Clonidine

FDA Indications:

- Attention-Deficit/Hyperactivity Disorder
    - ages 6-17, adjunct or monotherapy

Brand Names

- Kapvay (Clonidine ER)
- Catapres-TTS (Clonidine transdermal patch)

Off-label Uses:

- Motor tics
- Tourette Syndrome
- Oppositional defiance disorder
- Conduct disorder
- Pervasive developmental disorders
- Anxiety disorder (including PTSD and social anxiety disorder)

Mechanism of Action:

- Clonidine is an alpha-2 adrenergic agonist, which acts on central postsynaptic alpha-2 receptors in the prefrontal cortex
    - The prefrontal cortex is thought to be responsible for modulation of working memory, attention, impulse control, and planning

Dosages and Formulations:

- Clonidine is available in oral extended-release (ER) tablets (Kapvay), immediate-release (IR) tablets, and a transdermal patch. Certain pharmacies are also able to compound into liquid formulations.
- Usual dosage range for ADHD
    - ER: 0.1-0.4 mg/day in divided doses
    - IR: 0.2-0.6 mg/day in divided doses
- Dosage forms
    - ER: 0.1 mg, 0.2 mg
    - IR: 0.1 mg, 0.2 mg, 0.3 mg
    - Patch (7-day administration): 0.1 mg/24 hours, 0.2 mg/24 hours, 0.3 mg/24 hours
- How to dose
    - ER, oral: initial 0.1 mg at bedtime, can increase by 0.1 mg/day each week with twice daily dosing (either split evenly or larger dose at bedtime); max dose is typically 0.4 mg/day
    - IR, oral: weight-based
        - 27-40.5 kg: Initial- 0.05 mg at bedtime; increase as tolerated every 2 to 3 days in 0.05 mg/day increments given as 0.05 mg twice daily, then 3 times daily, then 4 times daily; max daily dose: 0.2 mg/day
        - 40.5 to 45 kg: Initial- 0.05 mg at bedtime; increase as tolerated every 2 to 3 days in 0.05 mg/day increments given as 0.05 mg twice daily, then 3 times daily, then 4 times daily; max daily dose: 0.3 mg/day

- >45 kg: Initial- 0.1 mg at bedtime; increase as tolerated every 2 to 3 days in 0.1 mg/day increments given as 0.1 mg twice daily, then 3 times daily, then 4 times daily; max daily dose: 0.4 mg/day

Side Effects:

- Sedation, dizziness, hypotension, fatigue, headache, dry mouth, constipation, nausea, vomiting
- Withdrawal syndrome: upon abrupt discontinuation, may experience rebound hypertension, diaphoresis, headache, and insomnia. Risk may be lower with transdermal clonidine administration due to a more gradual reduction in drug concentrations.

Precautions:

- Safety and efficacy are not established in children under the age of 6.
- Only contraindication is a proven allergy to clonidine.
- Use with caution in patients with renal impairment (possibly reduce dose), hepatic impairment, and cardiac impairment (particularly severe coronary insufficiency, conduction disturbances, recent MI, or cerebrovascular disease).

Pharmacokinetics and Drug Interactions:

- Half-life of IR formulation is 12-16 hours in adults; similar is observed for ER in adults.
- Metabolized by the liver (substrate of CYP2D6); excreted renally
- Increased depressive and sedative effects when taken with other CNS depressants

Clinical Pearls:

- Blood pressure and pulse should be measured at baseline and monitored following dose increases and periodically during treatment.
- For ADHD, it can take a few weeks to see maximum therapeutic benefits. Effects may be less robust than stimulants; however, may add to the efficacy of stimulants when used in combination.
- These meds may be helpful in targeting aggressive, impulsive, and oppositional behaviors associated with ADHD.
- Effects are consistent for 2-4 hours minimum. This, however, depends upon the patient and their age, particularly for IR formulation, which is why multiple doses may be needed for consistent clinical results over a 24-hour period.
- Compared to guanfacine, which is more selective for alpha-2a receptors, clonidine binds alpha-2a, -2b, and -2c receptors as well as imidazoline receptors, which may cause more sedation, hypotension, and side effects than guanfacine.
- Always taper when discontinuing; taper in decrements of 0.1 mg every 3-7 days to minimize risk of rebound hypertension.
- For some patients, transdermal patch may need to be switched out sooner (i.e., every 4-6 days) due to minor skin irritation or patch falling off skin.

References:

Clonidine: Drug Information. UpToDate. (n.d.). https://www.uptodate.com/contents/clonidine-drug-information?source=mostViewed_widget#F153510

Stahl, S. M., Grady, M. M., & Muntner, N. (2021). Stahl's essential psychopharmacology: Prescriber's Guide. Cambridge University Press.