SELEGILINE

**THERAPEUTICS**

**Brands**
- Zelapar, Eldepryl, Emsam

**Generic?**
Yes (as oral)

**Class**
- Monoamine oxidase type B (MAO-B) inhibitor

**Commonly Prescribed for**
*(FDA approved in bold)*
- Parkinson’s disease (PD)
- Major depressive disorder, treatment-refractory (patch only)
- Anxiety disorders
- Alzheimer’s and other dementias
- Migraine

**How the Drug Works**
- Selectively blocks monoamine oxidase type B (MAO-B) and inhibits metabolism of dopamine, increasing its effectiveness. At higher doses, starts to affect MAO-A as well as -B and inhibits metabolism of norepinephrine, serotonin, and tyramine, as well as dopamine

**How Long Until It Works**
- PD – weeks
- Depression, anxiety: usually months

**If It Works**
- PD – may require dose adjustments over time or augmentation with other agents. Most PD patients will eventually require carbidopa-levodopa to manage their symptoms

**If It Doesn’t Work**
- Bradykinesia, gait, and tremor should improve. If the patient has significantly impaired functioning, add carbidopa-levodopa with or without a dopamine agonist

**Best Augmenting Combos for Partial Response or Treatment-Resistance**
- For suboptimal effectiveness, add carbidopa-levodopa with or without a COMT inhibitor or a dopamine agonist

**Tests**
- Monitor for any changes in blood pressure

**ADVERSE EFFECTS (AEs)**

**How Drug Causes AEs**
- Increases concentration of peripheral and CNS dopamine. At higher doses affects serotonin and norepinephrine levels

**Notable AEs**
- Nausea, hallucinations, confusion, lightheadedness, loss of balance, insomnia, orthostatic hypotension, hypertension, weight gain

**Life-Threatening or Dangerous AEs**
- Hypertensive crisis, especially at higher doses that prevent breakdown of tyramine. Tyramine-containing foods include aged cheeses, liver, sauerkraut, cured and processed meats, soy, alcohol (especially chianti wine and vermouth), and avocado

**Weight Gain**
- Common

**Sedation**
- Unusual
What to Do About AEs
- Lower the dose or change to alternative PD medications

Best Augmenting Agents for AEs
- Orthostatic hypotension: adjust dose or stop antihypertensives, add supplemental salt, and consider fludrocortisone or midodrine

DOSING AND USE

Usual Dosage Range
- PD – 10 mg daily, divided into 2 daily doses taken at breakfast and lunch
- Depression – only the transdermal patch is indicated for the treatment of depression

Dosage Forms
- Tablets: 5 mg
- Capsules: 5 mg
- Orally disintegrating tablets: 1.25 mg
- Transdermal patch: 6, 9 or 12 mg per 24 hours

How to Dose
- Regular tablets: Start at 2.5 mg (regular tablets) twice daily (usually at breakfast and lunch) and increase to 5 mg twice a day in a few days if tolerated. After 3–4 days, may attempt to lower dose of carbidopa-levodopa
- Orally disintegrating tablets: Start at 1.25 mg in the morning before breakfast, and increase to 2.5 mg daily if tolerated and desired benefit not achieved
- Transdermal patch: Start at 6 mg per 24 hours. Increase every 2 weeks until desired effect achieved in 3 mg increments to a maximum of 12 mg/day

Dosing Tips
- Take orally disintegrating tablets before breakfast
- At doses above 10 mg, selegiline starts to become less selective and starts to have more MAO-A inhibition. This increases the risk of hypertensive crisis

Overdose
- Symptoms include dizziness, insomnia, hypotension or hypertension, headache, sedation, respiratory depression, and death. Symptoms of overdose can be delayed up to 12 hours, and maximal worsening may not occur until the next day

Long-Term Use
- Safe for long-term use. Effectiveness may decrease over time in PD

Habit Forming
- No

How to Stop
- No need to taper. Drug wears off in 2–3 weeks

Pharmacokinetics
- Orally disintegrating tablets (Tmax 10–15 minutes) have a more rapid absorption and greater bioavailability than the swallowed tablets (Tmax 40–90 minutes). The 2.5 mg disintegrating tablets have an effect similar to 10 mg of the regular tablets. Hepatic metabolism with metabolites, including L-methamphetamine and L-amphetamine. Metabolites are then excreted in the urine

Drug Interactions
- Increases the effect of levodopa, potentially requiring dose adjustments
- Multiple adverse CNS reactions reported when used with meperidine, including convulsions, coma, and death. Do not use meperidine within 2 weeks of drug
- Other analgesics, including methadone, tramadol, propoxyphene, and dextromethorphan, may also cause reactions
- Do not use within 2 weeks of tricyclic antidepressants, SSRIs, or SNRIs due to risk of serotonin syndrome (hyperthermia, myoclonus, rigidity, autonomic instability, mental status changes, or death.) Do not use within 5 weeks of fluoxetine
- Tramadol can increase risk of seizures
- Dopamine antagonists such as phenothiazines, metoclopramide may diminish effectiveness
- Use with caution in patients on antihypertensive medications due to risk of orthostatic hypotension
- At higher, non-selective doses can potentially interact with CNS stimulants due
to amphetamine metabolites. These include intravenous dopamine, norepinephrine and epinephrine, methylphenidate, nasal decongestants, sinus medications, asthma inhalers, diet pills or weight loss treatments, and even levodopa.

**Other Warnings/Precautions**
- Orally disintegrating tablets contain phenylalanine

**Do Not Use**
- Known hypersensitivity to the drug. Patients using meperidine, tricyclic antidepressants, SSRIs, or SNRIs

**SPECIAL POPULATIONS**

**Renal Impairment**
- No known effects

**Hepatic Impairment**
- May require lowering of dose

**Cardiac Impairment**
- No known effects

**Elderly**
- Start at a lower dose with careful titration. More likely to experience AEs

**Children and Adolescents**
- Not studied in children (PD is rare in pediatrics) and not recommended under age 16

**Pregnancy**
- Category C. Use only if benefits of medication outweigh risks

**Breast Feeding**
- Unknown if excreted in breast milk. Do not use

**THE ART OF NEUROPHARMACOLOGY**

**Potential Advantages**
- May delay need for carbidopa-levodopa or allow reduction of dose. Good initial treatment for patients with no cognitive dysfunction and significant disability. Better tolerated (less nausea) than dopamine agonists. May be useful for PD patients with comorbid depression

**Potential Disadvantages**
- Less effective than most PD treatments, including dopamine agonists, for motor dysfunction. Patients with significant motor disability, cognitive impairment, or patients older than 75 will require carbidopa-levodopa. Multiple drug interactions at doses greater than 10 mg limit titration and effectiveness

**Primary Target Symptoms**
- PD – motor dysfunction, including bradykinesia, hand function, gait and rest tremor

**Pearls**
- Well-tolerated adjunctive medication for PD. Favorable long-term AEs
- MAO-Is have drawn interest as possible neuroprotective agents in PD. Selegiline delays the need for levodopa compared to placebo, but this could be due to the symptomatic benefit of the drug. Newer studies of neuroprotection are evaluating rasagiline, another MAO-B inhibitor, which does not have methamphetamine as a metabolite
- May be useful in combination with other agents, such as donepezil, for the treatment of Alzheimer’s dementia
- For depression, use the transdermal patch. For PD, use oral selegiline
- At a dose of 10 mg or less, the drug is selective for MAO-B and dietary restrictions do not come into play
- MAO-I may be useful for the treatment of refractory migraine, but does not appear effective in some patients
Suggested Reading


