Guanfacine

FDA Indications:

- Attention-deficit/hyperactivity disorder (ADHD) in pediatric patients aged 6-17 years
- Hypertension (alone or in combination with other antihypertensive agents)

Off-label uses:

- Agitation/aggression
- Tourette syndrome and other tic disorders

Mechanism of Action:

- Guanfacine is an alpha-2 adrenergic agonist that acts centrally in the brain. By stimulating postsynaptic alpha-2A adrenergic receptors, guanfacine leads to the inhibition of norepinephrine release and reduced sympathetic outflow. By reducing sympathetic activity, guanfacine helps improve hyperactivity and aggression. Guanfacine is also thought to improve the delay-related firing of prefrontal cortex neurons, leading to an improvement in working memory and behavioral disinhibition.

Dosage Forms:

- Guanfacine is available in oral immediate-release tablets (Tenex) and extended-release tablet formulations (Intuniv). Certain pharmacies are also able to compound liquid formulations. Usual effective dose: 1-4 mg per day.
- Tenex – 1 mg, 2 mg; Intuniv –1 mg, 2 mg, 3 mg, 4 mg
- ADHD Dosing Guidelines:
- *Guanfacine immediate-release starting dose and titration schedule:*
- <45 kg: 0.5 mg nightly; titrate no faster than every 3-4 days in 0.5 mg increments BID, TID, or QID
- >45 kg: 1 mg nightly; titrate no faster than every 3-4 days in 1 mg increments BID, TID, or QID
- Maximum dose: 27-40.5 kg: 2 mg/day; 40.5-45 kg: 3 mg/day; >45 kg: 4 mg/day
- *Guanfacine extended-release starting dose and titration schedule:*
- 1 mg once daily, taken in the morning or evening. Titrate no faster than 1 mg per week.
- Maximum dose: Doses above 4 mg have been evaluated but are generally not prescribed due to the risk of hypotension. 25 to 33.9 kg: 2 to 3 mg/day; 34 to 41.4 kg: 2 to 4 mg/day; 41.5 to 49.4 kg: 3 to 5 mg/day; 49.5 to 58.4 kg: 3 to 6 mg/day; 58.5 to 91 kg: 4 to 7 mg/day; >91 kg: 5 to 7 mg/day.

Side Effects:

- Common side effects include somnolence, fatigue, dizziness/lightheadedness, dry mouth, constipation

- Less common side effects include: hypotension, bradycardia, syncope, depressive symptoms, abdominal pain, headache

Clinical Pearls:

- Regularly assess blood pressure in patients using guanfacine, as this medication may lead to hypotension.
- Sedation is common in the first several days after starting guanfacine or increasing the dose and often resolves with time. This side effect can be mitigated by starting guanfacine nightly at a low dose and gradually increasing the dose and later adding a daytime dose.
- Unlike stimulant ADHD medications, it may take several weeks for the clinical benefit of guanfacine to be observed.
- Guanfacine is often used to augment the effects of other ADHD medications in patients who have had an insufficient response to stimulants, cannot tolerate this class of medications, or have a contraindication to stimulants as it is generally considered to have inferior effectiveness compared to stimulants. In patients who have a tic disorder in addition to ADHD, guanfacine should be considered as a first-line option.
- Extended-release guanfacine (Intuniv) is thought to increase the elimination half-life modestly when compared to immediate-release guanfacine, though may be significantly more expensive and pills cannot be divided.
- Guanfacine may be more effective at managing ADHD symptoms of hyperactivity and impulsivity than inattention.

Precautions:

- Use with caution in patients with a history of hypotension, bradycardia, or cardiovascular disease.
- Gradual discontinuation is recommended to avoid rebound hypertension.

Drug Interactions:

- Guanfacine is primarily metabolized by CYP3A4 and excreted really. Much of the drug is excreted unchanged. There is no know inhibition or induction of the cytochrome system. Guanfacine may enhance the sedative effects of CNS depressants. Concurrent use with antihypertensive agents may lead to additive hypotensive effects.

Special Populations:

- Use with caution in patients with hepatic impairment, as guanfacine is primarily metabolized in the liver.
- Safety and effectiveness in pediatric patients under 6 years of age have not been established. If administered to patients under 6 years of age, patients with neurocognitive disorders, or patients with autism spectrum disorder, it is advised to start

at doses around 0.25-0.5 mg and increase the dose slowly to minimize the risk of adverse effects.

References:

1. Intuniv® (guanfacine) prescribing information. Shire US Inc.; Revised January 2023.

2. National Institute for Health and Care Excellence (NICE). Attention deficit hyperactivity disorder: diagnosis and management. Clinical Guideline [CG72]. Updated March 2013.

3. Lexicomp Online®. Hudson, OH: Lexi-Comp, Inc.; Accessed May 2023.

4. Pliszka S and AACAP Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *Am Acad Child Adolesc Psychiatry.* 2007;46(7):894-921.

5. Stahl, S. M., Grady, M. M., & Muntner, N. (2014). Stahl's essential psychopharmacology: the prescriber's guide. In Cambridge University Press eBooks. http://ci.nii.ac.jp/ncid/BB01427500