Primary Care Guide to Antidepressants		
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NHS
Nottinghamshire Area Prescribing Committee

PRIMARY CARE GUIDE TO ANTIDEPRESSANTS

PRESCRIBING, STOPPING & SWAPPING

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Treatment summary of NICE Guidance (NG222)

- Depression refers to a wide range of mental health problems characterised by the absence of a positive affect (a loss of interest and enjoyment in ordinary things), low mood, and a range of associated emotional, cognitive, physical, and behavioural symptoms.
- Depression severity exists along a continuum and is composed of symptoms, duration, and the impact on personal and social functioning. NICE guidance now defines episodes of depression as "less severe" or "more severe".
- Discuss treatment options with people who have a new episode of depression and match their choice of treatment to their clinical needs and preferences. Make a shared decision with the person about their treatment.
  Visual summary on discussing first line treatments for **less severe depression**
  Visual summary on discussing first line treatments for **more severe depression**

Talking therapies and sleep hygiene

Sleep Hygiene Resources

- https://www.nhs.uk/conditions/insomnia/
- https://www.mind.org.uk/information-support/types-of-mental-health-problems/sleep-problems/tips-to-improve-your-sleep/
- MIND - how to cope with sleep problems

Improving Access to Psychological Therapies (IAPT)

NHS
Nottingham and Nottinghamshire Talking Therapies

www.notts-talk.co.uk
Tel: 0333 188 1060

- Accept both GP and self-referral
- Provides a range of talking therapies, groups and computerised self-help materials
- For further information on referral and the support on offer visit the Nottingham and Nottinghamshire Talking Therapies website here

Initiating antidepressant treatment

- Do not routinely offer antidepressant medication as first line treatment for less severe depression (subthreshold symptoms or mild depression, defined in NG222 as depression scoring less than 16 on the PHQ-9 scale) unless that is the person's preference.

Initiating antidepressant treatment

- When offering medication for the treatment of depression, discuss and agree a management plan with the person. This should include:
  - The choices of antidepressant
  - Reason for offering medication
  - The dose, and how the dose may need to be adjusted
  - The benefits, covering what improvements the person would like to see in their life
  - Possible side effects (appendix one) including whether these are likely to be temporary or permanent
  - Any implications of taking antidepressants if the person is pregnant or planning pregnancy
  - Withdrawal symptoms and how these can be minimised by not missing doses and stopping the antidepressant in a planned manner with gradual dose reductions
  - How long it takes to see an effect (usually 4 weeks)
  - When their first review will be
  - Why regular monitoring is needed and how often they will need to attend for review
  - The importance of following instructions on how to take an antidepressant (e.g., time of day)
  - That treatment may need to continue for at least 6 months following the remission of symptoms
- Ensure the person has written information that is appropriate for their needs.

Monitoring antidepressant treatment

For those not considered to be at increased risk of suicide:

- Review within 2 weeks
- Review regularly in the first three months
- Thereafter review at longer intervals if the response is good

For those considered to present an increased risk of suicide or aged 18-25 years:

- Review after one week of starting the antidepressant or increasing the dose
- Review them again after this as often as needed, but no later than 4 weeks after the antidepressant was started
- Base the frequency and method of on-going review on their circumstances and any changes in suicidal ideation or assessed risk of suicide

During a review with a patient taking antidepressants the following should be discussed:

- Tolerability of the medication (directly ask about known side effects that may not be reported - e.g., adverse effect on sexual function with SSRIs).
- Adherence to the medication.
- Thoughts of hopelessness or suicide; including any specific intent or plans (particularly during the early stage of treatment or treatment changes).
- The person's depressive symptoms (i.e., response to treatment) using a validated rating scale such as the PHQ-9 (patient completion).
- Any ongoing stresses that may contribute to depression.

