**GUANFACINE**

**THERAPEUTICS**

**Brands**
- Tenex, Intuniv

**Generic?**
Yes (except extended release)

**Class**
- Antiadrenergic, alpha-2 agonist

**Commonly Prescribed for**
(FDA approved in bold)
- **Hypertension**
- Gilles de la Tourette syndrome (GTS)
- Tics
- Attention deficit hyperactivity disorder (ADHD)
- Neuropathic pain
- Opioid detoxification
- Alcohol withdrawal
- Hypertensive “urgency”
- Post-traumatic stress disorder

**How the Drug Works**
- Alpha-2 adrenergic agonist. Reduces sympathetic output from CNS, which decreases cardiac output, peripheral vascular resistance, and blood pressure
- Specifically targets alpha-2 receptors in the brainstem vasomotor center, decreasing presynaptic calcium levels and the release of norepinephrine
- Its effect in GTS and ADHD may be due to actions at the level of the prefrontal cortex

**How Long Until It Works**
- Hypertension, withdrawal – less than 2 hours
- GTS – weeks to months

**If It Works**
- In neurologic disorders, such as tics, continue to assess effect of the medication to see if it is still needed

**If It Doesn’t Work**
- GTS/tics – Neuroleptics are often effective, but their use should be reserved for patients with significant social isolation or embarrassment

**Best Augmenting Combos for Partial Response or Treatment-Resistance**
- In hypertension, combine with treatments less likely to cause orthostasis

**ADVERSE EFFECTS (AEs)**

**How Drug Causes AEs**
- Related to alpha-2 adrenergic agonist effect – hypotension and sedation

**Notable AEs**
- Dry mouth, drowsiness, dizziness, constipation, weakness, headache, depression, paresthesia, dermatitis, impotence, and syncope

**Life-Threatening or Dangerous AEs**
- Bradycardia and syncope. Rapid withdrawal can cause rebound hypertension with increased catecholamine levels

**Weight Gain**
- Unusual

**Sedation**
- Not unusual

**What to Do About AEs**
- Lower the dose and take the highest dose in the evening. Many AEs (especially sedation) improve with time

**Best Augmenting Agents for AEs**
- Most AEs cannot be improved by an augmenting agent
DOSSING AND USE

Usual Dosage Range
- 0.5–2 mg/day at night or in 2 divided doses
- Extended release: up to 4 mg at night

Dosage Forms
- Tablets: 1 mg, 2 mg
- Extended release: 1 mg, 2 mg, 3 mg, 4 mg

How to Dose
- Hypertension: start with 1 mg at night. If effect less than desired, increase to 1 mg twice daily or 2 mg at night.
- GTS/tics, ADHD: Start at 0.5 mg per day. Increase by 0.5 mg every 3–4 days as needed and tolerated. Average dose is 1.5 mg/day. Most patients take the entire dose at night.

Dosing Tips
- Start at bedtime only, and if well tolerated (little sedation) can divide doses
- Rebound hypertension usually occurs 2–4 days after discontinuation

Overdose
- Hypotension, bradycardia, drowsiness, and lethargy have been reported. Consider gastric lavage for large quantities

Long-Term Use
- Safe, but tolerance to antihypertensive effects is common

Habit Forming
- No

How to Stop
- Taper slowly to avoid rebound tachycardia and hypertension. Other withdrawal symptoms may include nervousness and anxiety

Pharmacokinetics
- Half-life is 17 hours, but shorter in younger patients. The peak effect is at 1–4 hours. Bioavailability is 80%, with about half of the drug metabolized into inactive metabolites and the other excreted unchanged in urine

Drug Interactions
- Use with other CNS depressants increases sedation

CYP-450 enzyme inducers (phenytoin, phenobarbital) lower elimination half-life and plasma levels. Increase daily dose and dose more frequently

Other Warnings/Precautions
- Do not discontinue perioperatively and monitor blood pressure closely
- Skin rash (exfoliative) has been reported

Do Not Use
- Known hypersensitivity

SPECIAL POPULATIONS

Renal Impairment
- Clearance is reduced but has little clinical effect. Consider using a lower dose

Hepatic Impairment
- No known effects

Cardiac Impairment
- Avoid using in patients with known coronary artery disease, conduction disturbances, recent myocardial infarction, or cerebrovascular events

Elderly
- No known effects

Children and Adolescents
- Children may be more sensitive to CNS AEs than adults. Doses for GTS and tics are similar to adults, but titrate more slowly. Consider giving the entire oral dose at night

Pregnancy
- Category B. Use only if there is a clear need

Breast Feeding
- Likely excreted in breast milk. Do not use

THE ART OF NEUROPHARMACOLOGY

Potential Advantages
- Fewer AEs than neuroleptics in the treatment of GTS and tic disorders. Less somnolence than clonidine
GUANFACINE (continued)

Potential Disadvantages
- Less effective than neuroleptics for GTS or tics. Hypotension and rebound hypertension may limit use

Primary Target Symptoms
- Tics, attention-deficit, and hyperactivity

Pearls
- The first decision in the treatment of GTS or tics is to decide if pharmacologic treatment is indicated. If the patient is not severely disabled, then reassure the patient and family that symptoms may improve and the prognosis is good. For patients with significant disability, guanfacine is a good initial choice due to lack of long-term AEs, especially in patients with coexisting ADHD
- In patients with severe ADHD, stimulants are more effective
- Clonidine, another alpha-2 adrenergic agonist, is often used for GTS or tics. Compared to guanfacine, more studies support its use but there was more somnolence. Rebound hypertension is greater and usually starts sooner after discontinuation compared to guanfacine
- Not an imidazoline ligand, which explains the lower incidence of somnolence compared to clonidine and tizanidine
- In children, case reports exist of guanfacine-related behavioral changes, including mania and aggression

Suggested Reading
