

Recommended drug-free intervals when changing from one antidepressant to another

For general information on switching between antidepressants, see *Therapeutic Guidelines*.

Changing from [NB1]	Changing to	Drug-free interval
a short-acting SSRI (CITALOPRAM, ESCITALOPRAM, PAROXETINE, SERTRALINE)	a short-acting SSRI (citalopram, escitalopram, paroxetine, sertraline)	nil
	fluvoxamine	nil
	fluoxetine	nil
	vortioxetine	nil
	mianserin, mirtazapine	2 to 4 days
	moclobemide	2 to 4 days [NB4]
	reboxetine	2 to 4 days
	an SNRI (desvenlafaxine, duloxetine, venlafaxine)	2 to 4 days
	a TCA (amitriptyline, clomipramine, dosulepin [dothiepin], doxepin, imipramine, nortriptyline)	2 to 4 days [NB5]
	an irreversible nonselective MAOI [NB2] (phenelzine, tranylcypromine)	1 week
FLUVOXAMINE	agomelatine [NB3]	1 to 2 days
	a short-acting SSRI (citalopram, escitalopram, paroxetine, sertraline)	nil
	fluoxetine	2 to 4 days
	vortioxetine	2 to 4 days
	mianserin, mirtazapine	2 to 4 days
	moclobemide	1 week
	reboxetine	2 to 4 days
	an SNRI (desvenlafaxine, duloxetine, venlafaxine)	2 to 4 days
	a TCA (amitriptyline, clomipramine, dosulepin [dothiepin], doxepin, imipramine, nortriptyline)	2 to 4 days [NB5]
	an irreversible nonselective MAOI [NB2] (phenelzine, tranylcypromine)	1 week
FLUOXETINE [NB6]	agomelatine [NB3]	1 to 2 days
	a short-acting SSRI (citalopram, escitalopram, paroxetine, sertraline)	1 week
	fluvoxamine	2 weeks
	vortioxetine	1 week
	mianserin, mirtazapine	1 week
	moclobemide	1 week
	reboxetine	2 to 4 days
	an SNRI (desvenlafaxine, duloxetine, venlafaxine)	1 week
	a TCA (amitriptyline, clomipramine, dosulepin [dothiepin], doxepin, imipramine, nortriptyline)	2 weeks [NB5]
	an irreversible nonselective MAOI [NB2] (phenelzine, tranylcypromine)	5 weeks
VORTIOXETINE	agomelatine [NB3]	2 to 4 days
	a short-acting SSRI (citalopram, escitalopram, paroxetine, sertraline)	nil
	fluvoxamine	nil
	fluoxetine	nil
	mianserin, mirtazapine	nil
	moclobemide	2 weeks
	reboxetine	nil
	an SNRI (desvenlafaxine, duloxetine, venlafaxine)	nil
	a TCA (amitriptyline, clomipramine, dosulepin [dothiepin], doxepin, imipramine, nortriptyline)	nil
	an irreversible nonselective MAOI [NB2] (phenelzine, tranylcypromine)	3 weeks
	agomelatine [NB3]	nil

Changing from [NB1]	Changing to	Drug-free interval
MIANSERIN or MIRTAZAPINE	a short-acting SSRI (citalopram, escitalopram, paroxetine, sertraline)	2 to 4 days
	fluvoxamine	2 to 4 days
	fluoxetine	2 to 4 days
	vortioxetine	2 to 4 days
	mianserin, mirtazapine	2 to 4 days
	moclobemide	2 to 4 days
	reboxetine	2 to 4 days
	an SNRI (desvenlafaxine, duloxetine, venlafaxine)	2 to 4 days
	a TCA (amitriptyline, clomipramine, dosulepin [dothiepin], doxepin, imipramine, nortriptyline)	2 to 4 days
	an irreversible nonselective MAOI [NB2] (phenelzine, tranylcypromine)	1 week
	agomelatine [NB3]	1 to 2 days
MOCLOBEMIDE [NB7]	a short-acting SSRI (citalopram, escitalopram, paroxetine, sertraline)	1 to 2 days
	fluvoxamine	1 to 2 days
	fluoxetine	1 to 2 days
	vortioxetine	1 to 2 days
	mianserin, mirtazapine	1 to 2 days
	reboxetine	1 to 2 days
	an SNRI (desvenlafaxine, duloxetine, venlafaxine)	1 to 2 days
	a TCA (amitriptyline, clomipramine, dosulepin [dothiepin], doxepin, imipramine, nortriptyline)	1 to 2 days
	an irreversible nonselective MAOI [NB2] (phenelzine, tranylcypromine)	nil
	agomelatine [NB3]	1 to 2 days
REBOXETINE	a short-acting SSRI (citalopram, escitalopram, paroxetine, sertraline)	1 to 2 days
	fluvoxamine	1 to 2 days
	fluoxetine	1 to 2 days
	vortioxetine	1 to 2 days
	mianserin, mirtazapine	1 to 2 days
	moclobemide	1 to 2 days
	an SNRI (desvenlafaxine, duloxetine, venlafaxine)	1 to 2 days
	a TCA (amitriptyline, clomipramine, dosulepin [dothiepin], doxepin, imipramine, nortriptyline)	1 to 2 days
	an irreversible nonselective MAOI [NB2] (phenelzine, tranylcypromine)	1 week
	agomelatine [NB3]	1 to 2 days
an SNRI (DESVENLAFAXINE, DULOXETINE, VENLAFAXINE)	a short-acting SSRI (citalopram, escitalopram, paroxetine, sertraline)	1 to 2 days
	fluvoxamine	1 to 2 days
	fluoxetine	1 to 2 days
	vortioxetine	1 to 2 days
	mianserin, mirtazapine	1 to 2 days
	moclobemide	1 to 2 days
	reboxetine	1 to 2 days
	an SNRI (desvenlafaxine, duloxetine, venlafaxine)	nil [NB8]
	a TCA (amitriptyline, clomipramine, dosulepin [dothiepin], doxepin, imipramine, nortriptyline)	1 to 2 days
	an irreversible nonselective MAOI [NB2] (phenelzine, tranylcypromine)	1 week
	agomelatine [NB3]	1 to 2 days

