GUANFACINE

**Brands**
- Intuniv (pending approval)
- Tenex

*see index for additional brand names*

**Generic?** Yes (not for guanfacine ER)

**Class**
- Centrally acting alpha 2A agonist; antihypertensive

**Commonly Prescribed for**
*(bold for FDA approved)*
- **Hypertension**
- Attention deficit hyperactivity disorder (ADHD) in children ages 6–17 (Intuniv, pending approval)
- Oppositional defiant disorder
- Pervasive developmental disorders
- Motor tics
- Tourette’s syndrome

**How the Drug Works**
- For hypertension, stimulates alpha 2A adrenergic receptors in the brain stem, reducing sympathetic outflow from the CNS and decreasing peripheral resistance, renal vascular resistance, heart rate, and blood pressure
- For ADHD, theoretically has central actions on postsynaptic alpha 2A receptors in the prefrontal cortex

**How Long Until It Works**
- For ADHD, can take a few weeks to see maximum therapeutic benefits
- Blood pressure may be lowered 30–60 minutes after first dose; greatest reduction seen after 2–4 hours
- May take several weeks to control blood pressure adequately

**If It Works (for ADHD)**
- The goal of treatment of ADHD is reduction of symptoms of inattentiveness, motor hyperactivity, and/or impulsiveness that disrupt social, school, and/or occupational functioning
- Continue treatment until all symptoms are under control or improvement is stable and then continue treatment indefinitely as long as improvement persists

**If Reevaluate the need for treatment periodically**
- Treatment for ADHD begun in childhood may need to be continued into adolescence and adulthood if continued benefit is documented

**If It Doesn’t Work (for ADHD)**
- Consider adjusting dose or switching to another agent
- Consider behavioral therapy
- Consider the presence of noncompliance and counsel patient and parents
- Consider evaluation for another diagnosis or for a comorbid condition (e.g., bipolar disorder, substance abuse, medical illness, etc.)

**Best Augmenting Combos for Partial Response or Treatment Resistance**
- Best to attempt another monotherapy prior to augmenting for ADHD
- Possibly combination with stimulants (with caution as benefits of combination poorly documented)
- Combinations for ADHD should be for the expert, while monitoring the patient closely, and when other treatment options have failed
- Chlorthalidone, thiazide-type diuretics, and furosemide for hypertension

**Tests**
- Blood pressure should be checked regularly during treatment

**SIDE EFFECTS**

**How Drug Causes Side Effects**
- Excessive actions on alpha 2A receptors

**Notable Side Effects**
- Sedation, dizziness
- Dry mouth, constipation
- Fatigue, weakness

**Life-Threatening or Dangerous Side Effects**
- Sinus bradycardia, hypotension

**Weight Gain**
- Reported but not expected
Sedation

- Occurs in significant minority
- Some patients may not tolerate it
- Can abate with time

- May be less sedation with controlled-release formulation (pending approval)

What to Do About Side Effects

- Wait
- Adjust dose
- If side effects persist, discontinue use

Best Augmenting Agents for Side Effects

- Dose reduction or switching to another agent may be more effective since most side effects cannot be improved with an augmenting agent

**DOSING AND USE**

**Usual Dosage Range**

- Immediate-release: 1–2 mg/day

**Dosage Forms**

- Immediate-release tablet 1 mg, 2 mg, 3 mg

**How To Dose**

- Immediate-release: initial 1 mg/day at bedtime; after 3–4 weeks can increase to 2 mg/day

**Dosing Tips**

- Adverse effects are dose-related and usually transient
- Doses greater than 2 mg/day are associated with increased side effects
- If guanfacine is terminated abruptly, rebound hypertension may occur within 2–4 days
- For hypertension, dose can be raised to 2 mg/day if 1 mg/day is ineffective, but 2 mg may have no more efficacy than 1 mg

**Overdose**

- Drowsiness, lethargy, bradycardia, hypotension

**SPECIAL POPULATIONS**

**Renal Impairment**

- Patients should receive lower doses

**Hepatic Impairment**

- Use with caution

**Cardiac Impairment**

- Use with caution in patients with recent myocardial infarction, severe coronary insufficiency, cerebrovascular disease

**Elderly**

- Elimination half-life may be longer in elderly patients

**Long Term Use**

- Shown to be safe and effective for treatment of hypertension

**Habit Forming**

- No

**How to Stop**

- Taper to avoid rebound effects (nervousness, increased blood pressure)

**Pharmacokinetics**

- Elimination half-life approximately 17 hours

**Drug Interactions**

- Increased depressive effects when taken with other CNS depressants
- Phenobarbital and phenytoin may reduce plasma concentrations of guanfacine

**Other Warnings/Precautions**

- Excessive heat (e.g., saunas) may exacerbate some of the side effects, such as dizziness and drowsiness
- Use with caution in patients with severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease, or chronic renal or hepatic failure

**Do Not Use**

- If there is a proven allergy to guanfacine
Elderly patients may be more sensitive to sedative effects.

**Children and Adolescents**
- Safety and efficacy not established in children under age 6
- Some reports of mania and aggressive behavior in ADHD patients taking guanfacine

**Pregnancy**
- Risk Category B [animal studies do not show adverse effects; no controlled studies in humans]
- Use in women of childbearing potential requires weighing potential benefits to the mother against potential risks to the fetus

**Breast Feeding**
- Unknown if guanfacine is secreted in human breast milk, but all psychotropics assumed to be secreted in breast milk
- Recommended either to discontinue drug or bottle feed

**Potential Disadvantages**
- Not well studied in adults with ADHD

**Primary Target Symptoms**
- Concentration
- Motor hyperactivity
- Oppositional and impulsive behavior
- High blood pressure

**Pearls**
- Guanfacine has been shown to be effective in both children and adults, and approval is pending for guanfacine extended-release in children ages 6–17
- Guanfacine can also be used to treat tic disorders, including Tourette’s syndrome
- Although both guanfacine and clonidine are alpha 2 adrenergic agonists, guanfacine is relatively selective for alpha 2A receptors, whereas clonidine binds not only alpha 2A, 2B, and 2C receptors but also imidazoline receptors, causing more sedation, hypotension, and side effects than guanfacine
- May be used as monotherapy or in combination with stimulants for the treatment of oppositional behavior in children with or without ADHD

**The Art of Psychopharmacology**

**Potential Advantages**
- No known abuse potential
- For oppositional behavior associated with ADHD
- Less sedation than clonidine

**Suggested Reading**