

**In large overdoses, VPA causes coma and multi-organ failure. Haemodialysis is indicated for life-threatening toxicity.**

## Toxicity / Risk Assessment

*Large overdoses may result in delayed onset of toxicity.*

*Patients may present asymptomatic. Peak serum*

*conc. may occur up to 16 hours post ingestion.*

*Toxicity may last days post massive overdose.*

Predicted toxicity by ingested dose:

< 200 mg/kg: mild sedation

200-1000 mg/kg: dose-dependent CNS depression

> 1000 mg/kg: coma likely requiring intubation, cerebral oedema, multi-organ failure and death

## Clinical features:

- CNS: ↓conscious state, ataxia, coma, seizures, cerebral oedema

- GI: nausea, vomiting, abdominal pain, hepatotoxicity, pancreatitis

- CVS: ↑HR, hypotension, ↑QT interval

- Metabolic: ↑ Na<sup>+</sup>, ↑ lactate, ↑ ammonia, ↓ Ca<sup>2+</sup>, ↓ glucose, metabolic acidosis

- Haematology: myelosuppression – leukopaenia and thrombocytopaenia

## Management

Supportive care with airway protection as required

## Decontamination:

**Activated charcoal 50 g** (Paediatric 1g/kg) within 4 hours of ingestion >200 mg/kg, OR at any time if the patient requires intubation (via NGT or orogastric tube). Consider **MDAC** if ingested >500 mg/kg (see below)

Consider **Whole Bowel Irrigation** if ingestion >1000 mg/kg, (*discuss with clinical toxicologist*)

Investigations - Check VPA serum concentration 4-6 hourly until decreasing

## Enhanced elimination

1. **MDAC** (see separate guideline) in cases >500 mg/kg requiring intubation (*discuss with clinical toxicologist*)

2. **Intermittent haemodialysis** is the preferred modality.

Indications: - Serum VPA concentration > 6000 µmol/L (850 mg/L) OR

- Severe toxicity including CVS instability/cerebral oedema/ metabolic acidosis pH <7.1

\*Endpoint: clinical improvement AND serum VPA concentration < 700 µmol/L (100 mg/L)

Carnitine (*Discuss with clinical toxicologist and see separate Carnitine guideline*)

- Consider carnitine in patients with any of the following:

*Severe metabolic acidosis (pH <7.1), NH<sub>3</sub> > 100 µmol/L, cerebral oedema, hepatotoxicity*

- Dose: 100 mg/kg IV loading dose (max 6 g) followed by 50 mg/kg IV 8 hourly (max 3 g per dose)

## Disposition:

>200 mg/kg: observe for at least 8 hours + decreasing VPA concentrations + VPA <3500 µmol/L (500 mg/L)

>500 mg/kg: observe for at least 12 hours + decreasing VPA concentrations + VPA <3500 µmol/L (500 mg/L)