GUANFACINE (Intuniv, Tenex) Fact Sheet [G]

BOTTOM LINE:
Guanfacine's advantages over stimulants include no worsening of tic disorders, lack of misuse potential, and no insomnia. It can also be used as an add-on to stimulant medication. However, its delayed onset of effect (two to four weeks) and lower efficacy rates make it a second-line choice for ADHD generally. ER is now available in generic and easier to use than IR. Commonly used off label for anxiety and insomnia, but efficacy data are limited.

PEDIATRIC FDA INDICATIONS:
ADHD (6–17 years [ER formulation only]), as monotherapy or adjunctive therapy to stimulants.

ADULT FDA INDICATIONS:
Hypertension.

OFF-LABEL USES:
Conduct disorder; Tourette's and motor tics; agitation in autistic kids; migraine prophylaxis; opioid withdrawal; anxiety and PTSD; insomnia.

DOSAGE FORMS:
- **IR tablets (Tenex, [G]):** 1 mg, 2 mg.
- **ER tablets (Intuniv, [G]):** 1 mg, 2 mg, 3 mg, 4 mg.

PEDIATRIC DOSAGE GUIDANCE:
- ADHD or anxiety:
  - IR dosing depends on weight:
    - 27–40.5 kg (55–90 lbs): Start 0.5 mg QHS, ↑ by 0.5 mg/day at weekly intervals up to 1.5 mg/day; may ↑ to 2 mg/day after two weeks; max 2 mg/day in two to four divided doses.
    - 40.5–45 kg (90–99 lbs): Start 0.5 mg QHS, ↑ by 0.5 mg/day at weekly intervals; max 1 mg per dose, 3 mg/day.
    - >45 kg (>99 lbs): Start 1 mg QHS, ↑ by 1 mg/day at weekly intervals up to 3 mg/day; may ↑ to 4 mg/day after two weeks; max 1 mg per dose, 4 mg/day.
  - ER: Start 1 mg QHS, ↑ by 1 mg/day at weekly intervals; max 4 mg/day. Alternative: 0.05–0.12 mg/kg QD or QHS; max 4 mg/day. Doses up to 7 mg/day ER studied as monotherapy in adolescents.
- Insomnia: Use IR: Start low, go slow, typically 0.5 mg QHS, increasing by 0.5 mg/day at weekly intervals; max 3 mg/day.

MONITORING: BP.

COST: $

SIDE EFFECTS:
- Most common: Dry mouth, somnolence, dizziness, constipation, fatigue, headache.
- Serious but rare: Hypotension, syncope, orthostasis.

MECHANISM, PHARMACOKINETICS, AND DRUG INTERACTIONS:
- Centrally acting, selective alpha-2 adrenergic agonist.
- Metabolized primarily through CYP3A4; t ½: 13–14 hours in children (16–18 hours in adults).
- Avoid use with MAOIs. Caution with 3A4 inhibitors (eg, clarithromycin, fluvoxamine) and inducers (eg, St. John's wort, carbamazepine).

EVIDENCE AND CLINICAL PEARLS:
- At least six randomized placebo-controlled trials and a meta-analysis show efficacy in children with ADHD.
- A pilot study of 83 children with GAD, separation anxiety, or social anxiety found guanfacine treatment resulted in greater subjective improvement of anxiety than placebo, but no improvement on other measures of anxiety.
- One negative randomized trial for insomnia in children with ADHD found decreased total sleep time of nearly an hour, with kids taking more time to fall asleep.
- Guanfacine IR and ER are not interchangeable on a mg:mg basis. When switching, taper and retitrate.
- Guanfacine tends to be less sedating than clonidine, another alpha-agonist.
- ER tablets should not be taken with a high-fat meal due to increased medication exposure.
- Minimize side effects, especially somnolence, by administering at bedtime.
- Monitor BP, especially during initial dosing titration.
- There is a risk of nervousness, anxiety, and possibly rebound hypertension two to four days after abrupt discontinuation. Taper dose in 1 mg/day decrements every three to seven days.
- If a child misses two or more consecutive doses, consider repeating titration.

FUN FACT:
Some prescribers have taken advantage of guanfacine's sympatholytic properties for the treatment of anxiety disorders in children as well as nightmares and dissociative symptoms in PTSD.