

Simplify IV N-Acetylcysteine for Acetaminophen Overdoses

Recent FDA approval for 2-step IV dosing is opening a bag of questions around using **N-acetylcysteine (NAC) for acetaminophen overdose**.

Acetaminophen poisonings are common. Poison control centers handled over 80,000 US cases in 2023.

NAC is the antidote...and has been used for decades. It deactivates a toxic acetaminophen metabolite that can cause deadly liver failure.

Many dosing strategies exist. NAC is classically given IV as a 3-bag regimen over 21 hours. But FDA approved an alternative 2-bag approach in late 2024...which many hospitals have used off-label for years.

Know how common NAC regimens compare. The original FDA-approved 3-bag regimen is given as 150 mg/kg infused over 1 hour...then 50 mg/kg over 4 hours...followed by 100 mg/kg over 16 hours.

On the other hand, the simpler 2-bag option is given as 200 mg/kg over 4 hours...then 100 mg/kg over 16 hours.

Be aware that the 2-bag approach has less side effects (itching, flushing, etc)...and similar liver protection. It also conserves IV fluids...and reduces mix-ups and delays.

But the 3-bag option may still be needed in some cases to give more NAC up front...such as when the acetaminophen overdose is very large.

In general, also expect to see the 3-bag option for patients who weigh 40 kg or less. The 2-bag labeling only applies to 41 kg and up.

Help prevent NAC errors. Address confusion between injectable and inhaled NAC products.

Both come in look-alike vials and 200 mg/mL strengths. NAC injection can be given orally...but NAC for nebulization CANNOT be used IV. Separate stock and use barcode scanning technology, if available.

Double-check diluents for either IV regimen. NAC can be diluted in 5% dextrose...1/2 normal saline...or sterile water.

And watch diluent volumes carefully. Too much volume can cause fluid overload...especially in kids. For example, patients under 40 kg generally need 500 mL bag sizes or smaller.

Advocate that bag labels state the regimen including the total dose...“N-acetylcysteine (2-bag regimen; 300 mg/kg)”...and bag order (“Bag 1,” etc).

Use this label info to prioritize prepping initial NAC bags ASAP. Patients have better liver protection the sooner NAC is started.

Read about other important antidotes in our chart, Drugs for Selected Medication Overdoses and Poisonings.

Key References:

- Gummin DD, Mowry JB, Beuhler MC, et al. 2023 Annual Report of the National Poison Data System (NPDS) from America's Poison Centers: 41st Annual Report. Clin Toxicol (Phila). 2024 Dec 17:1-35.
- Dart RC, Mullins ME, Matoushek T, et al. Management of Acetaminophen Poisoning in the US and Canada: A Consensus Statement. JAMA Netw Open. 2023 Aug 1;6(8):e2327739. Erratum in: JAMA Netw Open. 2023 Sep 5;6(9):e2337926.
- Cole JB, Oakland CL, Lee SC, et al. Is Two Better Than Three? A Systematic Review of Two-bag Intravenous

Cite this document as follows: Article, Simplify IV N-Acetylcysteine for Acetaminophen Overdoses, Hospital Pharmacy Technician's Letter, February 2025

The content of this article is provided for educational and informational purposes only, and is not a substitute for the advice, opinion or diagnosis of a trained medical professional. If your organization is interested in an enterprise subscription, email sales@trchealthcare.com.

© 2025 Therapeutic Research Center (TRC). TRC and Hospital Pharmacy Technician's Letter and the associated logo(s) are trademarks of Therapeutic Research Center. All Rights Reserved.

N-acetylcysteine Regimens for Acetaminophen Poisoning. West J Emerg Med. 2023 Nov;24(6):1131-1145.
-ISMP Canada. When the Antidote Causes Harm: Preventing Errors with Intravenous Acetylcysteine. Aug 24, 2023. <https://ismpcanada.ca/wp-content/uploads/ISMPCSB2023-i7-Acetylcysteine.pdf> (Accessed December 26, 2024).

Hospital Pharmacy Technician's Letter. February 2025, No. 410233

Cite this document as follows: Article, Simplify IV N-Acetylcysteine for Acetaminophen Overdoses, Hospital Pharmacy Technician's Letter, February 2025

The content of this article is provided for educational and informational purposes only, and is not a substitute for the advice, opinion or diagnosis of a trained medical professional. If your organization is interested in an enterprise subscription, email sales@trchealthcare.com.

© 2025 Therapeutic Research Center (TRC). TRC and Hospital Pharmacy Technician's Letter and the associated logo(s) are trademarks of Therapeutic Research Center. All Rights Reserved.