



Fomepizole for Acetaminophen Toxicity

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Background:

Fomepizole (4MP) is a Health Canada approved antidote for methanol and ethylene glycol toxicity. Recent studies have suggested that fomepizole may be considered for off-label use as an adjunct treatment for severe acetaminophen toxicity **in addition to** standard treatment with N-acetylcysteine.

Preclinical studies have suggested that fomepizole may have a role in mitigating acetaminophen toxicity through two mechanisms:

1. Inhibition of the enzyme (CYP 2E1) that metabolizes acetaminophen to the toxic metabolite (NAPQI)
2. Inhibition of activation of a protein (JNK) in the pathway of mitochondrial cell death

Adverse effects associated with fomepizole administration are minor and are rarely reported. These include headache, nausea, and burning at the infusion site.

Dosing of Fomepizole in Acetaminophen Toxicity

If on-call toxicologist recommends fomepizole to treat a patient with acetaminophen toxicity, dosing should be as follows:

1. 15 mg/kg (maximum 1.5 g) in 100mL of D5W or NS infused intravenously over 30 minutes

followed 12 hours later by

2. 10 mg/kg (maximum 1.5 g) in 100mL of D5W or NS infused intravenously over 30 minutes (i.e. total of 2 doses, then stop)

If the patient is receiving **intermittent hemodialysis**, and the patient has not received the two doses of fomepizole when dialysis was initiated, the fomepizole dosing interval should be increased to **10 mg/kg every 4 hours** for a total fomepizole treatment duration of 24 hours to account for clearance of fomepizole in the dialysate.

If the patient is receiving **continuous renal replacement therapy (CRRT) or similar**, and the patient has not received the two doses of fomepizole when dialysis was initiated, the fomepizole dosing interval should be increased to **10 mg/kg every 8 hours** for a total fomepizole treatment duration of 24 hours to account for clearance of fomepizole in the dialysate.

Note: Fomepizole is NOT a substitute for N-acetylcysteine treatment. N-acetylcysteine treatment should continue according to recommendations of the Poison Centre.

Fomepizole treatment in acetaminophen toxicity should be administered only in consultation with the Poison Centre. It does not constitute routine care of an acetaminophen poisoned patient.

References:

Archives of Toxicology (2022) 96:453–465 <https://doi.org/10.1007/s00204-021-03211-z>
Clinical Toxicology (2022) 60(4): 451–457 <https://doi.org/10.1080/15563650.2021.1980581>

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