 mg/kg administered over 60 minutes followed by a continuous infusion of 10 mg/kg/hr for 20 hours,[5] 14 mg/kg/hr for 20 hours,[4] or 15 mg/kg/hr.[28] In some studies, ½ NS was added to prevent hyponatremia, which has been reported with standard IV dosing.[5,6] **Advanced cerebral adrenoleukodystrophy:** Administration of NAC (140 mg/kg/day IV followed by 70 mg/kg *orally* 4 times a day) before (54–67 days) and after (114–250 days) hematopoietic stem cell transplant was noted to protect from fulminant demyelination in three children.[7] If mucositis developed after transplant the patient was given 70 mg/kg IV four times a day.[7] **Prevention of acute renal failure associated with nephrotoxic agents:** *Adult* studies have reported that both oral[8,9] and IV[9,29] NAC, in addition to appropriate hydration, can prevent renal dysfunction induced by radiographic contrast agents, but there are no pediatric studies with dosing recommendations. One study reported two cases in which NAC attenuated ifosfamide-induced acute renal failure. One patient received IV NAC (loading dose of 150 mg/kg over 60 minutes, followed by 50 mg/kg over 4 hours, then 100 mg/kg over 16 hours on days 1 and 2), and the other was given several days of oral NAC (600 mg BID).[10] **Prevention of acute kidney injury after cardiopulmonary bypass:** Several *adult* studies have reported no difference in prevention of acute kidney injury after cardiopulmonary bypass in patients receiving NAC compared to those receiving placebo.[11-15] One pediatric study including 21 neonates reported an improvement in urine output, time to negative fluid balance, and attenuation of rise in SCr after an IV bolus of NAC (100 mg/kg in D5W) followed by an infusion of NAC (10 mg/kg/hr) for 24 hours after separation from cardiopulmonary bypass.[16] **Prevention of bronchopulmonary dysplasia (BPD):** When compared to placebo, there was no difference in the development of BPD or death in 194 infants (500–999 g) who received a 6-day continuous infusion of NAC (16–32 mg/kg/day beginning within 36 hours of birth).[17]

Dosage *(cont.)*

Nonacetaminophen-induced hepatic disease: NAC reduced liver biochemistries and serum ferritin in three children with TPN (total parenteral nutrition)-associated liver disease. Each was begun on estimated maintenance requirements of cysteine (20–50 mg/kg/day of NAC). The NAC dose was increased by 10 mg/kg/day q 1–2 mo to maximum doses of 70, 120, and 135 mg/kg/day. Doses were infused over 12 hours and continued for 3–18 months. The improvements in liver function occurred with larger NAC dosages.[18] A prospective, randomized study of children and *adults* (1–64 years of age) with early liver toxicity due to allogenic hematopoietic stem cell transplantation reported that the introduction of NAC at the first sign of liver toxicity did not prevent progression of liver disease.[19] A retrospective review including 170 children with nonacetaminophen-induced acute liver failure compared standard of care (n = 59) and standard of care plus NAC (n = 111). NAC was given as a continuous infusion of 100 mg/kg/day until INR was <1.4, death, or liver transplantation. NAC was safe and associated with shorter length of hospital stay, higher incidence of native liver recovery without transplantation, and better survival after transplantation compared to the historical standard of care.[20] These findings are consistent with the *adult* literature.[21]

Dosage adjustment in organ dysfunction

Despite a threefold increase in NAC plasma concentrations in patients with hepatic cirrhosis, there are no recommendations for reduction of NAC dosing in patients with hepatic impairment.[2] No data are available to determine if dosage adjustment is needed for moderate or severe renal impairment.[2] Some suggest a 25% reduction in maintenance dose when the CrCl is <10 mL/min.[22]

Maximum dosage

Cumulative dose of 300 mg/kg per treatment course.[2] No adverse effects were noted following a mean rate of 4.2 mg/kg/hr for 24 hours in 10 preterm infants (gestational age: 25–31 weeks; weight: 500–1380 g) or following infusion of 0.1–1.3 mg/kg/hr for 6 days in six neonates (gestational age: 26–30 weeks; weight: 520–1335 g).[23] Also, in a study including 194 infants (weight: 500–999 g) receiving NAC at a constant infusion rate of 16–32 mg/kg/day for 6 days, no adverse effects associated with NAC were observed.[17]

Additives

Disodium edetate and sodium hydroxide[2]

Suitable diluents

D5W, ½NS, and SW.[2] Incompatible when administrated via Y-site with cefepime hydrochloride and ceftazidime.

Maximum concentration

Must be diluted prior to administration as Acetadote is hyperosmolar (2600 mOsmol/L).[2] Up to 50 mg/mL for loading dose and 10 mg/mL for maintenance dose. Adjust total volume as needed for patients' weight and those requiring fluid restriction.[2]

Weight (kg)	Loading Dose (150 mg/kg over 60 minutes)		2nd Dose (50 mg/kg over 4 hours)		3rd Dose (100 mg/kg over 16 hours)	
	Acetadote (mL)*	Diluent (mL)	Acetadote (mL)	Diluent (mL)	Acetadote (mL)	Diluent (mL)
10	7.5	30	2.5	70	5	140
15	11.25	45	3.75	105	7.5	210
20	15	60	5	140	10	280
25	18.75	100	6.25	250	12.5	500
30	22.5	100	7.5	250	15	500
40	30	200	10	500	20	1000
50	37.5		12.5		25	
60	45		15		30	
70	52.5		17.5		35	
80	60		20		40	
90	67.5		22.5		45	
100	75		25		50	

*200 mg/mL concentration