- The impact of any current psychological interventions or the potential benefit of this type of treatment if not undertaken so far
- The benefits of exercise and structured activity (where possible) to the outcome of antidepressant treatment
- Ask about alcohol and recreational drug use
- Any hypomanic symptoms

Continuation of antidepressant treatment and relapse prevention

- The continuation of antidepressant treatment after full or partial remission may reduce the risk of relapse and help people to stay well.
- Discuss with the person and reach a shared decision on whether to continue treatment based on their clinical needs and preferences. Visual summary on preventing relapse.
- Consider that the following factors may increase the risk of relapse:
  - A history of recurrent episodes of depression, particularly if these have occurred frequently or within the last 2 years
  - Any other chronic physical health or mental health problems
  - Any residual symptoms or history of incomplete response to treatment
  - Unhelpful coping styles (for example avoidance and rumination)
  - History of severe depression (including severe functional impairment)
  - Personal, social, and environmental factors that contributed to their depression and are still present (e.g., ongoing stress, relationship problems, poverty, isolation, unemployment)
- Consider the potential risks of continuing with antidepressants long term:
  - Side effects, such as increased bleeding risk or long-term effects on sexual function
  - Difficulty stopping antidepressants
- For people continuing with antidepressant medication to prevent relapse, hold reviews every 6 months. At each review:
  - Monitor mood state using a formal validated rating scale, for example the PHQ-9
  - Review side effects
  - Review any personal, social, and environmental factors that may impact on the risk of relapse
  - Discuss with them if they wish to continue treatment or not
- For people who choose not to continue antidepressant medication to prevent relapse, advise them:
  - How to stop antidepressant medication
  - To seek help as soon as possible if the symptoms return or residual symptoms worsen

Further line antidepressant treatment

- If a person's depression has not responded at all after 4 weeks of antidepressant medication, at a recognised therapeutic dose, discuss with them:
  - Any personal, social, or environmental factors or physical or other mental health conditions that might explain why treatment is not working.
  - If there are any problems with adhering to the treatment plan (e.g. stopping or reducing antidepressant medication because of side effects).

- If a person's depression has had no, or limited, response to treatment with antidepressant medication alone, and no obvious cause can be identified, discuss the following treatment options:
    - Adding a group exercise intervention
    - Switching to psychological therapy
    - Continuing antidepressant medication and increasing the dose (only do this if it's well tolerated). Higher doses may not be more effective and can lead to increased side effects.
    - Switching to another antidepressant medication in the same class (e.g., another SSRI). Many patients who can't tolerate one SSRI will tolerate another.
    - Switching to an antidepressant medication of a different class (e.g., SNRI).
    - Changing to a combination of psychological therapy and antidepressant medication.

- The choice of medication beyond the first SSRI should be individual and patient based. It should be informed by several factors that are unique to each patient:
    - Response to current medication/historical success
    - Specific characteristics of the depression (e.g., insomnia, anxiety)
    - Side effects or issues the patient would wish to avoid (e.g., weight gain with mirtazapine)
    - Other medications (potential drug-drug interactions) or any contraindications/cautions
    - Additional medical or psychiatric diagnoses
    - For women of childbearing potential avoid paroxetine where possible (due to some indications of excess foetal heart malformation and the higher level of discontinuation effects - meaning any decision to stop may be more difficult)
    - **Do not switch to/start dosulepin or amitriptyline because evidence supporting tolerability relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose.**
    - The preferred tricyclic antidepressant (TCA) for prescribing in primary care is lofepramine (due to a consistently low toxicity index), though nortriptyline may be an alternative following discussion with secondary care.
    - If a patient with depression is taking amitriptyline (or another tricyclic) for pain or other medical condition, assess the need for this given risk in overdose.

Switching antidepressants

- Specific advice on switching antidepressants, including examples, is available in appendix two.
- When changing from one antidepressant to another, abrupt withdrawal should be avoided unless there has been a serious adverse effect.
- In most cases, cross-tapering is the preferred method of switching antidepressants.
- In some cases, it may be possible to taper the current antidepressant to the usual starting dose and start the new antidepressant on the next day (i.e., a direct switch). This method may be preferred if a patient has been on the first antidepressant for a short duration or if there are intolerable side effects.
- The co-administration of some antidepressants, even when cross-tapering, is absolutely contraindicated (e.g. MAOIs with SSRI/SNRIs).
- The potential risks of co-administering two antidepressants include serotonin syndrome, additive side effects and drug interactions (e.g., some SSRIs elevate tricyclic plasma levels).

