Guidelines on Choice and Selection of Antidepressants for the Management of Depression

1. Introduction

This guidance should be considered as part of a stepped care approach in the management of depressive disorders. The most current NICE guidance should always be consulted wherever possible to obtain the most up to date information.

Antidepressants are not routinely recommended for the initial treatment of sub-threshold depressive symptoms or mild depression[6].

Drug treatment should be considered in the following circumstances[6];

- if mild depression complicates the care of physical health problems or,
- presentation of sub-threshold or mild depression in those with past history of moderate or severe depression, or
- sub-threshold or mild depression that persists after other interventions or
- sub-threshold depressive symptoms persisting for a long period of time (i.e. 2 years).

There is more evidence for the effectiveness of antidepressant medication in moderate to severe depression, in combination with psychotherapy/cognitive behavioural therapy (CBT)[6].

2. Purpose and Scope

To provide guidance on the safe and effective prescribing of antidepressant medication to patients within Hertfordshire Partnership University NHS Foundation Trust.

This guideline has been developed to act as a framework for prescribing for the treatment of moderate to severe depression in children and adults.

Detailed information on the treatment of depression in children and adolescents can be found in section 6.2. Further guidance on prescribing for older adults and for antenatal/postnatal service users can be found in section 6.1 and section 6.3, respectively.

These guidelines act as a guide only, they are to be used alongside the following reference sources and NICE:-

- Maudsley Prescribing Guidelines
- Psychotropic Drug Directory
- BNF
- Lactmed Database (for breastfeeding information) http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm
- UK Teratology Information Service (UKTIS) (for pregnancy and some breastfeeding information) www.uktis.org Tel 0344 892 0909

3. Recommended Pharmacological Treatment for Depression

Pharmacological Treatment of Depression in Adults

Patients under 18 years
Fluoxetine is the recommended first line treatment in patients under 18 years[7]. It is licensed for the treatment of moderate to severe depression from 8 years onwards. **See section 6.2.**[5,7]

SSRIs potentially interact with concomitant medication or physical illness (see section 5 below)

FIRST LINE
SSRI - Citalopram, Fluoxetine or Sertraline

Older Adults >65 years
Recommend monitoring for antidepressant – induced hyponatraemia. Increased risk of GI bleeding. See section 6.1.[5,6]

There is a risk of a dose dependant QT prolongation with **citalopram**, do NOT prescribe in patients with known QTc prolongation, congenital long QT syndrome or in those with medications that are known to prolong QTc.

SECOND LINE
Alternative SSRI or Venlafaxine or Mirtazapine

Antenatal and Postnatal Prescribing
SSRIs have low known risk, most experience with fluoxetine and sertraline. TCAs also have low teratogenic risk.
Imipramine, nortriptyline and sertraline considered safest in breastfeeding. See section 6.3.[5,8,10]

THIRD LINE
Alternative 2nd line agent (see above)
Consider vortioxetine* or other options (MAOI, TCA)

Consider a combination of two different antidepressants
Consider augmentation with an antipsychotic or lithium
With appropriate physical health monitoring

For specialist initiation only

*Refer to prescribing notes, page 8

4. Pharmacological Treatment for Depression

Basic principles of prescribing in depression[5];

- Discuss with the patient choice of drug and availability of other non-pharmacological treatments.
- Discuss with the patient likely outcomes, such as gradual relief from depressive symptoms over several weeks.
- Prescribe a dose of antidepressant (after titration, if necessary) that is likely to be effective.
- For a single episode, continue treatment for at least 6-9 months after resolution of symptoms (those at risk of relapse should continue for at least 2 years).
- Withdraw antidepressants gradually; always inform patients on the risk and nature of discontinuation symptoms.

Choice of antidepressant[5,6];

Consider a baseline assessment for severity of depression and regularly review symptoms both clinically and using a standard severity rating scales. Initially normally choose a generic SSRI whilst taking the following into account;

- Fluoxetine, fluvoxamine and paroxetine have the higher propensity for drug interactions (fluvoxamine and paroxetine are the least preferred SSRI's). It may be appropriate to consider sertraline and citalopram in patients who have chronic health problems, as these have a lower propensity for interactions with medications for physical health.
- SSRI's are associated with an increased risk of bleeding – consider prescribing a gastro-protective drug (e.g. omeprazole) in older adults who are taking NSAIDs and/or aspirin.

