

Acetylcysteine (intravenous) (Acetadote®)

Acetaminophen is a commonly used analgesic and antipyretic. Acetaminophen toxicity may occur acutely when supratherapeutic amounts are ingested purposefully or unintentionally, or chronically when supratherapeutic amounts are ingested over an extended period of time. Liver failure, including coagulopathy and hepatic encephalopathy, and kidney failure may occur in severe toxicity. However, if treated early, patients with acetaminophen poisoning generally recover uneventfully.

Mechanism/Indications: Acetaminophen is metabolized to a toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI), that is detoxified by conjugation with glutathione. In overdose, hepatic stores of glutathione are depleted and NAPQI binding to hepatocytes induces cell death and hepatic necrosis. Acetylcysteine replenishes hepatic glutathione and may also act as a glutathione substitute, combining directly with the toxic metabolite. Additionally, acetylcysteine acts as a free radical scavenger, reducing the cytotoxic effect of NAPQI. Intravenous acetylcysteine is indicated in adults and children who present with a history of acetaminophen overdose within the past 8-10 hours, patients unable to tolerate oral acetylcysteine, and patients who present with evidence of fulminant hepatic failure.

Adverse Effects/Contraindications: Caution should be used in patients who have experienced previous hypersensitivity or anaphylactoid reactions with IV acetylcysteine, as well as in patients with asthma. The most common anaphylactoid reactions include rash, flushing, and bronchospasm.

Dosing: Adults and children should receive 150 mg/kg administered over 60 minutes, followed by 50 mg/kg administered over 4 hours, followed by 100 mg/kg administered 16 hours. The total dose is 300 mg/kg delivered over 21 hours. AST/ALT, INR, and acetaminophen level should be checked before discontinuing the IV acetylcysteine after 21 hours, because longer infusions may be necessary in some patients based on these and other criteria. Dilution volume should be reduced in patients weighing < 40 kg in order to avoid complications of fluid overload. Please call the Maryland Poison Center for specific dosing information for adults and pediatrics.

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For more on oral acetylcysteine:

- Howland MA, Hendrickson RG. *Antidotes in Depth: N-Acetylcysteine*. In: Flomenbaum NE, Goldfrank LR, Hoffman RS et al, eds: *Goldfrank's Toxicologic Emergencies*. New York NY, 2011;500-507.
- Doyon S, Klein-Schwartz W. *Hepatotoxicity despite early administration of intravenous N-acetylcysteine for acute acetaminophen overdose*. *Acad Emerg Med* 2009; 16(1): 34-39.
- Klein-Schwartz W, Doyon S. *Intravenous acetylcysteine for the treatment of acetaminophen overdose*. *Expert Opin Pharmacother* 2011; 12(1): 119-30.
- Yarema MC, Johnson DW, Berlin RJ, et al. *Comparison of the 20-hour intravenous and 72-hour oral acetylcysteine protocols for the treatment of acetaminophen poisoning*. *Ann Emerg Med* 2009; 54(4): 606-614.