- Exercise particular caution when switching:
  - From fluoxetine to other antidepressants (fluoxetine has a long half-life).
  - From fluoxetine or paroxetine to a tricyclic (both medications inhibit the metabolism of tricyclics). A lower starting dose of the tricyclic will be required, particularly if switching from fluoxetine.
  - From a MAOI (e.g., phenelzine, isocarboxazid or tranylcypromine) to other antidepressants. A washout period is required. Even a single dose of a SSRI during this time can cause a severe serotonin syndrome. Some other general medical treatments (such as opiates) also release serotonin and there should be caution in using these with MAOIs, or within the washout period. These risks are greatest with irreversible MAOIs but should also be considered with reversible MAOIs (e.g. moclobemide).
- Further information on switching antidepressants is also available at NICE CKS - depression.
- Further information specifically on switching from dosulepin is available here.

Deprescribing antidepressants

- A general rule is that antidepressants taken for months should be withdrawn over weeks, and if taken for years withdrawn over months.
- People may have concerns about stopping antidepressant medication (withdrawal effects or that their depression may return) and may need support to stop successfully. Support may include details of online/written resources or increased support from a clinician (for example regular check-in phone calls or seeing them more frequently).
- When stopping antidepressant medication:
  - Consider the half-life of the antidepressant - those with a shorter half-life such as venlafaxine and paroxetine will need to be tapered more slowly.
  - Consider the duration of treatment – patients prescribed antidepressants for longer may require a slower taper.
  - Slowly reduce the antidepressant dose to zero in a step wise fashion, at each step prescribing a proportion of the previous dose (e.g., 50%). Consider smaller reductions (e.g., 25%) as the dose becomes lower and consider liquid preparations or tapering strips if necessary, where these are available.
  - The speed and duration of withdrawal should be led and agreed by the patient.
  - Ensure any withdrawal symptoms have resolved, or are tolerable, before making the next reduction.
  - If there are serious or intolerable adverse effects, consider a faster withdrawal.
  - Recognise that withdrawal may take weeks or months to complete successfully.
  - Monitor the person for withdrawal symptoms and for the return of symptoms of depression.

Withdrawal symptoms

- Withdrawal symptoms can be understood through reversal of adaptive brain changes developed during the period of antidepressant use.
- Withdrawal symptoms can be experienced with a wide range of antidepressant medication.
- Withdrawal symptoms are more likely if a person stops taking antidepressant medication abruptly, misses doses or doesn't take the full dose.

- Symptoms may include: dizziness, vertigo, altered sensations (e.g., electric shocks sensations), irritability, anxiety, low mood, tearfulness, confusion, irrational fears, restlessness, agitation, insomnia, sweating, nausea, tiredness, palpitations, headaches and muscle aches.
- The onset and severity of withdrawal symptoms are related to the pharmacological properties of antidepressants, including elimination half-life.
  - Some antidepressants including venlafaxine and paroxetine are associated with more severe withdrawal symptoms, which should be discussed at the point of initiation.
  - Antidepressants with longer half-lives, e.g., fluoxetine, have fewer reported withdrawal effects, though there is a possibility that these may be delayed by 2-6 weeks in some people.
- Withdrawal symptoms are typically distinguished from relapse by their rapid onset (days, rather than weeks), a rapid response to reintroduction of the antidepressant and the presence of somatic and psychological symptoms distinct from the original illness (e.g., brain zaps, dizziness).
- Withdrawal symptoms can be mild and self-limiting (usually go away within 1-2 weeks). However, there is substantial variation in people's experiences. For some patients, symptoms can last much longer and be more severe.
- If a person has mild withdrawal symptoms:
  - Monitor the symptoms
  - Provide reassurances that symptoms are common and usually self-limiting
  - Advise them to contact you if the symptoms do not improve or get any worse.
- If a person has more severe withdrawal symptoms:
  - Consider restarting the antidepressant medication at the previous dose
  - Attempt dose reduction at a slower rate after symptoms have resolved

Drug interactions

- This section is not exhaustive. For a full list of drug interactions with antidepressants please consult the individual product literature.
- Common drug interactions to be aware of:
  - SSRIs and SNRIs: risk of gastrointestinal side effects when administered with NSAIDs.
  - SSRIs and SNRIs: risk of bleeding when concomitantly administered with medicines that affect platelet function (e.g., anticoagulants and NSAIDs). Consider proton pump inhibitor cover for upper GI bleeding in higher risk patients.
  - Most antidepressants: risk of hyponatraemia when concomitantly administered with diuretics.
  - SSRIs: reports of increased lamotrigine concentrations and toxicity when concomitantly administered with sertraline. Consider the possibility of an interaction if a patient presents with troublesome adverse effects including agitation/insomnia or skin rash/blistering/fever.
  - Fluoxetine is a strong inhibitor of CYP2D6 enzyme, concomitant therapy with medications also metabolised by this enzyme system may lead to drug interactions (e.g. increased serum levels of some antipsychotic medications).
  - Risk of QTc interval prolongation if some antidepressants are administered concomitantly with other agents known to cause this effect (see MHRA alert for QT interval prolongation with citalopram and escitalopram).
  - Additive CNS effects when classes of antidepressants with similar mechanisms of action are prescribed for separate indications (e.g. a tricyclic for neuropathic pain and a SNRI for depressive illness).