Discuss choice of antidepressant, covering;

- Patient choice, the perception of the efficacy and tolerability.
- Existing co-morbid psychiatric disorders such as obsessive compulsive disorder, anxiety etc., through accurate history taking.
- Anticipated adverse events, e.g. agitation, nausea and vomiting with SSRIs, and discontinuation symptoms. See appendix 1 for table of relative side effects of antidepressants.
- Potential interactions with concomitant medication or physical illness[5,11];

Medication for physical health problem	Recommended antidepressant(s)
NSAIDs (non-steroidal anti-inflammatory drugs)	Try to avoid SSRI's – but if no suitable alternatives can be identified, offer gastro-protective medicines (e.g. omeprazole) together with the SSRI[5,11]. Consider mirtazapine, moclobemide or trazodone.
Warfarin or heparin	Do not normally offer SSRI's[5,11]. Consider mirtazapine.
Theophylline or methadone	Offer citalopram or sertraline (sertraline may increase methadone levels).
Clozapine	Consider citalopram or sertraline (small to modest increases in plasma clozapine levels may occur, particularly with sertraline)[2, 16].
'Triptan' drugs for migraine	Do not offer SSRI's, offer mirtazapine or trazodone.
Aspirin	Use SSRI's with caution, if no suitable alternatives can be identified, offer gastro-protective medicines together with the SSRI. Consider trazodone when aspirin is used as a single agent, alternatively consider mirtazapine.
Monoamine-oxidase B inhibitors, e.g. selegiline or	Do not normally offer SSRI's, offer mirtazapine or trazodone.

rasagiline	
Flecainide or propafenone	Offer sertraline as the preferred antidepressant, mirtazapine or moclobemide may also be used.

- Switch treatments early (e.g. after 1-2 weeks) if adverse effects are intolerable or if no improvement at all is seen by 3-4 weeks. Antidepressants have a fairly prompt onset of action and non-response at 2-6 weeks is a good predictor of overall response. See Appendix 2 for table of swapping and stopping advice taken directly from the Maudsley Prescribing Guidelines 12th Edition[5].
- The absence of any improvement at all at 3-4 weeks should normally provoke a change in treatment. If there is some improvement at this time, continue and assess for a further 2-3weeks.
- For advice on switching treatments please refer to the Psychotropic Drug Directory[4], The Maudsley Prescribing Guidelines[5] or contact the pharmacy team for advice.

5. HPFT Formulary Drugs for the treatment of Depression in Adults[1,5]

Drug	Drug Class	Formulation	Additional Prescribing Information
Amitriptyline	Tricyclic antidepressant (TCA)	10mg, 25mg and 50mg tablets 25mg/5ml and 50mg/5ml oral solution	Consider TCAs in patients presenting with pain and physical symptoms. Avoid in patients at risk of arrhythmias. Consider ECG at higher dose or when co-administered with other drugs that may increase the risk e.g. fluoxetine. Increased cholinergic burden, especially when co-prescribed with other anticholinergic drugs.
Citalopram	Selective serotonin reuptake inhibitor (SSRI)	10mg, 20mg, 40mg tablets 40mg/ml oral drops (1 drop=2mg) 4 drops (8mg) = 10mg tablet	SSRI with lowest propensity for drug interactions. Suitable choice in renal impairment. Citalopram: QT interval prolongation—new maximum daily dose restrictions (including in elderly patients), contraindications, and warnings. Citalopram most toxic of SSRI's in overdose (coma, seizures, arrhythmia)[5]. Contraindicated with other QT prolonging medications. Baseline ECG advised in patients with cardiac disease.
Clomipramine	TCA	10mg, 25mg and 50mg capsules	As for amitriptyline.
Duloxetine	Serotonin and noradrenaline reuptake inhibitor (SNRI)	30mg and 60mg capsules	Second line SNRI only after venlafaxine.
Fluoxetine	SSRI	20mg capsules 20mg/5ml oral liquid (can also be used sublingually)	60mg capsules NOT approved. Good option for patents with poor medication compliance due to its long half-life.
Imipramine	TCA	10mg and 25mg tablets 25mg/5ml oral solution	As for amitriptyline.
Lofepramine	TCA	70mg tablets	As for amitriptyline.

