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IV Form of NAC Receives FDA sNDA to Prevent, Lessen Liver Injury After Ingesting Toxic Quantities of Acetaminophen

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Key Takeaways

- The FDA approved a simplified NAC dosing regimen to present liver injury from acetaminophen overdose, enhancing patient outcome and reducing adverse events.
- Acetaminophen is a leading cause of acute liver failure in the US, with thousands affected annually by overdose.

Two Studies found a 2-bag regime of N-acetylcysteine (NAC) resulted in fewer and shorter delays in treatment as well as decreases in cutaneous non-allergic anaphylactoid reactions

The FDA approved a supplemental new drug application (sNDA) for the injectable N-acetylcysteine (NAC, Acetadote; Cumberland Pharmaceuticals), an intravenous (IV) formulation to prevent or lessen liver injury following the ingestion of potentially toxic

quantities of the OTC pain reliever and fever reducer acetaminophen.

According to experts, acetaminophen is the leading cause of acute liver failure in the US. Every year, thousands of US individuals experience accidental or intentional acetaminophen poisoning, which can lead to serious liver damage.

The new dosing regimen of NAC simplifies the administration by combining the first 2 bags of the standard regimen into a slower single infusion. This new approach, according to the experts, has been implemented in hospitals and demonstrated the ability to reduce the frequency of medication errors as well as potentially serious non-allergic anaphylactoid reactions (NAARs) while not compromising the efficacy of NAC. The simplification of this new NAC dosing regimen allows health care professionals to administer the life-saving treatment more efficiently and potentially improve patient outcomes.

"This FDA [sNDA] approval is a significant step forward in the treatment of acetaminophen overdose," said Rick Dart, MD, PhD, director at the Rocky Mountain Poison and Drug Center, in a news release. "By streamlining the administration of NAC, we can improve patient outcomes and reduce the risk of adverse events (AEs). This simplified dosing regimen is a valuable tool for health care providers in managing this potentially life-threatening condition."

Findings of a 2022 retrospective cohort study published in *Clinical Toxicology* (Philadelphia) demonstrated that a 2- day regimen of IV NAC was associated with significantly fewer and shorter delays when treating patients for acetaminophen (referred to as paracetamol in the study) overdose. Patients who were treated with a 3-bag regimen 1rom October 2009 to October 2013 In= 271) were compared to patients treated with a 2.-bag regimen 1rom

February 2.014 to May 2020 (n = 598). The start times of each in1usion were sourced from medical records, and delay-.; were calculated by comparing the actual infusion times against prescribed times. Additionally, evidence of AEs, including gastrointestinal reactions as well as cutaneous and systemic NAARs - were also recorded.

In addition to finding that the 2-bag method resulted in less and much shorter delays (median delay: 35 minutes [IQR 15, 70] vs 65 minutes (IQR: 40, 105), P <: .01), delays longer than an hour were found to be less frequent (2-bag: 31%, 3-bag: 51%; P< .01). NAARs were also observed to be associated with significantly longer delays in both cohorts but were more frequent in the 3-bag cohort.

Further, a similar retrospective cohort study published in Annals of Pharmacotherapy3 compared 3-bag with 2-bag NAC regimens for acetaminophen toxicity in pediatric patients, with the primary outcome being incidence of NAARs and secondary outcomes being rates of medication errors (MEs) and relevant hospital outcomes, such as length of stay {LOS), intensive care unit {ICU) admission, liver transplant, and death."

A total of 243 patients with a median age of 15 years were enrolled, of which 62% (n = 150) received the 3-bag NAC regimen and the remaining 38% (n = 93) the 2-bag NAC. Although there was no difference observed in overall NAARs (2-bag: 2%, n = 2; 3-bag: 10%, n = 15), there were fewer cutaneous NAARs in the 2-bag group. MEs were also found 10 be significantly decreased with the 2-bag regimen {2-bag: 23%, n = 21; 3-bag: 39%, n = 59), and there were no statistical differences observed in LOS, ICU admissions, transplant, or death.

"We are thrilled to announce the FDA [sNDA] approval to this simplified dosing regimen tor [NAC]." said A.J

Kazimi, CEO of Cumberland Pharmaceuticals, in the news release. "This important milestone underscores our commitment to improving patient care and providing innovative solutions for urgent medical needs. By streamlining the administration process, we aim to enhance patient outcomes and reduce the burden on health care providers."