- TCAs are anticholinergic. This effect can be exacerbated by other anticholinergic drugs – consider calculating the anticholinergic burden score - http://www.acbcalc.com/.
- TCAs – caution with other drugs that can alter cardiac conduction.
- Lithium – interaction with NSAIDs, ACE inhibitors, angiotensin receptor blockers and diuretic medications, with the potential to significantly increase lithium levels and cause toxicity.
- MAOIs – potentially fatal interaction with other medications that increase serotonin levels (including SSRIs, SNRIs, some opiates and ziprasidone); and potential for stroke with medications that cause pressor effects (including some over-the-counter cold remedies). Patients should always be encouraged to tell professionals they are taking MAOIs, including for over-the-counter medications.

Serotonin syndrome

- Serotonin syndrome is caused by excessive central and peripheral serotonergic activity.
- Serotonin syndrome can occur with a single serotonergic drug at a therapeutic dose or more frequently in combination of serotonergic drugs or overdose.
- The most severe cases have involved a MAOI (including moclobemide) and a serotonin reuptake inhibitor but any combination of a MAOI and another medication increasing central serotonin levels has the potential to cause fatal serotonin toxicity.
- Some serotonergic agents are not associated with the treatment of depression and include opioids (e.g. fentanyl, tramadol, oxycodone), triptans, Parkinson's disease treatments (e.g. selegiline, rasagiline, safinamide), antiemetics (e.g. ondansetron, metoclopramide), bupropion and St John's Wort amongst others – see UKMi summary for a comprehensive list.
- Onset of symptoms can occur within hours or days of increase in serotonergic medication.
- It is classed as poisoning, severe symptoms will need urgent management in an acute setting.

Symptoms of serotonin syndrome:

Alteration of mental status	Neuromuscular abnormalities	Autonomic hyperactivity
agitation	tremors	hypertension
anxiety	clonus	tachycardia
disorientation	hyperreflexia	tachypnea
restlessness	muscle rigidity	hyperthermia
excitement	bilateral babinski signs	mydriasis
		diaphoresis
		dry mucous membranes
		flushed skin
		shivering
		vomiting
		diarrhoea
		hyperactive bowel sounds
		arrhythmias

Patient Information

- A patient information leaflet on antidepressants is available from MIND.
- https://www.nhs.uk/mental-health/talking-therapies-medicine-treatments/medicines-and-psychiatry/antidepressants/
- https://www.rcpsych.ac.uk/mental-health/treatments-and-wellbeing/antidepressants

- For information on stopping antidepressants:
  - https://www.nhs.uk/mental-health/talking-therapies-medicine-treatments/medicines-and-psychiatry/stopping-or-coming-off-antidepressants /
  - https://www.rcpsych.ac.uk/mental-health/treatments-and-wellbeing/antidepressants
  - Antidepressants and withdrawal effects – MIND

References

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Version Control - **Primary Care Guide to Antidepressants**			
Version	Author(s)	Date	Changes
1.0	Nick Sherwood, Mental Health Efficiencies Pharmacist, NHS Nottingham and Nottinghamshire CCG	September 2019	
2.0	Hannah Godden, Specialist Mental Health Interface Pharmacist, NHS Nottingham and Nottinghamshire ICB	September 2022	1. Updated as per NICE guideline 222. 2. Added agomelatine and bupropion to appendices one and two. 3. Antidepressant switch examples added to appendix two.
2.1		July 23	Updated the link to access Talking Therapies
2.2	Irina Varlan, Interface Pharmacist	Nov 23	Changed traffic light for Vortioxetine from A2 to A3 to match formulary entry

