

# Switching Antidepressants

There are instances where a particular antidepressant medication will need to be discontinued despite the continued need for treatment. This happens when the medication is not effective, the patient is unable to tolerate its side effects, or in the presence of significant drug-drug interactions.

Identifying the need to switch to another agent is easier if there are intolerable side effects or drug-drug interactions, but it is sometimes not as clear in the case of a poor antidepressant effect. After ensuring that the patient has been adherent to an adequate dose of the medication, non-response is defined as  $\leq 25\%$  decrease in symptom severity compared to baseline, and a partial response as 26-49% decrease. This can be measured using rating scales like the PHQ-9 for depression or the GAD-7 for generalized anxiety, or directly asking the patient *“How much do you think you have improved as a percentage since you started taking your medication?”*

There are three ways of doing a switch: a direct switch, a cross-taper, or a gradual discontinuation with a wash-out period. It is important to consider the risk of drug-drug interactions, discontinuation symptoms, risk of relapse, and patient preferences.

## Direct switch

The initial medication is stopped and an equivalent dose of the second medication is started the following day. When switching from a high dose an initial gradual reduction of the first agent should be followed by a direct switch after a moderate dose has been approached.

## Cross-taper

The dose of the initial medication is gradually reduced to zero while the new antidepressant is initiated at a low dose and slowly increased to a therapeutic one. The gradual discontinuation can be done either by percentage of dose (25-50% of dose reduction in every interval) or a fixed milligram amount (e.g. for fluoxetine 10-20mg reduction in every interval).

## Gradual discontinuation with a wash-out period

The dose of the initial antidepressant is gradually lowered, and after a wash-out period, a new agent is started and slowly increased to a therapeutic dose. The duration of the wash-out depends on the half-life of the initial antidepressant, which is usually 5 days (longer for fluoxetine and MAIOs).



Direct switch	Cross-taper	Discontinuation with wash-out
<p>Only an alternative when switching <i>within a class</i> from and to SSRIs or SNRIs, or <i>out of class</i> from SSRIs to SNRIs or from SNRIs to SSRIs.</p>	<p>An alternative for most medication switches <i>within a class</i> and <i>out of a class</i>, except switches involving MAOIs.</p>	<p>If switching from MAOIs, a strict 2 weeks washout period is essential to minimize the risk of developing serotonin syndrome.</p>
<p><b>DAY 1:</b> Escitalopram 10mg</p> <p><b>DAY 2:</b> Start sertraline 50mg</p> <p><b>From a high dose:</b></p> <p><b>INITIAL DOSE:</b> Escitalopram 20mg</p> <p><b>WEEK 1:</b> Escitalopram 15mg</p> <p><b>WEEK 2:</b> Escitalopram 10mg Direct switch at the end of week 2</p>	<p><b>INITIAL DOSE:</b> Mirtazapine 45mg</p> <p><b>WEEK 1:</b> Mirtazapine 30mg + escitalopram 5mg</p> <p><b>WEEK 2:</b> Mirtazapine 15mg + escitalopram 10mg</p> <p><b>WEEK 3:</b> Discontinue mirtazapine + continue escitalopram 10mg or increase to 15 or 20mg</p>	<p><b>INITIAL DOSE:</b> Bupropion XL 450mg</p> <p><b>WEEK 1:</b> Bupropion XL 300mg</p> <p><b>WEEK 2:</b> Bupropion XL 150mg</p> <p><b>WEEK 3:</b> discontinue bupropion</p> <p><b>WEEK 4:</b> Venlafaxine 37.5mg and continue titrating accordingly</p>

In summary, not all switching strategies are an option depending on the medications involved. When presenting and discussing alternatives with our patients, special attention should be given to the risks of drug-drug interactions, side effects, withdrawals and relapses so they can make a more informed decision.

**References:**

1. Boyce, P. et al. Switching antidepressants in the treatment of major depression: When, how and what to switch to?. *Journal of Affective Disorders* 2020, 261:160-163
2. Ogle, N., Akkerman, S. Guidance for the discontinuation or switching of antidepressant therapies in adults. *Journal of Pharmacy Practice* 2013, 26(4):389-96