Wisconsin Poison Center
Serving people of all ages.
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Wisconsin Poison Center Recommendations for Dosing of N-acetylcysteine

The Wisconsin Poison Center (WPC) recently updated recommendations for IV N-acetylcysteine (NAC) dosing in the setting of known or potential acetaminophen overdose. Current FDA-approved dosing for Acetadote® is based upon a regimen proposed in the UK nearly 40 years ago. This regimen involves the preparation of three different IV bags run at different infusion rates and has never been optimized or formally validated. In recent years, it's become apparent that this regimen provides inadequate NAC for treating at least some patients.[1-5]

Errors in NAC dosing are common and are consequential.[7,8] A British study found that use of the FDA-approved dosing regimen for IV Acetadote® resulted in a compounding dosing error of at least 20% in 1/3 of patients treated and 8% of treatments led to a dosing error greater than 50%. A subsequent, independent study confirmed IV NAC dosing errors in 1/3 of patients. Others centers are reporting similar experience.

Because the oral route and dosing delivers antidote directly to the liver, is substantially less expensive and has a better safety profile, this remains the preferred route and regimen, whenever feasible. If a patient is unable to tolerate oral dosing and needs IV NAC, a substantially lower dose would be delivered to the liver. This is simply not enough drug for some patients, and most sources agree that the lowest dose of the FDA-approved regimen is inadequate for some patients / situations. A simplified method of IV NAC preparation is warranted.

When dosing of NAC is indicated and required, the WPC recommends that only one oral or one IV dosing regimen be prepared and utilized:

Product	Route	Current Regimens	Comments
PO NAC (e.g. Mucomyst)	Oral	140 mg/kg load 70 mg/kg every 4 hours	Provides 490 mg/kg in first 24 hours
IV NAC (e.g. Acetadote®)	IV	150 mg/kg load 12.5 mg/kg/hr x 20 hours or more	Provides 400 mg/kg in first 21 hours

NAC solutions are compatible with and can be prepared in DsW, 0.45 NS or 0.9 NS. Because of concern for volume overload and possible hyponatremia, the volume (i.e., concentration) must be adjusted in patients who weigh less than 40 kg. The best current evidence suggests that, because of its poor lipid solubility, continued escalation of dose is not needed in obese patients whose weight exceeds 100 kg, so the loading IV dose need not exceed 15,000 mg and the IV infusion need not exceed 1,250 mg/hr in most cases. Doses may need to be adjusted during hemodialysis or other extracorporeal processes.

As always, the Wisconsin Poison Center is available 24 hours a day to assist you in caring for these patients. Thank you for your interest and for supporting your poison center.

1. Chiew A, et al. Massive paracetamol overdose: an observation study of the effect of activated charcoal and increased acetylcysteine dose (ATOM-2). *Clin Toxicol.* 2017:1-11.

2. Gummin D, et al. A Liver's Rise and Fall with Changes in NAC Dosing. *C/in Toxico/.* 2016;54(8):754.

3. Bateman N, et al. New regimens for intravenous acetylcysteine, where are we now? *Clin Toxico/.* 2015;54(2): 1-4.

4. Chiew A, et al. Evidence for the changing regimens of acetylcysteine. *Br J Clin Pharmacol.* 2015;53(3):471-481.

5. Waring WS. Novel acetylcysteine regimens for the treatment of paracetamol overdose. *Ther Adv Drug Sat.* 2012;3(6):305-315.

6. Rumack B, Bateman ON. Acetaminophen and acetylcysteine dose and duration: Past, present and future. *Clin Toxicol.* 2012;50(2):91-98.

7. Hayes BO, Klein-Schwartz W, Doyon S. Frequency of Medication Errors with Intravenous Acetylcysteine for Acetaminophen Overdose. *Ann Pharmacother* 2008;42:766-70.

8. Ferner RE, et al. Random and systematic medication errors in routine clinical practice: a multicenter study of infusions, using acetylcysteine as an example. *Br J Clin Pharmacol.* 2001;52:573-577.