Appendix One: Info on medications

Medication	Traffic Light Status	Class	Relative common adverse effect (Maudsley and BNF)						Minimum effective dose (BNF, Maudsley)	Common side effects (most common first, not a comprehensive list (SPCs))	How to respond *In all cases, discuss with patient whether acceptable s/e based on benefit.* *In many cases side effects will reduce after several weeks.*
			Sedation	Hypotension	Cardiac Conduction	Anticholinergic effects	Nausea/ Vomiting	Sexual Dysfunction			
Agomelatine	Amb2		+	-	-	-	-	-	25mg/day	Headache, nausea, dizziness Liver function monitoring required – see APC prescribing information	Generally transient within first 2 weeks of treatment
Amitriptyline (not recommended)	Grey	TCA	+++	+++	+++	+++	+	+++	50mg/day (10mg initially >65 years old)	Sedation, postural hypotension, tachycardia, anticholinergic effects	Take at bedtime, exercise good dental hygiene
Bupropion	Amb2	NRI and DRI	-	-	-	-	-	-	150mg/day	Insomnia, agitation, increased seizure potential, tremor	Avoid bedtime dose
Citalopram	Green	SSRI	-	-	+	-	++	+++	20mg/day (10mg >65years old)	GI disturbances, rash, sweating, agitation. MHRA drug safety update - QT interval prolongation	Take with food, in the morning.
Clomipramine	Green	TCA	++	+++	+++	++	++	+++	10mg/day	Sedation, postural hypotension, tachycardia, anticholinergic effects	Take at bedtime, exercise good dental hygiene
Doxepin (not recommended)	Grey	TCA	+++	++	+++	+++	+	+	75mg/day	Sedation, postural hypotension, tachycardia, anticholinergic effects	Take at bedtime, exercise good dental hygiene
Duloxetine	Amb2	SNRI	-	-	-	-	++	++	60mg/day	Nausea, insomnia, headache, dizziness, dry mouth	Exercise good dental hygiene
Escitalopram	Green	SSRI	-	-	+	-	++	+++	10mg/day (5mg >65years old)	GI disturbances, rash, sweating, agitation. MHRA drug safety update - QT interval prolongation	Take with food, in the morning.

Fluoxetine	Green	SSRI	-	-	-	-	++	+++	20mg/day	Insomnia, agitation, rash, GI disturbances	Take with food, in the morning.
Imipramine	Green	TCA	++	+++	+++	+++	+	+	75mg/day (10mg/day initially >65 years old)	Sedation, postural hypotension, tachycardia, anticholinergic effects	Take at bedtime, exercise good dental hygiene
Isocarboxazid	Amb2	MAOI	+	++	+	++	+	+	10mg/day (lower for elderly)	Postural hypotension, dizziness, drowsiness, insomnia, dry mouth	Take at bedtime
Lofepramine	Green	TCA	+	+	+	++	+	+	140mg/day (lower for elderly)	Less sedative, less anticholinergic and less cardiotoxic than other TCAs	Take at bedtime.
Mirtazapine	Green	Piperazinoazepine	+++	+	-	+	+	-	15mg- 30mg/day	Increased appetite (weight gain), drowsiness, dizziness, oedema	Take at bedtime
Moclobemide	Amb2	Reversible MAOI	-	-	-	-	+	+	300mg/day	Sleep disturbances, nausea, agitation, confusion	Side effects should abate after several weeks.
Nortriptyline	Green	TCA	+	++	++	+	+	+	Initiate at low dose, 75mg/day	Sedation, postural hypotension, tachycardia, anticholinergic effects.	Take at bedtime, exercise good dental hygiene
Phenelzine	Amb2	MAOI	+	+	+	+	+	+	45mg/day (divided doses)	Postural hypotension, dizziness, drowsiness, insomnia, headaches	Take at bedtime
Sertraline	Green	SSRI	-	-	-	-	++	+++	50mg/day	GI disturbances, rash, sweating, agitation	Take with food, in the morning.
Tranylcypromine	Red	MAOI	-	+	+	+	+	+	10mg/day	Insomnia, postural hypotension, dizziness	Giving last dose of the day by 3pm
Trazodone	Green	Triazolopyridine	+++	+	+	+	+	+	150mg/day (divided doses) – 100mg/day for >65 years old	Sedation, dizziness, headache, nausea, and vomiting.	Don't take with alcohol, benzos or hypnotics.
Venlafaxine	Green	SNRI	-	-	+	-	+++	+++	75mg/day	Nausea, insomnia, dry mouth, somnolence, dizziness	Exercise good dental hygiene
Vortioxetine	Amb3	SSRI	-	+	-	-	++	+	10mg/day (5mg/day for >65 years old	Nausea, decreased appetite, abnormal dreams, dizziness,	Generally transient, within first 2 weeks

+++ high incidence/severity, ++moderate, + low, - very low/none.

