

**Overdose can cause rapid onset of seizures, coma, and severe metabolic acidosis. Pyridoxine is the specific antidote.**

## Toxicity / Risk Assessment

*Isoniazid inhibits pyridoxine metabolism, preventing the conversion of glutamate to GABA. Reduction in central nervous system GABA leads to seizures.*

*Toxicity is dose dependent.*

*Onset of clinical effects is rapid (30 – 120 minutes).*

*>1.5 g (20mg/kg): severe toxicity possible*

## Clinical features:

- **CNS:** lethargy, blurred vision, slurred speech, ataxia, mydriasis, confusion, coma, seizures
- **GI:** nausea and vomiting
- **CVS:** tachycardia and hypotension (late)
- **Metabolic:** severe lactic acidosis
- **Other:** complications of prolonged seizures – hyperthermia, pulmonary aspiration, rhabdomyolysis, weak MAO inhibitor effects

*Isoniazid blood concentrations do not correlate with toxicity and are not routinely available.*

**Management** Discuss all cases with a clinical toxicologist.

Patients with coma or seizure activity should be treated with prompt intubation and ventilation.

## Decontamination:

Activated charcoal 50 g (1g/kg children) via NGT if intubated

## Antidote: (Pyridoxine)

Pyridoxine is the specific antidote (70mg/kg IV, maximum 5 grams) - *see separate pyridoxine guideline.*

**Indications:** seizures, coma, metabolic acidosis

## Seizures

Whilst pyridoxine is being sourced administer IV diazepam 5-10mg and repeat if seizures continue.

If refractory seizure activity despite treatment with pyridoxine and benzodiazepines – Propofol or phenobarbitone (20mg/kg [max. 2000 mg] IV over 20 minutes) are suitable second line treatments

**Enhanced elimination:** There is no role for extracorporeal elimination techniques unless pyridoxine is not available (or there is inadequate supply) and the patient has ongoing seizure activity refractory to the above treatments.

## Disposition:

Discharge pending mental health assessment if asymptomatic at 6 hours post-exposure.

All patients with neurotoxicity should be admitted to a HDU environment.