		70mg/5ml oral suspension	Lower incidence of side-effects and less dangerous in overdose. Less cardiotoxic than other TCAs. It is an option in SSRI induced hyponatraemia. Can cause raised liver function tests.
Mianserin	Tetracyclic antidepressant	10mg tablets and 30mg tablets	**For specialist initiation only** in line with NICE CG 90 (for combining with an another antidepressant).
Mirtazapine	Noradrenaline and specific serotonin antidepressant (NaSSa)	15mg, 30mg and 45mg tablets and orodispersible tablets 5mg/ml oral solution	Oral solution should only be used when orodispersible tablets are unsuitable. Safer option in patients at high risk of GI bleed e.g. older adults + NSAIDs. Consider if SSRI has not benefited or SSRI not appropriate. Good choice if sedation required.
Moclobemide	Reversible Monoamine oxidase inhibitor (MAOI)	150mg and 300mg tablets	**For specialist initiation only.** Reversible MAOI. Reduced risk of major food and drug interactions, however patients should still be advised to avoid large quantities of tyramine rich foods and sympathomimetic drugs. See BNF for details on initiating treatment after another antidepressant has been stopped. MAOIs not recommended in cardiovascular disease.
Nortriptyline	TCA	10mg and 25mg tablets	As for amitriptyline.
Paroxetine	SSRI	20mg and 30mg tablets 10mg/5ml oral suspension	Less preferred choice. SSRI with greatest risk of withdrawal reactions.
Phenelzine	MAOI	15mg tablets	**For specialist initiation only.** As for moclobemide. Preferred MAOI – probably the most safest.
Reboxetine	Selective inhibitor of noradrenaline re-uptake	4mg tablets	Reboxetine should be used with caution in patients with renal or hepatic impairment. It should also be used under close supervision in patients with bipolar disorder, urinary retention, benign prostatic hyperplasia, glaucoma, or a history of epilepsy or cardiac disorders.

Sertraline	SSRI	50mg and 100mg tablets	Drug of choice for those with cardiovascular disease (recent MI or unstable angina) or renal impairment. Reduced propensity for drug interactions.
Trazodone	Tricyclic-related Antidepressant	50mg and 100mg capsules 150mg tablets 50mg/5ml sugar free oral solution	Oral liquid significantly more expensive than tabs/caps. Restricted to those unable to swallow solid dose forms.
Trimipramine	TCA	10mg and 25mg tablets 50mg capsules	As for amitriptyline.
Venlafaxine	SNRI	37.5mg and 75mg tablets 37.5mg, 75mg, 150mg and 225mg MR tablets	Immediate-release venlafaxine (BD dosage) is considerably less expensive than once daily (MR) formulations. The MR formulation should only be used if the immediate-release formulation is not tolerated or if concordance with a twice daily regimen is difficult. If MR preparation is required then MR tablets should be prescribed rather than MR capsules as these are more cost-effective. Existing patients on MR preparations must not be switched to IR tablets without involvement/agreement of psychiatrist. Avoid use in patients with high risk of cardiac arrhythmia. Monitor blood pressure in doses above 150mg. Consider ECG at higher dose. Do not prescribe venlafaxine for patients with[11]: ▪ Uncontrolled hypertension ▪ Recent myocardial infarction ▪ High risk of cardiac arrhythmia ▪ Monitor BP at initiation and regularly during treatment (particularly during dose titration) ▪ Monitor for signs and symptoms of cardiac dysfunction ▪ Doses of 300 mg daily or more should only be prescribed under the supervision or advice of a specialist mental

			health practitioner.
Vortioxetine	Serotonin modulator and stimulator (SMS)	5mg, 10mg and 20mg tablets	**GPs can initiate once specialist advice has been sought from a HPFT Consultant Psychiatrist.** NICE recommends that vortioxetine is an option for treating major depression in adults who have responded inadequately to two antidepressants within the current episode of depression[9]. However, **NICE considered that there was no convincing evidence that vortioxetine was more or less effective than other antidepressants[9]**. Low toxicity in overdose. Dose adjustment not required in renal impairment although caution in severe renal impairment and in severe hepatic impairment as data is limited[15]. Trial data suggest no effect on QTc or on coagulation parameters. Treatment can be stopped abruptly as it has a long half-life (66hours) and there is no evidence of clinically important discontinuation symptoms[15].

Escitalopram and Agomelatine are non-formulary within HPFT. Requests to use these drugs will need to be made via a named patient request form.

Dosulepin: DO NOT SWITCH TO, OR START dosulepin because evidence supporting its tolerability relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose. NICE CG90[1,6]

6. Prescribing antidepressants in specialist groups

6.1 Older Adults (>65 years)[5,6]

SSRIs are generally used first-line; they offer considerable advantages over TCAs including potentially fewer side effects, safety in overdose, less dosage titration, once a day administration and greater patient adherence. Fluoxetine may not be considered first line in this patient group, due to its longer duration of action, risk of accumulation and multiple drug interactions. Potential side effects such as sedation and consequent risk of falls should be taken into account when selecting an antidepressant. TCAs (except lofepramine) may be less suitable due to the antimuscarinic adverse effects.

Due to changes in pharmacodynamic sensitivity and pharmacokinetics older adults usually take longer to respond to antidepressants, and are more sensitive to their side effects. Therefore a minimum of six weeks treatment should be given before considering the treatment to be ineffective,

SSRIs increase the risk of gastrointestinal (GI) bleeds, particularly in the very elderly and those with established risk factors such as history of bleeds or treatment with non-steroidal anti-inflammatory drug (NSAID), steroid or warfarin. The elderly are also particularly prone to developing hyponatraemia with SSRIs as well as postural hypotension and falls.

