

Cyproheptadine

Serotonin syndrome is a potentially fatal adverse drug reaction resulting from excessive central or peripheral serotonergic activity. Ingestion of multiple therapeutic proserotonergic drugs, and less frequently with overdoses of single agents, are contributors to this syndrome. The syndrome encompasses a wide range of clinical findings, which generally occur within the first 24 hours of multiple proserotonergic drugs ingestion. Clinical features of serotonin syndrome include a triad of altered mental status, autonomic dysfunction, and neuromuscular changes. Symptoms may range from agitation, diarrhea, tachycardia, diaphoresis, mydriasis, tremor, myoclonus, and hyperreflexia in mild to moderate cases to delirium, coma, hyperthermia, muscle rigidity, hypertonicity and in severe cases.

Mechanism/Indications: Cyproheptadine is a histamine-1 receptor antagonist with nonspecific 5-hydroxytryptamine (5-HT)-1A and 5-HT_{2A} antagonistic properties. It is the recommended antidote for the treatment of serotonin syndrome in the setting of incomplete response with supportive therapy including aggressive cooling and benzodiazepines. While it exerts weak anticholinergic actions, cyproheptadine's antidotal properties are attributed to the blockade and competition of 5-HT receptor sites receptors. A dose of 12–32 mg will bind 85%–95% of serotonin receptors.

Dosing: The adult dose is 12 mg orally initially, then 2 mg given every 2 hours if patient remains symptomatic. The adult maximum dose is 32 mg in 24 hours. Children should receive 0.25 mg/kg/day divided every 6 hours with a maximum of 12 mg/day. It is available as a 2 mg/5 oral syrup and a 4 mg tablet, which may be crushed and administered via a nasogastric tube. Cyproheptadine is not available for IV use. For both children and adults, the dose should be titrated up until the maximum recommended daily dosage is achieved or the patient becomes asymptomatic.

Adverse Effects/Contraindications: Cyproheptadine may lead to sedation, but this side effect is consistent with the goals of management and should not deter clinicians from its use. It may also produce transient hypotension due to the reversal of serotonin-mediated increases in vascular tone. Common side effects of cyproheptadine may include nausea, vomiting, diarrhea, abdominal discomfort, weight gain, thick sputum and dryness of the mouth. Cyproheptadine should be avoided or used with caution in:

- Patients with hypersensitivity to cyproheptadine products
- Narrow angle glaucoma patients
- Bladder neck obstruction patients and symptomatic prostatic hyperplasia patients since anticholinergic properties may exacerbate urinary retention
- Pyloroduodenal obstruction and stenosing peptic ulcer patients since anticholinergic properties may increase occlusion of gastric outlet

Cyproheptadine has an atropine-like action and, therefore, should be used with caution in patients with a history of bronchial asthma, increased intraocular pressure, hyperthyroidism and cardiovascular disease. Cyproheptadine is considered relatively safe in pregnancy (pregnancy risk category B).

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For more on cyproheptadine:

- Boyer E, Shannon M. The serotonin syndrome. *N Engl J Med* 2005; 352: 1112-1120.
- Graudins A, Stearman A, Chan B. Treatment of the serotonin syndrome with cyproheptadine. *J Emerg Med* 1998; 16: 615-9.
- Kapur S, Zipursky RB, Jones C, Wilson AA, DaSilva JD, Houle S. Cyproheptadine: a potent in vivo serotonin antagonist. *Am J Psychiatry* 1997; 154(6):884.
- Manini AF. Monoamine Oxidase Inhibitors. In: Nelson LS, Lewin NA, Howland MA, Hoffman RS, Goldfrank LR, Flomenbaum NE, editors. *Goldfrank's toxicologic emergencies*. 9th ed. New York: McGraw Hill; 2011;1034-1035.

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