

Overview

Potent SNRI with potentially life-threatening OD. Often causes seizures and, in large ingestions, cardiotoxicity.

Toxic mechanism

SNRI & NaBlockade actions.

Toxicokinetics

Well abs but extensive 1st pass metab. Peak 2-3hrs (or 6-8 if XR). Vd 5-7L/kg. Metabolised by liver CYP2D6 to active metabolite O-Desmethylvenlafaxine (ODV - peak 4-5h) and renally excreted. $T_{1/2}$ = 5h (15h XR)

Clinical features

Dysphoria, anxiety, mydriasis, sweating, tremor, clonus, ↑HR, ↑BP are common.

Generalised seizures may be delayed up to 18h with XR. Coma not a feature.

Serotonin toxicity is common & ↑risk of being severe if another serotonergic co-ingestant.

With large ingestions ↓BP & arrhythmias (↑QRS & occ ↑QTc) may occur. Case reports suggest the possibility of tako-tsubo cardiomyopathy may occasionally occur.

Investigations

Screening: serial ECGs (freq dependent on size of OD), paracetamol, BSL

Other: CK if serotonin toxicity

Risk assessment

Dose	Effect
<1.5g	5% risk of seizures
1.5-3.0g	10% risk of seizures
3.1-4.5g	>30% risk of seizures
4.6-7g	~100% risk of seizures. Risk of ↓BP, ↑QRS & ↑QTc
>7g	Hypotension & arrhythmias

About 15% have seizures overall.

If serotonergic co-ingestant → risk of significant serotonin toxicity even with small ODs.

For children <30mg/kg is safe.

Management

Resus: Early intubation indicated if large OD (>7g) suspected.

Supportive Care:

- Treat agitation early & seizures (prophylactically & actively) with BDZs
- Treat NaBlockade with **bicarbonate**
- Seek & treat ↑↑T, serotonin toxicity (up to & incl intubation, paralysis & active cooling.)

Decontamination: Activated charcoal PO if alert and <2hrs post >1g OD, or by NG if >7-8g, severe features and intubated. Consider WBI if intubated.

Disposition

Because of risk of delayed seizures, all need admission for observation for ≥16h. Cardiac monitoring may be stopped if ECG normal after 6h when OD≤4.5g or 12h when OD>4.5g.

If severe features or serotonin syndrome → ICU.

Notes

Duloxetine, another SNRI, is not generally assoc with cardiotoxicity or seizures in lone OD.