
DOPAMINE AGONISTS (Mirapex, Neupro, Requip, Sinemet)

Fact Sheet [G]

Bottom Line:

Dopamine agonists are effective first-line agents for restless legs syndrome (RLS), though rates of problematic impulsive or compulsive behaviors can be high. Reserve carbidopa/levodopa for intermittent use.

FDA Indications:

Parkinson's disease; RLS (except Sinemet, only approved for Parkinson's).

Off-Label Uses:

Treatment-resistant depression; cluster headache.

Dosage Forms:

- **Carbidopa/levodopa tablets (Sinemet, Sinemet CR, [G]):** IR: 10/100 mg, 25/100 mg, 25/250 mg; ER: 25/100 mg, 50/200 mg; ODT: 10/100 mg, 25/100 mg, 25/250 mg.
- **Pramipexole tablets (Mirapex, Mirapex ER, [G]):** IR: 0.125 mg, 0.25 mg, 0.5 mg, 0.75 mg, 1 mg, 1.5 mg; ER: 0.375 mg, 0.75 mg, 1.5 mg, 2.25 mg, 3 mg, 3.75 mg, 4.5 mg.
- **Ropinirole tablets (Requip, Requip XL, [G]):** IR: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg, 5 mg; ER: 2 mg, 4 mg, 6 mg, 8 mg, 12 mg.
- **Rotigotine transdermal patches (Neupro):** 1 mg, 2 mg, 3 mg, 4 mg, 6 mg, 8 mg.

Dosage Guidance:

- Carbidopa/levodopa: Start ½ of 25/100 mg tablet QHS PRN, then increase by ½ tablet every three days as necessary to max three 25/100 mg tablets.
- Pramipexole: Start 0.125 mg taken one to three hours before HS, then double dose Q4–7 days; max 0.5 mg/day.
- Ropinirole: Start 0.25 mg taken one to three hours before HS, then increase to 0.5 mg after two to three days, 1 mg after seven days, then increase by 0.5 mg weekly until 3 mg/day, then increase by 1 mg/day to maximum 4 mg/day if necessary.
- Rotigotine transdermal patch: Start 1 mg/24 hours applied QD, can increase by 1 mg/24 hours at weekly intervals to maximum 3 mg/24 hours.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: \$; pramipexole ER: \$\$; rotigotine: \$\$\$\$

Side Effects:

- Most common: Nausea, headache, dizziness, anxiety, insomnia. Newer data suggest nearly half of patients will develop compulsive behaviors (eg, gambling, shopping, eating, sexual activity).
- Serious but rare: Hallucinations, agitation (less common than when treating Parkinson's).
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Dopamine agonist.
- Metabolized primarily by: CYP450 (carbidopa/levodopa, rotigotine), renal elimination (pramipexole), CYP1A2 (ropinirole); t ½: 0.75–1.5 hours (carbidopa/levodopa), 8 hours (pramipexole), 6 hours (ropinirole), 5–7 hours (rotigotine).

Clinical Pearls:

- Avoid rotigotine in patients with sulfite allergies because it contains sodium metabisulfite, which may induce anaphylaxis or respiratory symptoms in sensitive patients. Those with history of asthma have an increased risk of sulfite sensitivity.
- Lower doses are used for RLS compared to Parkinson's (eg, pramipexole max daily dose is 0.5 mg for RLS vs 4.5 mg for Parkinson's).
- Onset of action: Pramipexole takes effect upon first dose. Ropinirole takes four to 10 days. Rotigotine has onset with first dose but may require up to one week for full effect.
- Caution patients about compulsive behaviors (gambling, shopping, eating). These occur commonly and can be devastating. Lower dose if such behaviors develop or discontinue if severe.
- Pramipexole showed modest efficacy for treatment-resistant depression in a controlled study. Open-label studies suggest it may work in patients who have not responded to electroconvulsive therapy. Start with 0.125–0.25 mg QHS and increase to target dose of 0.75–2 mg QHS.

Fun Fact:

Some Parkinson's patients have experienced an increased sex drive when taking these medications, sparking off-label use of these agents for managing low libido. Mirasex, anyone?