MONOAMINE OXIDASE INHIBITOR

Tranylcypromine

Parnate

Activating irreversible MAO inhibitor with amphetamine-like structure, reserved for treatment-resistant depression under strict dietary control.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
30-60 mg/day PO divided	1.5-3.2 h; MAO recovery 2 wks	Oxidation; renal excretion	2-4 wks; 6 wks full effect

⚠ FDA BOXED WARNING

Hypertensive crisis: sometimes fatal crises can occur with tyramine-rich food or beverages and with interacting drugs; monitor blood pressure and enforce dietary restrictions. Suicidal thoughts and behaviors: antidepressants increased risk in children, adolescents, and young adults; monitor closely early in treatment.

INDICATIONS

- FDA-approved for the treatment of major depressive disorder without melancholia in adults who have not responded to other therapy.
- The label restricts use to patients in whom other antidepressant treatments have failed, reflecting the required dietary vigilance.
- Off-label for treatment-resistant bipolar depression, where its activating profile can help anergic and hypersomnic presentations.
- Off-label for social anxiety disorder and panic disorder after first-line and second-line pharmacotherapy have proved inadequate.
- Often chosen over phenelzine when sedation and weight gain would be unacceptable, since it is stimulating rather than sedating.
- Not approved for pediatric use; safety and effectiveness in patients under 18 years have not been established.

DOSING & TITRATION

- Start **30 mg/day PO in divided doses**, typically 20 mg in the morning and 10 mg in the afternoon to limit insomnia.
- If there is no response after 2 weeks, increase by **10 mg/day** at intervals of 1 to 3 weeks up to the maximum of **60 mg/day**.
- Avoid dosing after mid-afternoon because the activating effect commonly produces initial insomnia and agitation.
- Supplied only as 10 mg tablets; the tyramine-restricted diet begins with the first dose and continues 2 weeks past the last dose.
- Some experts exceed 60 mg/day in refractory cases, but this is off-label and requires intensive blood pressure monitoring.
- Taper gradually when stopping and observe a **14-day washout** before any serotonergic or sympathomimetic agent is started.

MECHANISM OF ACTION

- Irreversibly inhibits both MAO-A and MAO-B, so monoamine oxidase activity recovers only through new enzyme synthesis over roughly 2 weeks.
- Structurally a cyclopropylamine analogue of amphetamine, which gives it mild releasing and reuptake-inhibiting properties beyond enzyme blockade.
- These amphetamine-like actions explain the activating profile, the potential for insomnia, and occasional reports of misuse at high doses.
- Gut and hepatic MAO-A inhibition abolishes first-pass metabolism of dietary tyramine, allowing pressor amines into the systemic circulation.
- Elevated synaptic serotonin, norepinephrine, and dopamine account for both antidepressant efficacy and the risk of serotonin syndrome.

PHARMACOKINETICS

- Rapidly absorbed with peak plasma concentrations at about 1 to 2 hours; divided daily dosing is used despite the irreversible effect.
- Plasma half-life is only about 1.5 to 3.2 hours, which bears no relation to the duration of pharmacologic action.
- Cleared largely by oxidative metabolism with subsequent renal excretion of metabolites; ring hydroxylation and N-acetylation both occur.
- Enzyme activity returns over approximately 1 to 2 weeks after the last dose, which defines the mandatory washout interval.
- It is a weak inhibitor of CYP2A6 and CYP2C19, though the clinically dominant interactions are pharmacodynamic rather than metabolic.

ADVERSE EFFECTS

- Insomnia and overstimulation are the most characteristic effects and often require the last dose to be moved earlier in the day.
- Orthostatic hypotension is common and dose limiting despite the stimulant profile, and it contributes to falls in older adults.
- Hypertensive crisis presents with severe occipital headache, palpitations, neck stiffness, nausea, sweating, and photophobia.
- Serotonin syndrome with hyperthermia, clonus, rigidity, and autonomic instability can be fatal when serotonergic drugs are combined.
- Weight gain is less than with phenelzine, but sexual dysfunction, dry mouth, and edema remain frequent complaints.
- Rare hepatocellular injury, and abuse or dependence at supratherapeutic doses, have both been described with this agent.

MONITORING

- Measure supine and standing blood pressure at every visit and instruct the patient in home monitoring during titration.
- Provide written tyramine dietary instructions before the first dose and reinforce that they continue 2 weeks after stopping.
- Teach the patient to seek emergency care for sudden severe headache, chest pain, or palpitations rather than self-treating.
- Review every prescription, over-the-counter product, and supplement at each visit, since new agents drive most serious events.
- Obtain baseline liver enzymes and recheck if malaise, anorexia, or jaundice develops during long-term treatment.

INTERACTIONS & CAUTIONS

- Contraindicated with SSRIs, SNRIs, tricyclics, triptans, tramadol, meperidine, linezolid, methylene blue, and St. John's wort.
- Contraindicated with all sympathomimetics including pseudoephedrine, phenylephrine, amphetamines, and with dextromethorphan and buspirone.
- Requires a **14-day washout** in both directions for most antidepressants, and a **5-week washout** after stopping fluoxetine.
- Contraindicated in pheochromocytoma, cerebrovascular disease, cardiovascular disease, and significant hepatic impairment.
- Avoid meperidine absolutely; morphine, fentanyl, and hydromorphone are the preferred opioids when analgesia is unavoidable.

SPECIAL POPULATIONS

- Human pregnancy data are very limited and the drug crosses the placenta; alternatives are preferred unless the depression is refractory.
- Lactation data are essentially absent, so breastfeeding is generally discouraged during treatment with this agent.
- Safety and effectiveness in patients under 18 years have not been established, and pediatric use is not recommended.
- Older adults are at higher risk of orthostatic hypotension and falls; start at **10 mg daily** and increase very gradually.
- Contraindicated in hepatic disease; use cautiously with renal impairment because metabolites are renally eliminated.

PRESCRIBING PEARLS

- The most activating MAOI; keep the last dose before mid-afternoon to protect sleep.
- Less weight gain and sedation than phenelzine, but the same absolute diet and drug restrictions.
- Hypertensive crisis is a boxed warning here, not just a precaution.

References

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NOTE

References follow APA 7th edition style. Dosing, boxed warnings, and interaction data change; confirm every clinical decision against the current FDA prescribing information (DailyMed) and your institution's formulary. This sheet is an educational quick reference and does not replace the full label or clinical judgment.