Appendix Two: Switching antidepressants

(Information from Maudsley prescribing guidelines[4])

FROM \ TO	**Agomelatine**	**Bupropion**	**Clomipramine**	**Fluoxetine**	**Mirtazapine**	**Moclobemide**	**MAOI** Phenelzine Isocarboxazid Tranylcypromine	**SNRI** Venlafaxine Duloxetine	**SSRI** Sertraline, Citalopram Escitalopram	**Trazodone**	**Tricyclics (except clomipramine)** Lofepramine, Imipramine Nortriptyline	**Vortioxetine**
Agomelatine		Stop agomelatine then start bupropion	Stop agomelatine then start clomipramine	Stop agomelatine then start fluoxetine	Stop agomelatine then start mirtazapine	Stop agomelatine then start moclobemide	Stop agomelatine then start MAOI	Stop agomelatine then start SNRI	Stop agomelatine then start SSRI	Stop agomelatine then start trazodone	Stop agomelatine then start TCA	Stop agomelatine then start vortioxetine
Bupropion	Cross taper cautiously		Cross taper cautiously with low dose clomipramine	Cross taper cautiously	Cross taper cautiously	Taper and stop then start moclobemide	Taper and stop, wait for 2 weeks then start MAOI	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously with low dose TCA	Cross taper cautiously
Clomipramine	Cross taper cautiously	Cross taper cautiously		Taper and stop, then start fluoxetine at 10mg/day	Cross taper cautiously	Taper and stop, wait for 1 week, then start moclobemide	Taper and stop, wait for 3 weeks then start MAOI	Taper and stop. Start low dose SNRI	Taper and stop, then start low dose SSRI	Cross taper cautiously	Cross-taper cautiously	Taper and stop, then start at low dose
Fluoxetine	Cross taper cautiously	Taper and stop fluoxetine. Wait 4-7 days then start bupropion	Taper and stop fluoxetine. Wait 2 weeks, then start low dose clomipramine (initially 10mg)		Cross taper cautiously	Taper and stop, wait 5-6 weeks, then start moclobemide	Taper and stop, wait 5-6 weeks, then start MAOI at low dose	Taper and stop fluoxetine. Wait 4-7 days then start SNRI at low dose	Taper and stop fluoxetine. Wait 4-7 days, then start other SSRI at low dose	Cross taper cautiously	Taper and stop fluoxetine. Wait 4-7 days, then start TCA at low dose	Taper and stop fluoxetine. Wait 4-7 days, then start vortioxetine at low dose
Mirtazapine	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously		Taper and stop, wait for 1 week then start moclobemide	Taper and stop, wait for 2 weeks then start MAOI	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously
Moclobemide	Taper and stop, wait 24 hours then start agomelatine	Taper and stop, wait for 24 hours then start bupropion	Taper and stop, wait for 24 hours then start clomipramine	Taper and stop, wait for 24 hours then start fluoxetine	Taper and stop, wait for 24 hours then start mirtazapine		Taper and stop, wait for 24 hours then start MAOI	Taper and stop, wait for 24 hours then start SNRI	Taper and stop, wait for 24 hours then start SSRI	Taper and stop, wait for 24 hours then start trazodone	Taper and stop, wait for 24 hours then start TCA	Taper and stop, wait for 24 hours then start vortioxetine
MAOIs Phenelzine Isocarboxazid Tranylcypromine	Cross taper cautiously	Taper and stop, then wait for 2 weeks	Taper and stop, wait for 3 weeks then start clomipramine	Taper and stop, wait for 2 weeks then start fluoxetine	Taper and stop, wait for 2 weeks then start mirtazapine	Taper and stop, wait for 2 weeks then start moclobemide	Taper and stop, wait for 2 weeks then start alternative MAOI	Taper and stop, wait for 2 weeks then start SNRI	Taper and stop, wait 2 weeks then start SSRI	Taper and stop, wait for 2 weeks then start trazodone	Taper and stop, wait for 2 weeks then start TCA	Taper and stop, wait for 2 weeks then start vortioxetine
SNRI Venlafaxine Duloxetine	Cross taper cautiously	Cross taper cautiously	Taper and stop SNRI. Then start low dose clomipramine.	Direct switch or cautious cross-taper. See information below.	Cross-taper cautiously	Taper and stop. Wait for 1 week, then start moclobemide	Taper and stop. Wait for 1 week, then start MAOI	Direct switch or cautious cross-taper. See information below.	Direct switch or cautious cross-taper. See information below.	Cross taper cautiously	Cross taper cautiously, starting with a low dose TCA	Direct switch possible. See information below
SSRIs; Sertraline Citalopram Escitalopram	Cross taper cautiously	Cross taper cautiously	Taper and stop, then start low dose clomipramine	Direct switch or cautious cross-taper. See information below.	Cross- taper cautiously	Taper and stop, wait for 1 week then start moclobemide	Taper and stop, wait 1 week then start MAOI	Direct switch or cautious cross-taper. See information below.	Direct switch or cautious cross-taper. See information below.	Cross taper cautiously	Cross taper cautiously, start with low dose TCA	Direct switch or cautious cross-taper. See information below.

