

Table 3.2 Serotonin syndrome [9, 13, 16–23]

Onset	<ul style="list-style-type: none"> • Typically rapid • 60% of cases present within 6 h after initial use or dosage adjustment of medication and 75% within 24 h
Signs and symptoms	<ul style="list-style-type: none"> • Mild: tachycardia, shivering, diaphoresis, mydriasis, intermittent tremor, myoclonus or hyperreflexia • Moderate: mild symptoms plus hypertension, hyperthermia, hyperactive bowel sounds, diarrhea, hyperreflexia and clonus greater in lower extremities, mild agitation or hypervigilance, pressured speech • Severe: previous symptoms plus severe hypertension and tachycardia, agitated delirium, muscular rigidity, hyperreflexia, rhabdomyolysis
Monitoring parameters	<ul style="list-style-type: none"> • Heart rate • Temperature (severe cases >40°C) • Blood pressure • Neurologic examination • Basic metabolic panel (increased serum creatinine and metabolic acidosis in severe cases)
Associated drugs	<p>High risk:</p> <ul style="list-style-type: none"> • Antibiotics: linezolid (nonselectively inhibits MAO) • Dietary supplements: Hypericum perforatum (St. John's Wort), tryptophan, S-adenosyl-methionine (SAMe) • Ethylcysteinate: methylphenidylmethamphetamine (MEDMA), lysergic acid diethylamide (LSD), cocaine • MAOIs: tranylcypromine, phenelzine, moclobemide • SNRIs: venlafaxine • SSRIs: citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline • Serotonin releaser stimulants: amphetamine • TCAs: clomipramine, imipramine <p>Low risk:</p> <ul style="list-style-type: none"> • Anticonvulsants: carbamazepine, valproate • Antiemetics: ondansetron, metoclopramide • Antimigraine drugs: sumatriptan, dihydroergotamine • Cyclobenzaprine (controversial, mimic TCA chemical structure) • Lithium • Methylene blue (inhibits MAO-A) • Misc. Antidepressants: buspirone, trazodone • Opioid analgesics: fentanyl, meperidine, pentazocine, tramadol, dexmethylorphan

If serotonin syndrome is suspected, all serotonergic medications should be promptly discontinued. When supportive therapy is necessary treatment may include stabilization of autonomic dysregulation and control of hyperthermia and agitation. In some cases benzodiazepine treatment may be necessary to treat agitation. In severe cases, limited data suggest administration of 12 mg of the 5HT_{2A} antagonist cyproheptadine followed by 4–8 mg every 6 h may be beneficial for some patients [8, 23, 26]. Most cases of serotonin syndrome subside within 24 h of discontinuing the offending agent [9].

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