Using the New Zealand Formulary: Guide for switching antidepressants

In most cases, selective serotonin re-uptake inhibitors (SSRIs) are the first-line pharmacological treatment for depression. They are better tolerated and have a wider safety margin than tricyclic antidperessants (TCAs) and irreversible non-selective monoamine oxidase inhibitors (MAOIs). However, choice of antidepressant is also based on individual patient factors, and different medicines may need to be trialled to find the most effective and well-tolerated treatment.

Improvement in symptoms is usually seen within two weeks of starting an antidepressant at a therapeutic dose. If after approximately four weeks (or longer), there is no response or only minimal improvement, changing to a different antidepressant may be considered, along with adding or changing psychological therapies. Switching antidepressants may also be considered if the maximum dose of an antidepressant has been reached, with no further improvement in symptoms, or if adverse effects of a particular antidepressant cannot be tolerated.

There is no particular method in choosing which antidepressant to switch to, however, often switching to a medicine within the same class is tried, before switching to a medicine from a different antidepressant class. Patients should be very carefully monitored when switching, and should be assessed on an individual basis to determine how quickly a switch can be performed.

Factors to take into consideration when changing antidepressants include:

- The patient's severity of illness and the urgency of switching
- Co-morbidities
- Concurrent medicines; serotonin syndrome is more likely to occur if the patient is taking other medicines with serotonergic activity, e.g. triptans, pethidine, tramadol, lithium
- Current dose of antidepressant
- Duration of antidepressant treatment (if less than six weeks it may be possible to stop the antidepressant abruptly)
- The need for a "washout period" (antidepressant-free interval) to avoid interactions
- Tapering of doses, e.g. slowly reducing higher doses of an antidepressant before switching to a new antidepressant, which is started at a low dose and increased as required
- History of discontinuation reactions and management of discontinuation syndrome, should it occur. Symptoms may include dizziness, nausea, anxiety, vivid dreams and headache with SSRIs, and cholinergic rebound (hypersalivation, abdominal cramping, diarrhoea and sleep disturbance) with TCAs.

For further information see: "Pharmacological management of depression in adults", Best Practice Special Edition, July 2009.

A comprehensive table on how to safely and effectively switch between antidepressants is available in Section 4.3 ("Antidepressant drugs") of the New Zealand Formulary (NZF).

This table can be found by clicking on Section 4.3 in the left-hand navigation panel of the NZF. A "printer friendly" PDF version can also be downloaded.

Available from: **nzf.org.nz/nzf/resource/Antidepressant_Switching_Table.pdf**

Short acting SSRIs including citalopram, escitalopram, paroxetine and sertraline can generally be stopped without tapering, and a different SSRI started the next day.

Discontinuation symptoms are unlikely because SSRIs have the same mechanism of action, and any effects will be covered by the new SSRI, which should be started at a low dose.

Fluoxetine has a longer half-life than other SSRIs. Discontinuation symptoms are unlikely with fluoxetine, however, more vigilance is required when changing from this medicine. A four to seven day wash-out period is recommended to allow concentrations of fluoxetine and its active metabolite to decrease.

MAOIs and moclobemide should never be adminstered with another antidepressant, and clomipramine should never be administered with SSRIs or venlafaxine.

Antidepressant Switching Table

Changing from \ Changing to	short-acting SSRI [a]	fluoxetine	TCAs [b]	venlafaxine	mirtazapine (or mianserin)	bupropion	moclobemide	irreversible nonselective MAOIs [c]
short-acting SSRIs [a]	Stop 1st SSRI [d] then start 2nd SSRI the following day	Stop 1st SSRI [d] then start fluoxetine	Cross taper cautiously with very low dose TCA [f] [g]	Stop SSRI [d] then start venlafaxine the next day at 37.5mg/day and increase very slowly	Withdraw before starting mirtazapine cautiously	Withdraw then start bupropion	Withdraw, wait 1 week, start moclobemide	Withdraw and wait 1 week
fluoxetine [h]	Stop fluoxetine, wait 4-7 days, start SSRI at low dose [e]	—	Stop fluoxetine, wait 4-7 days, start TCA at very low dose and increase very slowly [f][g]	Stop fluoxetine, wait 4-7 days, start venlafaxine at 37.5mg/day and increase very slowly	Stop fluoxetine, wait 4-7 days, start mirtazapine cautiously	Stop fluoxetine, wait 4-7 days, start bupropion	Stop fluoxetine, wait 5 weeks, start moclobemide	Stop fluoxetine and wait 5 weeks [h]
TCAs [b]	Halve dose, add SSRI, then slowly withdraw TCA [g]	Halve dose, add fluoxetine, then slowly withdraw TCA [g]	Cross taper cautiously	Cross taper cautiously starting with venlafaxine 37.5mg/day [g]	Withdraw, start mirtazapine cautiously	Cross taper cautiously	Withdraw, wait 7 days, start moclobemide	Withdraw and wait 7 days
venlafaxine	Cross taper cautiously starting with low dose SSRI [e]	Cross taper cautiously starting with fluoxetine 20mg on alternate days	Cross taper cautiously with very low dose TCA [g]	—	Withdraw, start mirtazapine cautiously	Withdraw, start bupropion cautiously	Withdraw, wait 7 days, start moclobemide	Withdraw and wait 7 days
mirtazapine/ mianserin	Withdraw then start SSRI	Withdraw then start fluoxetine	Withdraw then start TCA	Withdraw then start venlafaxine	—	Withdraw, start bupropion cautiously	Withdraw, wait 7 days, start moclobemide	Withdraw and wait 7 days
bupropion	Withdraw then start SSRI	Withdraw then start fluoxetine	Withdraw then start TCA at a low dose.	Withdraw, start venlafaxine at 37.5mg and increase slowly	Withdrawn, start mirtazapine cautiously	—	Withdraw, wait 7 days, start moclobemide	Withdraw and wait 7 days
moclobemide	Withdraw, wait 24 hours, start SSRI	Withdraw, wait 24 hours, start fluoxetine	Withdraw, wait 24 hours, start TCA	Withdraw, wait 24 hours, start venlafaxine	Withdraw, wait 24 hours, start mirtazapine	Withdraw, wait 24 hours, start bupropion	—	Withdraw and wait 24 hours
irreversible nonselective MAOIs	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks	Withdraw and wait 2 weeks

[a] Short-acting SSRIs are citalopram, escitalopram, paroxetine, and sertraline.
[b] TCAs are amitriptyline, clomipramine (refer to note g), dothiepin, doxepin, imipramine, nortriptyline, trimipramine.
[c] Irreversible nonselective MAOIs (phenelzine or tranylcypromine) should be commenced with caution after all other antidepressants because of the risk of hypertensive crisis and serotonin toxicity. Allowance should be made for the washout period (5 half-lives) and individual patient differences in pharmacokinetics.
[d] Abrupt withdrawal is usually possible, however if patients are likely to experience problems with discontinuation symptoms then a slower withdrawal may be required.
[e] Low Dose= citalopram 10mg/day; escitalopram 5mg/day; paroxetine 10mg/day; sertraline 25mg/day; fluoxetine 20mg on alternate days
[f] If changing from paroxetine or fluoxetine, TCA concentration may be elevated for at least several weeks due to persisting SSRI-induced cytochrome P450 inhibition.
[g] Do not co-administer clomipramine with SSRIs or venlafaxine.
[h] Care is required when changing from fluoxetine to another antidepressant as it has a longer half-life than other SSRIs, leading to significant concentrations of fluoxetine or its active metabolite being present for about five weeks after cessation.

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