MONOAMINE OXIDASE INHIBITOR

Selegiline (Transdermal)

Emsam

Transdermal MAO inhibitor that bypasses gut MAO-A, so the 6 mg/24 h patch needs no tyramine diet while higher strengths still do.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
6-12 mg/24 h transdermal	18-25 h; patch worn 24 h	CYP2B6, CYP2C19, CYP3A4	2-4 wks; 6 wks full effect

⚠ FDA BOXED WARNING

Suicidal thoughts and behaviors: antidepressants increased the risk in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders. Monitor closely for clinical worsening and emergence of suicidality; safety and effectiveness in pediatric patients have not been established.

INDICATIONS

- FDA-approved for the treatment of major depressive disorder in adults, delivered as a once-daily transdermal system.
- Practical option for patients who need MAO inhibition but cannot reliably follow a tyramine-restricted diet at the 6 mg strength.
- Off-label for treatment-resistant depression, atypical depression, and depression with prominent anergia and hypersomnia.
- Off-label for social anxiety disorder, extrapolating from oral MAO inhibitor evidence rather than transdermal trial data.
- Oral selegiline is approved for Parkinson disease, but the transdermal system is not indicated or dosed for that condition.
- Safety and effectiveness in pediatric patients have not been established, and pediatric trials did not demonstrate efficacy.

DOSING & TITRATION

- Start at **6 mg/24 h** applied to dry intact skin on the upper torso, upper thigh, or outer upper arm, and change the patch daily.
- Increase in **3 mg/24 h** increments no more often than every 2 weeks, to a maximum of **12 mg/24 h** in adults.
- No dietary tyramine restriction is required at **6 mg/24 h**; a tyramine-restricted diet is mandatory at 9 and 12 mg/24 h.
- Rotate application sites daily and do not reapply to the same site for several days to limit local skin reactions.
- In older adults or those with hepatic or renal impairment, remain at **6 mg/24 h** unless a higher dose is clearly needed.
- Discontinue at least 10 days before elective surgery, and observe a **14-day washout** before any serotonergic agent is started.

MECHANISM OF ACTION

- Irreversibly inhibits MAO-A and MAO-B in the brain, raising synaptic serotonin, norepinephrine, and dopamine as with oral MAO inhibitors.
- Transdermal delivery bypasses the gastrointestinal tract, so intestinal MAO-A remains largely intact and dietary tyramine is still degraded.
- That preserved gut metabolism is why the **6 mg/24 h** patch requires no dietary tyramine restriction in the current US label.
- At **9 and 12 mg/24 h** the higher systemic exposure begins to inhibit gut MAO-A, so a tyramine-restricted diet becomes mandatory.
- Selegiline is selective for MAO-B at low oral doses, but the concentrations achieved transdermally inhibit both isoenzymes centrally.

PHARMACOKINETICS

- About 25 to 30 percent of the patch content is absorbed over 24 hours, giving far higher systemic exposure than an equal oral dose.
- Elimination half-life is roughly 18 to 25 hours, and steady state is reached after approximately 5 days of daily patch changes.
- Metabolized by CYP2B6, CYP2C19, and CYP3A4 to N-desmethylselegiline, l-amphetamine, and l-methamphetamine.
- Those amphetamine metabolites can cause a positive amphetamine result on urine drug immunoassays and require confirmatory testing.
- Heat sources such as heating pads, saunas, and prolonged direct sun over the patch can increase absorption and should be avoided.

ADVERSE EFFECTS

- Application site reactions occur in roughly 24 percent of patients versus 12 percent with placebo and are the most common complaint.
- Headache, insomnia, diarrhea, dry mouth, and dyspepsia are the other frequent adverse events reported in registration trials.
- Orthostatic hypotension occurs but is less prominent than with oral phenelzine or tranylcypromine at comparable efficacy.
- Sexual dysfunction and weight gain are notably less frequent than with oral MAO inhibitors or with SSRIs at usual doses.
- Hypertensive crisis can still occur if a contraindicated sympathomimetic or serotonergic agent is added, regardless of patch strength.
- Serotonin syndrome remains a fatal risk with concurrent serotonergic drugs and is not mitigated by transdermal delivery.

MONITORING

- Check blood pressure supine and standing at each visit, particularly during titration above the **6 mg/24 h** starting strength.
- Confirm and document dietary counseling whenever the dose is raised to 9 or 12 mg/24 h, since restrictions then apply.
- Inspect application sites and rotate them daily; persistent dermatitis may require topical treatment or discontinuation.
- Review all prescription, over-the-counter, and herbal products at every visit because pharmacodynamic interactions drive serious harm.
- Warn patients and testing programs that urine immunoassays may read positive for amphetamine because of metabolite formation.

INTERACTIONS & CAUTIONS

- Contraindicated with SSRIs, SNRIs, tricyclics, bupropion, mirtazapine, meperidine, tramadol, methadone, and St. John's wort.
- Contraindicated with carbamazepine, oxcarbazepine, cyclobenzaprine, dextromethorphan, linezolid, methylene blue, and buspirone.
- Requires a **14-day washout** in both directions with most antidepressants and a **5-week washout** after stopping fluoxetine.
- Contraindicated with sympathomimetic amines including pseudoephedrine, phenylephrine, amphetamines, and with pheochromocytoma.
- Avoid tyramine-rich foods entirely at 9 and 12 mg/24 h, and avoid supplements containing tyramine or phenylalanine at any dose.

SPECIAL POPULATIONS

- Human pregnancy data are limited; animal studies show developmental toxicity, so use only if the benefit clearly outweighs the risk.
- Lactation data are essentially absent and the amphetamine metabolites raise theoretical concern, so alternatives are preferred.
- Pediatric trials did not establish efficacy, and adolescents carry the class suicidality warning if the drug is used off-label.
- In adults 65 and older, exposure is higher and the label advises maintaining the **6 mg/24 h** dose rather than escalating.
- No specific renal or hepatic dose adjustment is defined, but mild to moderate impairment raises exposure and argues for the lowest strength.

PRESCRIBING PEARLS

- Only the **6 mg/24 h** patch is diet-free; 9 and 12 mg/24 h require full tyramine restriction.
- Metabolites can trigger a positive urine amphetamine screen; confirm with mass spectrometry.
- Stop the patch at least 10 days before elective surgery involving general anesthesia.

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.