Changing from [NB1]	Changing to	Drug-free interval
a TCA (AMITRIPTYLINE, CLOMIPRAMINE, DOSULEPIN [DOTHIEPIN], DOXEPIN, IMIPRAMINE, NORTRIPTYLINE)	a short-acting SSRI (citalopram, escitalopram, paroxetine, sertraline)	2 to 4 days
	fluvoxamine	2 to 4 days
	fluoxetine	2 to 4 days
	vortioxetine	2 to 4 days
	mianserin, mirtazapine	2 to 4 days
	moclobemide	clomipramine: 1 week [NB9] other TCAs: 2 to 4 days [NB9]
	reboxetine	2 to 4 days
	an SNRI (desvenlafaxine, duloxetine, venlafaxine)	2 to 4 days
	a TCA (amitriptyline, clomipramine, dosulepin [dothiepin], doxepin, imipramine, nortriptyline)	nil
	an irreversible nonselective MAOI [NB2] (phenelzine, tranylcypromine)	1 week
an irreversible nonselective MAOI (PHENELZINE, TRANYLCYPROMINE)	agomelatine [NB3]	1 to 2 days
	a short-acting SSRI (citalopram, escitalopram, paroxetine, sertraline)	2 weeks
	fluvoxamine	2 weeks
	fluoxetine	2 weeks
	vortioxetine	2 weeks
	mianserin, mirtazapine	2 weeks
	moclobemide	nil [NB10]
	reboxetine	2 weeks
	an SNRI (desvenlafaxine, duloxetine, venlafaxine)	2 weeks
	a TCA (amitriptyline, clomipramine, dosulepin [dothiepin], doxepin, imipramine, nortriptyline)	2 weeks
AGOMELATINE [NB3]	an irreversible nonselective MAOI [NB2] (phenelzine, tranylcypromine)	2 weeks
	agomelatine [NB3]	1 to 2 days
	a short-acting SSRI (citalopram, escitalopram, paroxetine, sertraline)	nil
	fluvoxamine	nil
	fluoxetine	nil
	vortioxetine	nil
	mianserin, mirtazapine	nil
	moclobemide	nil
	reboxetine	nil
	an SNRI (desvenlafaxine, duloxetine, venlafaxine)	nil
	a TCA (amitriptyline, clomipramine, dosulepin [dothiepin], doxepin, imipramine, nortriptyline)	nil
	an irreversible nonselective MAOI [NB2] (phenelzine, tranylcypromine)	1 to 2 days

nil = start the new antidepressant the next day; MAOI = monoamine oxidase inhibitor;
SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin and noradrenaline reuptake inhibitor; TCA = tricyclic antidepressant

NB1: Interpret these recommendations in the context of each patient's situation (eg doses of drugs, concurrent drugs, physical health). Higher doses of antidepressant should generally be reduced before starting the new drug and the new drug should usually be started at a low dose.

NB2: Exercise caution when switching to an irreversible nonselective MAOI because of the risk of severe hypertension, stroke and serotonin toxicity. If necessary, adjust the drug-free interval to accommodate individual patient differences in pharmacokinetics.

NB3: Data on antidepressant-free intervals when changing to and from agomelatine are limited.

NB4: If changing from a low or moderate dose of the short-acting SSRIs (citalopram, escitalopram, paroxetine or sertraline), the dose of moclobemide should not exceed 300 mg daily for the first week. The dose of moclobemide may subsequently be increased if necessary. If changing from a high dose of a short-acting SSRI, seek expert advice.

NB5: The TCA concentration may be elevated for several weeks due to persisting SSRI-induced cytochrome P450 inhibition.

NB6: Because of the long half-life of fluoxetine, clinically relevant concentrations persist for approximately 5 weeks after it is stopped. Exercise caution when changing to another antidepressant.

NB7: The recommended drug-free intervals apply when switching from a low or moderate dose of moclobemide to a low or moderate dose of the new antidepressant—if the patient is treated with a high dose of moclobemide, gradually reduce the dose before switching.

NB8: Because a drug-free interval is not needed when changing from one SNRI to another, cross-tapering or a rapid switch may be used. If switching to duloxetine using one of these methods, start at 30 mg daily and increase the duloxetine dose slowly.

NB9: If changing from a low or moderate dose of a TCA (eg less than 150 mg imipramine), the dose of moclobemide should not exceed 300 mg daily for the first week. The dose of moclobemide may subsequently be increased if necessary. If changing from a high dose of a TCA, seek expert advice.

NB10: This recommendation applies if moderate or low doses of both drugs are involved—if changing from a high dose of an irreversible nonselective MAOI, seek expert advice. Continue to adhere to irreversible nonselective MAOI dietary guidelines (see *Therapeutic Guidelines*) for 2 weeks after switching to moclobemide.