GUANFACINE

**THERAPEUTICS**

**Brands**
- Intuniv
- Tenex

*see index for additional brand names*

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

**Class**
- Neuroscience-based Nomenclature: norepinephrine receptor agonist (N-RA)
- Centrally acting alpha 2A agonist; antihypertensive; nonstimulant for ADHD

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

**How the Drug Works**
- For ADHD, theoretically has central actions on postsynaptic alpha 2A receptors in the prefrontal cortex
- Guanfacine is 15–20 times more selective for alpha 2A receptors than for alpha 2B or alpha 2C receptors
- The prefrontal cortex is thought to be responsible for modulation of working memory, attention, impulse, control, and planning
- 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

**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**
- 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
- Some studies of up to 2 years
- 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**
- 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)
- 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, nonselective actions on alpha 2B and alpha 2C receptors

**Notable Side Effects**
- Sedation, dizziness
- Dry mouth, constipation, abdominal pain
GUANFACINE (continued)

- Fatigue, weakness
- Hypotension

**Life-Threatening or Dangerous Side Effects**
- Sinus bradycardia, hypotension (dose-related)

**Weight Gain**

- Reported but not expected

**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
- For extended-release formulation, do not administer with high-fat meals because this increases exposure
- Extended-release tablets should not be crushed, chewed, or broken
- Extended-release and immediate-release tablets have different pharmacokinetic properties, so do not substitute on a mg-per-mg basis
- Consider dosing extended-release on a mg/kg basis (0.05 mg/kg to 0.12 mg/kg)

**Overdose**
- Drowsiness, lethargy, bradycardia, hypotension

**Long-Term Use**
- Shown to be safe and effective for treatment of hypertension
- Studies of up to 2 years in ADHD

**Habit Forming**
- No

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

**Pharmacokinetics**
- Pharmacokinetic properties differ for immediate- and extended-release formulations
- Metabolized by CYP450 3A4

**Drug Interactions**
- CYP450 3A inhibitors such as nefazodone, fluoxetine, fluvoxamine, and ketoconazole, may decrease clearance of guanfacine and raise guanfacine levels significantly
- CYP450 3A inducers may increase clearance of guanfacine and lower guanfacine levels significantly

### DOSING AND USE

**Usual Dosage Range**
- Immediate-release: 1–2 mg/day
- Extended-release: 1–4 mg/day

**Dosage Forms**
- Immediate-release tablet: 1 mg, 2 mg, 3 mg
- Extended-release: 1 mg, 2 mg, 3 mg, 4 mg

**How to Dose**
- Immediate-release: initial 1 mg/day at bedtime; after 3–4 weeks can increase to 2 mg/day
- Extended-release: initial 1 mg/day; can increase by 1 mg/week; maximum dose 4 mg/day

**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

**Fatigue, weakness**

**Hypotension**

**Life-Threatening or Dangerous Side Effects**
- Sinus bradycardia, hypotension (dose-related)

**Weight Gain**

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**Sedation**

- Many experience and/or can be significant in amount
- Some patients may not tolerate it
- Can abate with time
- May be less sedation with extended-release formulation

**Overdose**
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Pregnancy

- Effective June 30, 2015, the US FDA requires changes to the content and format of pregnancy and lactation information in prescription drug labels, including the elimination of the pregnancy letter categories; the Pregnancy and Lactation Labeling Rule (PLLR or final rule) applies only to prescription drugs and will be phased in gradually for drugs approved on or after June 30, 2001.
- Controlled studies have not been conducted in pregnant women.
- Animal studies do not show adverse effects.
- 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.

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.

Do not administer extended-release with high-fat meals, because this increases exposure.

Combined use with valproate may increase plasma concentrations of valproate.

Increased depressive effects when taken with other CNS depressants.

Phenobarbital and phenytoin may reduce plasma concentrations of guanfacine.

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.
- Use with caution in patients at risk for hypotension, bradycardia, heart block, or syncope.

Elderly

- Elimination half-life may be longer in elderly patients.
- 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.

Guanfacine has been shown to be effective in both children and adults, and guanfacine extended-release is approved for ADHD in children ages 6–17.

THE ART OF PSYCHOPHARMACOLOGY

Potential Advantages

- No known abuse potential; not a controlled substance.
- Not a stimulant.
- For oppositional behavior associated with ADHD.
- Less sedation than clonidine.

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 guanfacine extended-release is approved for ADHD 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.

Suggested Reading


