Antidepressant crosstaper matrix

FROM and TO with method, overlap, and watchouts. Plus MAOI washout rules. Reviewed against current guidelines as of June 8, 2026.

Three patterns cover almost every antidepressant switch. Direct switch (stop one, start the next day). Cross-taper (overlap with opposite dose adjustments). Wash and switch (fully discontinue, then start). Default when unsure: cross-taper over 1 to 2 weeks. It's rarely wrong.

The switching matrix

FROM	TO	Method	Overlap approach	Watchouts
SSRI	Different SSRI	Direct or short cross-taper	Same day or 3 to 7 day overlap	Watch for serotonin syndrome if both high dose
SSRI	SNRI	Direct or short cross-taper	3 to 7 days at reduced doses	Blood pressure at SNRI titration
SSRI	Bupropion	Cross-taper or wash	Bupropion starts after SSRI reduced	Anxiety re-emergence with bupropion
SSRI	Mirtazapine	Direct or overlap	Overlap safe (California rocket fuel evidence)	Sedation, weight
SSRI	TCA	Cross-taper	Fluoxetine and paroxetine raise TCA levels via 2D6	TCA levels can rise sharply
SSRI	MAOI	Wash	14 days (5 weeks for fluoxetine)	Serotonin syndrome
SSRI	Vortioxetine	Direct or short cross-taper	3 to 7 day overlap	Nausea common
SNRI	SSRI	Cross-taper	1 to 2 weeks (venlafaxine discontinuation)	Discontinuation from venlafaxine, duloxetine
SNRI	Different SNRI	Direct if equipotent	Venlafaxine to duloxetine: usually direct	Watch BP
SNRI	Bupropion	Cross-taper	Reduce SNRI first	Venlafaxine discontinuation
SNRI	Mirtazapine	Direct or overlap	Overlap safe	Sedation
SNRI	MAOI	Wash	14 days	Serotonin syndrome
Paroxetine	Anything	Cross-taper, slowly	Reduce paroxetine over 2 to 4 weeks	Severe discontinuation syndrome
Fluoxetine	Anything	Direct or short cross-taper	Self-tapers due to long half-life	5-week wait before MAOI; 2D6 lingers

Fluoxetine	Fast 2D6 substrate (TCA, atomoxetine)	Cross-taper carefully	2D6 inhibition persists weeks after stopping	Watch TCA or atomoxetine levels
TCA	SSRI	Cross-taper	Reduce TCA over 1 to 2 weeks	Fluoxetine or paroxetine raise TCA via 2D6
TCA	MAOI	Wash	14 days	Serotonin syndrome, hypertensive crisis
Bupropion	Anything	Direct	Bupropion has minimal discontinuation issues	Anxiety re-emergence if it was covering
Mirtazapine	Anything	Direct or overlap	Easy to overlap safely	Sedation carry-over if abrupt
MAOI	Anything serotonergic	Wash	14 days	Serotonin syndrome
MAOI	Different MAOI	Wash	14 days (enzyme regeneration)	
Vortioxetine	SSRI or SNRI	Direct or short overlap	Vortioxetine half-life 66 hours	Nausea if incoming drug titrated fast
Vilazodone	SSRI	Direct	Vilazodone half-life 25 hours	Take with food matters for vilazodone

MAOI washout rules

Direction	Rule
Before starting an MAOI, after stopping most SSRIs, SNRIs, TCAs, mirtazapine	Wait 14 days
Before starting an MAOI, after stopping fluoxetine	Wait 5 weeks (norfluoxetine t1/2 7 to 15 days)
Before starting an MAOI, after stopping another MAOI	Wait 14 days (enzyme regeneration)
Before starting an MAOI, after stopping bupropion	At least 24 hours; some sources 14 days
Never combine with an active MAOI	Meperidine, tramadol, dextromethorphan, linezolid, methylene blue
Before starting a serotonergic drug after an MAOI	Wait 14 days after last MAOI dose
Selegiline transdermal 6 mg per 24 hr	No dietary restrictions, but same 14-day washouts apply

Special cases worth calling out

- Paroxetine to anything. Discontinuation is intense: nausea, dizziness, brain zaps, flu-like symptoms. Cross-taper over 2 to 4 weeks. Consider liquid formulation at the low end. If incoming drug is bupropion, expect discontinuation to happen even during overlap.
- Venlafaxine to duloxetine. Usually direct: venlafaxine 150 XR to duloxetine 60 next day. Watch BP.
- TCA to fluoxetine or paroxetine. 2D6 inhibition raises TCA levels 2 to 4-fold. Check a level first, reduce TCA meaningfully, or pick sertraline, citalopram, or escitalopram.

- Serotonin syndrome risk during overlap. At typical doses, well-tolerated. Warning signs: agitation, diaphoresis, hyperreflexia, clonus (especially lower extremity), tremor, tachycardia, GI symptoms. If clonus, temp over 38C, or altered mental status: stop both and treat.

Not medical advice.