MONOAMINE OXIDASE INHIBITORS (MAOIs) Fact Sheet [G]

Bottom Line:
MAOIs are not commonly used due to side effects, dietary restrictions, and drug interactions; however, they should be considered for appropriate patients who do not tolerate or respond to other antidepressants.

FDA Indications:
Major depression.

Off-Label Uses:
Treatment-resistant depression; panic disorder; social anxiety disorder.

Dosage Forms:
- **Isocarboxazid, tablets (Marplan):** 10 mg (scored).
- **Phenelzine, tablets (Nardil, [G]):** 15 mg.
- **Tranylcypromine, tablets (Parnate, [G]):** 10 mg.

Dosage Guidance:
- Isocarboxazid: Start 10 mg BID, ↑ by 10 mg/day every two to four days, to 40 mg/day by end of the first week (divided BID–QID). After first week, may ↑ by up to 20 mg weekly to max 60 mg/day. Use caution in patients on >40 mg/day.
- Phenelzine: Start 15 mg BID, ↑ by 15 mg/day every two to four days, up to 60–90 mg/day divided BID.
- Tranylcypromine: Start 10 mg BID, ↑ by 10 mg/day every two to three weeks to maximum of 60 mg/day divided BID.
- Dose timing: Tranylcypromine is the best tolerated of the MAOIs, but it can be activating, so prescribe it in the morning initially. Since larger doses may cause orthostasis if taken at once, you may need to split up the dose as you titrate up, but the PM dose should be taken no later than noon.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: Isocarboxazid: $$$$$; phenelzine: $; tranylcypromine: $$$

Side Effects:
- Most common: Dizziness, headache, orthostatic hypotension, dry mouth, constipation, drowsiness, tremor, sweating, peripheral edema, sexual side effects, weight gain.
- Serious but rare: Hypertensive crisis (see drug interactions below).
- Tranylcypromine is the best tolerated for most patients.
- Pregnancy/breastfeeding: Generally not recommended.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Non-selective monoamine oxidase inhibitors.
- Metabolized primarily through liver, limited data though likely through oxidative CYP450; t ½ irrelevant as irreversible inhibition effects continue for two weeks after discontinuation.
- Avoid with other antidepressants, serotonergic agents, stimulants, sympathomimetics, dextromethorphan, disulfiram, and meperidine. Do not use within five weeks of fluoxetine discontinuation or two weeks of other antidepressant discontinuation. Discontinue at least 10 days prior to elective surgery. Antihypertensives may exaggerate hypotensive effects.
- Avoid use with foods or supplements high in tyramine, tryptophan, phenylalanine, or tyrosine. Examples include aged cheese, air-dried or cured meats (eg, salami), fava or broad bean pods, tap/draft beers, Marmite concentrate, sauerkraut, soy sauce, or spoiled foods.
- See Table A3 in Appendix A for more information on diet and drug interactions with MAOIs.

Clinical Pearls:
- Studies in the 1970s and 1980s showed that MAOIs were more effective than TCAs for atypical depression, characterized by overeating, oversleeping, rejection sensitivity, and mood reactivity.
- Rough dose equivalents: 20 mg of tranylcypromine = 40 mg of isocarboxazid = 45 mg phenelzine.
- When switching from an MAOI to another antidepressant, wait two weeks after MAOI discontinuation. This is because monoamine enzymes are irreversibly inhibited by MAOIs, and regeneration of enzymes takes two to three weeks after discontinuation.

Fun Fact:
MAOIs were the first antidepressants developed, after tuberculosis patients given the antibacterial agent isoniazid (INH) were found to have an elevated mood. Isoniazid was found to be an MAOI and was developed as the first antidepressant in the late 1950s.