

Guanfacine Extended Release

Guanfacine, like clonidine, is a central alpha-2 receptor agonist classically considered an antihypertensive agent. In recent years, however, an extended-release (ER) formulation has been marketed under the trade name Intuniv® for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents. A generic formulation has also been available since December 2014. Its mechanism of action as a treatment for ADHD is related to its ability to bind post-synaptic alpha-2a receptors in the prefrontal cortex. This in turn is theorized to improve delayed firing of prefrontal cortex neurons resulting in effects on underlying working memory and behavioral inhibition. This drug is not associated with a high propensity for abuse.

The increasing use of guanfacine in the management of ADHD is associated with an increase in the number of pediatric case reports of both unintentional and deliberate poisonings. In the first 12 months after Intuniv® was approved, the number of prescriptions dispensed per month increased from 98,000 to 212,000 in the United States (*Pediatr Emerg Care 2012;28:1060-1061*). Reasons for exposures in the pediatric population appear to be age-related. Unintentional exposures were more common in children under 6 years of age. Between the ages of 6 and 12, therapeutic error was the most common reason behind toxicities, and intentional ingestion was most associated with children over the age of 13 (*Pediatr Emerg Care 2013;29:1033-1036*). There is also the potential for medication errors within the healthcare setting by picking or prescribing the wrong formulation to administer or dispense to the patient.

Clinical effects associated with guanfacine overdose are predominately cardiovascular and neurologic. Cardiovascular effects include transient hypertension (due to peripheral alpha-2 agonist activity in vascular smooth muscle, causing vasoconstriction), bradycardia, QTc prolongation, and hypotension, which can be delayed. Neurologic effects include drowsiness, lethargy, and miosis. In children with guanfacine exposures, the most common effects reported to poison centers were CNS depression (77%), bradycardia (30%), and hypotension (26%) (*Ann Pharmacother 2002;36:1698-1703*).

Toxicities associated with guanfacine extended release are the same as those seen with immediate release, but the time course is prolonged. Most ingestions of guanfacine ER should be observed in the emergency department for 8 to 14 hours, and admitted for at least 24 hours of observation if they are symptomatic. Activated charcoal is recommended if the ingestion was recent and the patient is alert and able to protect his/her airway. Atropine can be used for symptomatic bradycardia. Hypertension normally does not need to be treated, but one may consider a calcium channel blocker or nitroprusside if it persists. Beta-blockers should not be used because they can worsen hypertension due to unopposed alpha-1 stimulation. Hypotension is treated with fluid boluses and, if refractory, with vasopressors. Guanfacine may cause the release of endogenous opioids through central alpha stimulation; therefore, naloxone may reverse CNS depression. Serum concentrations of guanfacine are not routinely available or useful.

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Did you know?

Guanfacine ER (Intuniv®) is not the only extended-release alpha-2 agonist being used in the treatment of ADHD

Clonidine also is available in an ER formulation (Kapvay®) for the treatment of ADHD. A toxic exposure involving this product will look very similar to that of guanfacine ER; however, clonidine could present with more severe symptomology. Clonidine is less specific for alpha-2a receptors alone, and due to its affinity for alpha-2b and 2c in the locus ceruleus and medulla, it can cause more sedation. It also shows affinity for the imidazoline receptors in the medulla, which can produce more pronounced hypotension. Like guanfacine, naloxone can be considered but results have been inconsistent. Clonidine also has a faster absorption and shorter half-life than guanfacine (*Pediatr Emerg Care 2013;29:1033-1036*). Triage and treatment for these overdoses should be handled in the same way as guanfacine ER.

