

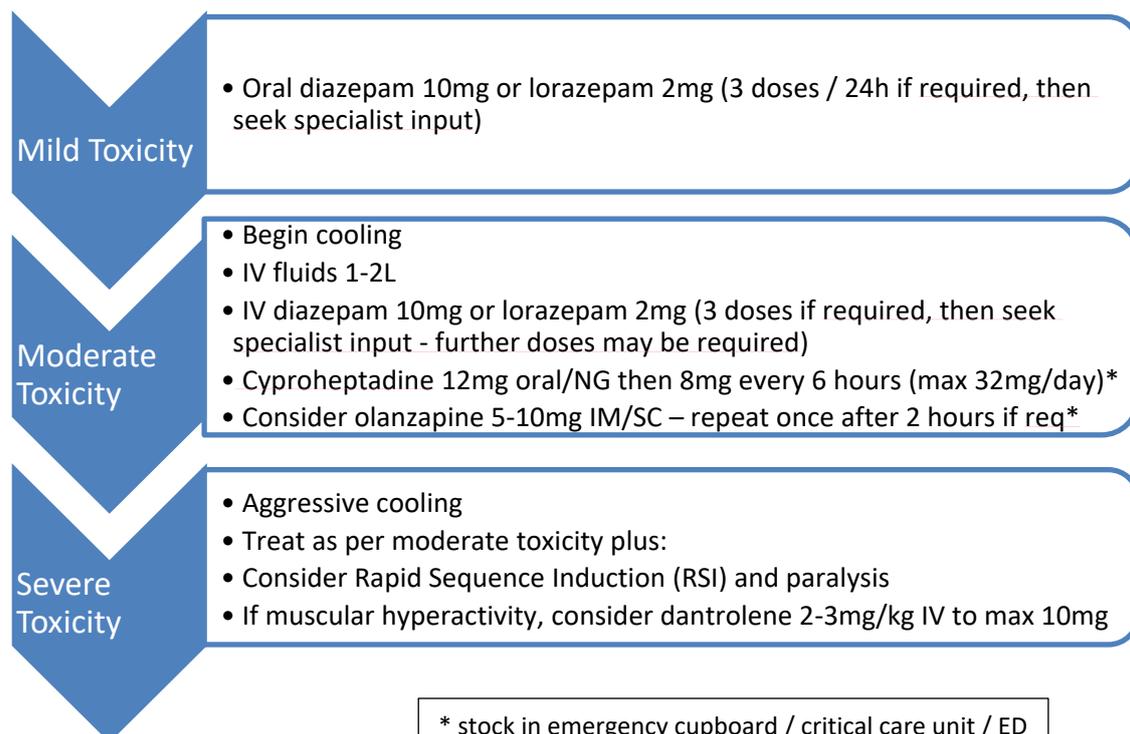
## SEROTONIN SYNDROME - ADULT

<b>TARGET AUDIENCE</b>	Board-wide
<b>PATIENT GROUP</b>	For treatment – adult critical care & ED For information - All adult, including mental health

### Clinical Guidelines Summary

#### MANAGEMENT OF SEROTONIN SYNDROME IN ADULTS <sup>1,2,3</sup>

- **Withdraw causative drugs** (including fentanyl patches if worn). Mild cases typically resolve within 24-48 hours, depending on drug half-life.
- **Moderate to severe cases** require acute medical facility management.



#### **Supportive care may be required for:**

- Pyrexia: Cooled IV fluids, ambient Bair Hugger, ice packs. **NB.** Paracetamol is ineffective as the temperature is not hypothalamic in origin.
- Hypoglycaemia, hyperkalaemia, rhabdomyolysis (consider 1.26% bicarbonate therapy).

#### **RSI AND SEROTONIN SYNDROME**

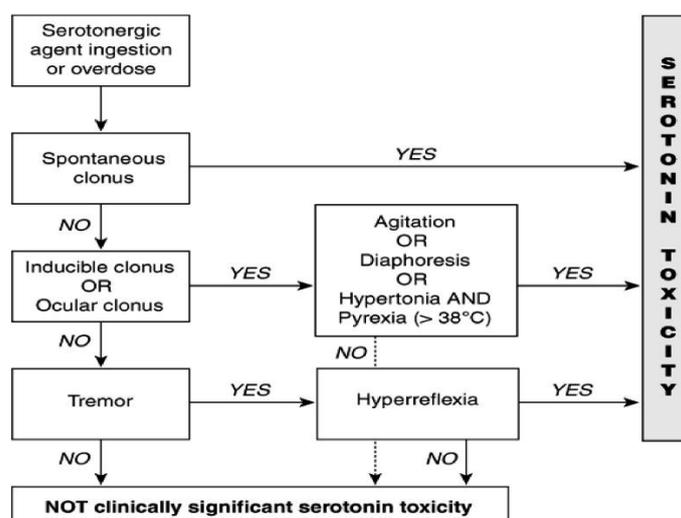
- Avoid opioids with serotonergic activity (e.g. fentanils).
- Avoid suxamethonium (risk of hyperkalaemia) - **rocuronium** is preferred.

