



## Appendix D: Switching Antidepressants

Switching antidepressants can be accomplished by the following strategies:

1. **Direct switch:** stop the first antidepressant abruptly and start new antidepressant the next day.
2. **Taper & switch immediately:** gradually taper the first antidepressant, then start the new antidepressant immediately after discontinuation.
3. **Taper & switch after a washout:** gradually withdraw the first antidepressant, then start the new antidepressant after a washout period.
4. **Cross-tapering:** taper the first antidepressant (usually over 1-2 week or longer), and build up the dose of the new antidepressant simultaneously.

The following table is intended for general guidance only. Whichever strategy is used, patients should be closely monitored for symptoms and adverse events. The duration of tapering should be determined individually for each patient. Physicians should balance the risk of discontinuation symptoms versus risk of delay in new treatment. The washout period is mostly dependent on the  $t_{1/2}$  of the first drug.

Switching From	To →	SSRIs (except fluoxetine)	Fluoxetine	SNRIs	NDRI (bupropion)	NaSSA (mirtazapine)	RIMA (moclobemide)	TCA
SSRIs (except fluoxetine)	→	Taper & stop, then start new SSRI at a low dose <sup>1,†</sup>	Taper & stop, then start fluoxetine at low dose (10 mg daily) <sup>1,†</sup>	Taper & stop <sup>5</sup> (or to low dose), <sup>1</sup> then start low dose SNRI & ↑ very slowly. <sup>1,3,5,†</sup>	Taper & stop <sup>5</sup> (or to low dose), <sup>2</sup> then start bupropion.	Taper & stop <sup>5</sup> (or to low dose), <sup>1</sup> then start mirtazapine cautiously.	Taper & stop, wait 1 week, then start moclobemide. <sup>1,5</sup>	Cross-taper cautiously with very low dose TCA. <sup>1,3,5,§</sup>
Fluoxetine*	→	Stop fluoxetine, wait 4-7 days. Start the new SSRI at low dose & ↑ slowly. <sup>1,2,5</sup>		Stop fluoxetine, wait 4-7 days. Start with low dose SNRI & ↑ very slowly. <sup>3,5</sup>	Stop fluoxetine, wait 4-7 days. Start bupropion. <sup>5</sup>	Stop fluoxetine, wait 4-7 days, then start mirtazapine cautiously. <sup>5</sup>	Stop fluoxetine, wait 5 weeks, start moclobemide. <sup>3,5</sup>	Stop fluoxetine, wait 4-7 days. Start TCA at very low dose & ↑ very slowly. <sup>1,5,§</sup>
SNRIs	→	Cross-taper cautiously with low dose of SSRI. <sup>1,5</sup>	Cross-taper cautiously with low dose of fluoxetine. <sup>1,5</sup>	Taper & stop, then start new SNRI. <sup>1</sup>	Taper & stop (or to low dose), then start bupropion cautiously. <sup>5</sup>	Cross-taper cautiously. <sup>1</sup>	Taper & stop, wait 1 week, then start moclobemide. <sup>1,5</sup>	Cross-taper cautiously with very low dose of TCA. <sup>1,5,§</sup>
NDRI (bupropion)	→	Taper & stop, then start SSRI (consider lower starting dose). <sup>4,5</sup>	Taper & stop, then start fluoxetine (consider lower starting dose). <sup>4,5</sup>	Taper & stop, then start SNRI at low dose & ↑ slowly. <sup>4,5</sup>		Taper & stop, then start mirtazapine cautiously (consider lower starting dose). <sup>4,5</sup>	Taper & stop, wait 1 week, then start moclobemide. <sup>5</sup>	Taper & stop, then start TCA at a low dose & ↑ slowly. <sup>5</sup>
NaSSA (mirtazapine)	→	Taper & stop <sup>5</sup> (or to low dose), <sup>1</sup> then start SSRI cautiously.	Taper & stop <sup>5</sup> (or to low dose), <sup>1</sup> then start fluoxetine cautiously.	Taper & stop <sup>5</sup> (or to low dose), <sup>1</sup> then start SNRI cautiously.	Taper & stop, then start bupropion cautiously. <sup>5</sup>		Taper & stop, wait 1 week, then start moclobemide. <sup>1</sup>	Taper & stop <sup>5</sup> (or to low dose), <sup>1</sup> then start cautiously with low dose of TCA.
RIMA (moclobemide)	→	Taper & stop, wait 24 hours, start SSRI. <sup>1,5</sup>	Taper & stop, wait 24 hours, start fluoxetine. <sup>1,5</sup>	Taper & stop, wait 24 hours, start SNRI. <sup>1,5</sup>	Taper & stop, wait 24 hours, start bupropion. <sup>1,5</sup>	Taper & stop, wait 24 hours, start SNRI. <sup>1,5</sup>		Taper & stop, wait 24 hours, start TCA. <sup>1,5</sup>
TCA	→	Gradually ↓ dose by up to 50% & start SSRI at normal starting dose, then slowly withdraw TCA over few weeks. <sup>1,5,§</sup>	Gradually ↓ dose by up to 50% & start fluoxetine at normal starting dose, then slowly withdraw TCA over few weeks. <sup>1,5,§</sup>	Cross-taper cautiously, start with low dose SNRI. <sup>1,5</sup>	Taper & stop <sup>4</sup> (or to low dose), <sup>5</sup> then start bupropion cautiously.	Taper & stop (or to low dose), <sup>1,5</sup> then start mirtazapine cautiously.	Taper & stop, wait 1 week, then start moclobemide. <sup>1</sup>	Cross-taper cautiously <sup>1,5</sup> (switching is of questionable benefit). <sup>4</sup>

**Abbreviations:** mg milligrams; **NaSSA** noradrenergic/specific serotonergic antidepressant; **NDRI** norepinephrine dopamine reuptake inhibitor; **RIMA** reversible inhibitor of monoamine oxidase A; **SNRI** serotonin norepinephrine reuptake inhibitor; **SSRI** selective serotonin reuptake inhibitor; **TCA** tricyclic antidepressants.

**Footnotes:**

\* Exercise particular caution when switching from fluoxetine to other antidepressant. Significant concentrations of fluoxetine or its active metabolite may be present for 5 weeks after stopping.<sup>1,3,5</sup>

† Direct switching may also be possible, but precise equivalent doses of SSRIs and SNRIs have not been established.<sup>2,3,5</sup>

‡ Fluvoxamine (CYP450 1A2 inhibitor), paroxetine and fluoxetine (CYP450 2D6 inhibitors) can cause ↑TCA blood levels for several weeks.<sup>3,5</sup>

§ Do not co-administer clomipramine with SSRIs or SNRIs.<sup>1,5</sup>

**References**

1. Luft B. Antidepressant switching strategies. Graylands Hospital Drug Bulletin North Metropolitan Health Services - Mental Health. 2013;20(1).
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