

Clinical toxicity is characterised by adrenergic stimulation and delayed-onset seizures. Opioid toxidrome may also occur (Tapentadol > Tramadol).

Toxicity / Risk Assessment

	Opioid effects	Adrenergic effects	Serotonergic effects
Tramadol	++	+++	++
Tapentadol	+++	++	+

- Toxic dose is poorly defined. Patients who are more susceptible to toxicity: children, patients with a low seizure threshold (e.g., history of seizure disorder) or severe liver impairment
- Ingestion > 2g = significant risk of seizures

Clinical features: (delayed > 6 hours with SR preparations)

- **Seizures:** often delayed, may be >6 hours post-ingestion and up to 24 hours if slow-release preparation
- **Adrenergic effects** - Agitation and autonomic hyperactivity
- **Opioid effects:** CNS and respiratory depression. More common in tapentadol. Less prominent with tramadol unless exposure to high doses.
- **Serotonin toxicity:** is only expected with co-ingestion of other serotonergic agents or MAOI
- Nausea & vomiting are common
- Hypoglycaemia occurs rarely with tramadol

Management - Attention to ABC and termination of seizures are main priorities

Decontamination: Offer 50g activated charcoal in alert cooperative patients: -

- < 2 hours post ingestion of > 2 g immediate-release preparation
- < 4 hours post ingestion of > 2 g slow-release preparation

Seizures

Benzodiazepines: Diazepam 5 mg IV every 5 minutes as necessary

Naloxone: Seizures are NOT responsive to naloxone

Agitation & Autonomic hyperactivity

Benzodiazepines: Diazepam 2.5-5 mg IV 10 minutely or 5-10 mg PO 30 minutely until sedated

CNS and Respiratory Depression

- Naloxone:** place 400 mcg naloxone in 10 mL syringe and make up to 10 mL with N/saline (40 mcg per mL)
- Titrate IV every 60 seconds to response – 1 mL, 2 mL, 3 mL, 4 mL (40 mcg, 80 mcg, 120 mcg, 160 mcg)
 - Further increments of 200 mcg may be required up to a total dose of 2000 mcg (then consider other DDx)
 - Paediatric naloxone dose - bolus 10 mcg/kg up to 400 mcg, repeat as required

Disposition

- Observe for at least 12 hours if immediate release preparation
- Observe for at least 24 hours if slow-release preparation
- Do not discharge at night. Observe all patients until asymptomatic