

## Fomepizole for Acetaminophen Toxicity

### 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 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

When fomepizole is recommended, administer two doses as follows:

1. **15 mg/kg** (max 1.5 g) in 100 mL D5W or NS IV over 30 minutes
2. **10 mg/kg** (max 1.5 g) in 100 mL D5W or NS IV over 30 minutes, given 12 hours after dose 1

If dialysis is initiated before the patient has received two doses of fomepizole, increase the dosing frequency to account for fomepizole clearance in the dialysate:

- **Intermittent hemodialysis:** 10 mg/kg every 4 hours for 24 hours
- **CRRT (or equivalent):** 10 mg/kg every 8 hours for 24 hours

**NOTE:** Fomepizole is not a substitute for acetylcysteine and does not constitute routine care in acetaminophen poisoning. Acetylcysteine should continue per Poison Centre recommendations. Fomepizole should only be administered in consultation with the Poison Centre.