Trazodone	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously, starting with low dose clomipramine	Cross taper cautiously	Cross taper cautiously	Taper and stop, wait for 1 week then start moclobemide	Taper and stop, wait for 1 week then start MAOI	Cross-taper cautiously	Cross taper cautiously		Cross taper cautiously, starting with low dose TCA	Cross taper cautiously
Tricyclics (except clomipramine): Lofepramine Amitriptyline Imipramine Nortriptyline Dosulepin Doxepin	Cross taper cautiously	Taper TCA to half dose, then add bupropion and slow withdrawal of TCA	Direct switch possible. See information below.	Taper TCA to half dose, then add fluoxetine 10mg and cross taper cautiously	Cross-taper cautiously	Taper and stop, wait for 1 week then start moclobemide	Taper and stop, wait for 2 weeks then start MAOI (wait 3 weeks in case of imipramine)	Cross taper cautiously, start SNRI at low dose	Taper TCA to half dose, then add SSRI and slow withdrawal of TCA over next 5-7 days	Taper TCA to half dose, then add trazodone, Slow withdrawal of TCA	Direct switch or cautious cross-taper. See information below.	Taper TCA to half dose, then add vortioxetine and Slow withdrawal of TCA
Vortioxetine	Cross taper cautiously	Cross taper cautiously	Taper and stop, then start low dose clomipramine	Direct switch or cautious cross-taper See information below.	Cross taper cautiously	Taper and stop, wait for 1 week then start moclobemide	Taper and stop, wait for 3 weeks then start MAOI	Direct switch or cautious cross-taper. See information below.	Direct switch or cautious cross-taper See information below.	Cross taper cautiously	Cross taper cautiously, start with low dose TCA	

1) **"Direct switch"** In some instances (e.g. short duration on first antidepressant or intolerable side effects) it may be possible to gradually taper the current antidepressant to the usual starting dose and start the new antidepressant on the next day.

Example		Week 1	Week 2	Week 3	Week 4
Withdrawing sertraline	150mg once daily	100mg once daily	50mg once daily	Nil	Nil
Introducing escitalopram	Nil	Nil	Nil	10mg once daily	10mg once daily Titrate according to response and tolerability

2) **"Cross taper cautiously"** Usually over 2-4 weeks. The dose of the ineffective or poorly tolerated drug is slowly reduced while the new drug is slowly introduced. The speed of cross tapering is best judged by monitoring patient tolerability.

Example		Week 1	Week 2	Week 3	Week 4
Withdrawing citalopram	40mg once daily	20mg once daily	10mg once daily	Nil	Nil
Introducing mirtazapine	Nil	15mg at night	30mg at night	30mg at night	30mg at night

					Titrate according to response and tolerability

3) **"Cross taper cautiously, starting with low dose"** This means the new dose should be started more cautiously. For example, venlafaxine being introduced at a low dose would be 37.5mg (the lowest dose available).

Example		**Week 1**	**Week 2**	**Week 3**	**Week 4**
Withdrawing dosulepin	150mg once daily	75mg once daily	50mg once daily	25mg once daily	Nil
Introducing venlafaxine MR	Nil	Nil	37.5mg once daily	75mg once daily	75mg once daily Titrate according to response and tolerability