## Serotonin Syndrome – ADULT

### BACKGROUND

Serotonin syndrome is a potentially life-threatening condition associated with increased intra-synaptic serotonin in the central nervous system (CNS). It is usually caused by therapeutic medication use (uncommon), drug interactions, or overdose (common). It is classically described as a triad of mental status changes, autonomic hyperactivity, and neuromuscular abnormalities, but actually a spectrum of toxicity ranging from mild (underreported) to life-threatening.

### DIAGNOSIS (HUNTER CRITERIA)<sup>1a</sup>



- Onset occurs within a few hours of serotonergic agent intake.
- Mild serotonin syndrome may not meet Hunter Criteria.

### DIFFERENTIAL DIAGNOSIS<sup>4</sup>

In the absence of serotonergic exposure or neuromuscular excitation (e.g. hyperreflexia, clonus), consider alternative diagnoses, including CNS infection, neuroleptic malignant syndrome, anticholinergic/sympathomimetic toxicity, or malignant hyperthermia.

### SPECTRUM OF SEROTONIN TOXICITY<sup>1</sup>

	SEVERITY	NEUROMUSCULAR	AUTONOMIC	MENTAL STATUS
	Serotonergic side effects	Brisk reflexes	Nausea, diarrhoea	Insomnia
	Mild	Inducible clonus, hyperreflexia	Hypertension, palpitations	Anxiety, restlessness
	Moderate	Sustained clonus, tremor	Mydriasis, flushing, diaphoresis, pyrexia, tachycardia	Agitation, hallucinations
	Severe	Rigidity, respiratory failure	Severe hyperthermia (>40°C)	Confusion, delirium

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## Serotonin Syndrome – ADULT

### AETIOLOGY

Can occur with drugs designed to increase serotonin (e.g. SSRIs) or those with unintended serotonergic effects (e.g. linezolid). Serious toxicity is attributed to 5-HT<sub>2</sub> receptor stimulation from combinations involving different mechanisms e.g. MAOI and SSRI combinations, necessitating washout periods to mitigate risk.<sup>2,4</sup> Drugs acting on other 5-HT receptors or serotonin antagonists (e.g., triptans, antipsychotics, anti-emetics, anticonvulsants) carry a lower risk.

### POSSIBLE CAUSATIVE AGENTS

Numerous medications can induce serotonin syndrome alone in high doses or in combination.

Antidepressants	Opioids	CNS stimulants	Others
MAOIs e.g. phenelzine	pethidine	amphetamines	St John's wort
TCAs e.g. amitriptyline	fentanils	cocaine	Sodium valproate
SSRIs e.g. fluoxetine	oxycodone	MDMA	lithium
SNRIs e.g. venlafaxine	tramadol	LSD	linezolid
trazodone	buprenorphine	methylphenidate	
vortioxetine	tapentadol		

### RESTARTING TREATMENT

Once symptoms resolve, serotonergic medication may be restarted at a lower dose under close monitoring. This should be done prior to hospital discharge in consultation with the appropriate specialty, e.g. liaison psychiatry for psychiatric medications. Alternative treatments with reduced serotonergic activity should be considered based on severity and cause of serotonin syndrome.

## References/Evidence

- 1) Chiew AL, Management of Serotonin Syndrome. *Br J Clin Pharmacol* 2024; DOI: 10111/bcp.16152.
- a) Hunter Serotonin Toxicity Criteria. Flow diagram based on the Hunter Serotonin Toxicity criteria. *Source:* Figure from Isbister et al. 2007. Figure reproduced with permission from: Chiew, A.L. and Isbister, G.K. (2025) 'Management of serotonin syndrome (toxicity)', *British journal of clinical pharmacology*, 91(3), pp. 654–661
- 2) Toxbase. Serotonin Syndrome. Updated 01/21. Accessed 6/12/24.
- 3) UpToDate. Serotonin Syndrome. Last updated 07/24. Accessed 6/12/24.
- 4) BMJ Best Practice. Serotonin Syndrome. Last updated 07/10/2022. Accessed 23/8/24.

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### Appendices

#### 1. Governance information for Guidance document

<b>Lead Author(s):</b>	Sarah Brady
<b>Endorsing Body:</b>	ADTC
<b>Version Number:</b>	2
<b>Approval date</b>	October 2025
<b>Review Date:</b>	October 2028
<b>Responsible Person (if different from lead author)</b>	

<b>CONSULTATION AND DISTRIBUTION RECORD</b>	
<b>Contributing Author / Authors</b>	Sarah Brady, Senior Pharmacist, UHH Dr Vanessa Vallance, Consultant Anaesthetist, UHH Lorna Templeton, Lead Pharmacist MHLd, UHW
<b>Consultation Process / Stakeholders:</b>	Iain Lang (original author) Anaesthetics teams Pharmacy surgery/critical care teams ED representative – Dr Alison Pollock, UHW
<b>Distribution</b>	All adult

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## Serotonin Syndrome – ADULT

CHANGE RECORD			
Date	Lead Author	Change	Version
December 2015	Iain Lang	Initial version – management of serotonin syndrome (focus on critical care)	1
May 2025	Sarah Brady	Review and extend guidance to cover more background and include non-critical care.	2
			3
			4
			5

### 2. You can include additional appendices with complimentary information that doesn't fit into the main text of your guideline, but is crucial and supports its understanding.

e.g. supporting documents for implementation of guideline, patient information, specific monitoring requirements for secondary and primary care clinicians, dosing regimen/considerations according to weight and/or creatinine clearance

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