Generally lower doses are required, and antidepressants should be initiated at lower doses than used for younger adults.

The average older adult takes at least four or more types of medicines, leading to a significant potential for drug-drug and drug-disease interactions.

6.2 Children and Adolescents (<18 years)[5,7]

Do not offer antidepressant drugs to a child or young person except in combination with a psychological therapy. The current NICE Guidelines recommend that in young people under the age of 18 if an antidepressant is to be prescribed this should only be following assessment and diagnosis by a Child and Adolescent Psychiatrist. In some instances where you are concerned about the severity of presentation and are of the view that an antidepressant would be necessary as a matter of urgency, kindly have a discussion with the Child and Adolescent Psychiatrist in the local Specialist CAMHS Clinic as a first step. NICE updated guidelines state clinicians should consider starting treatment with antidepressants and psychological therapy simultaneously for young people with moderate to severe depression.

Fluoxetine is the first line SSRI (licensed ≥ 8 years), NICE reports fluoxetine as the 'only antidepressant for which trials show the benefit outweighs the risks'. In the UK it is licensed for use for children and young people from 8-18 to treat moderate to severe major depression which is unresponsive to psychological therapy after 4-6 sessions. It is recommended that pharmacotherapy should be administered in combination with a concurrent psychological therapy.

Sertraline and citalopram may be considered as second line agents by specialists with caution. NICE specifically excludes paroxetine, venlafaxine, TCAs and St Johns Wort for the treatment of depression in this age group.

It is important to note that suicide-related behaviours (suicidal attempt and suicidal thoughts), and hostility (predominantly aggression, oppositional behaviour and anger) were more frequently observed in clinical trials among children and adolescents treated with antidepressants compared to those treated with placebo[14].

A child or young person prescribed an antidepressant should be closely monitored by the prescribing doctor and the healthcare professional delivering the psychological therapy for the emergence of suicidal behaviour, self-harm, or hostility, particularly at the beginning of treatment when the dose is changed.

6.3 Antenatal and Postnatal Prescribing [5,8]

Antenatal[5,8]

It is important to ensure that maternal mental health is treated appropriately. As such, antidepressants may be suitable for use in pregnancy, but the risks and benefits of use must be considered on a case-by-case basis. Initiation of antidepressant medication in pregnancy is for specialist initiation only.

Approximately 10% of pregnant women develop a depressive illness at some point during their pregnancy.

Antidepressants should be considered for women with mild depression during pregnancy if they have a history of severe depression and they decline, or their symptoms do not respond to psychological treatments.

Lowest known teratogenicity risk during pregnancy is with TCAs (amitriptyline and imipramine); however they are more likely to cause death if taken in overdose compared to SSRIs.

SSRI with lowest known teratogenic risk during pregnancy is fluoxetine. There is also experience with sertraline which has low infant exposure. However, if the patient is prescribed another SSRI, it is often prudent to continue the same SSRI (except paroxetine) to avoid risk of relapse. The risk of intrauterine growth retardation (although low) is greater in untreated major depression than with drugs like fluoxetine, hence it is advisable to continue the antidepressant drug in major depression.

Paroxetine has been specifically associated with cardiac malformations particularly after high dose (>25mg/day), first trimester exposure. Paroxetine is non-formulary and is not recommended.

Always obtain the most up-to-date advice by contacting a member of your pharmacy team or ring UKTIS specialist centre on 0344 892 0909.

Persistent pulmonary hypertension in the neonate is noted when SSRIs are taken after 20 weeks gestation.

High blood pressure with venlafaxine at high doses is noted, together with higher toxicity in overdose compared to SSRIs and some TCAs.

Withdrawal or toxicity in the neonate with all antidepressants, in particular paroxetine and venlafaxine (usually self-limiting).

Postnatal[5,8,13]

Much post-partum depression begins before birth. There is a significant increase in new psychiatric episodes in the first 3 months after delivery.

In each case, the benefits of breastfeeding to the mother and infant must be weighed against the risk of drug exposure to the infant.

Lowest levels in breast milk are noted with imipramine, nortriptyline and sertraline.

Highest levels in breast milk are noted with citalopram and fluoxetine.

Always obtain the most up-to-date advice by contacting a member of your pharmacy team or accessing the UKMI Lactmed database http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm

References

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Appendix 1 - Table of relative side effects of Antidepressants[4]

The following table can be used by prescribers in conjunction with patients to help guide choice of antidepressant therapy. Alternatively the Choice and Medication website provides information for patients on medicines used in mental health. Please note the Choice and Medication website may include information on medicines that have not been approved in Hertfordshire.

Selective Serotonin Reuptake inhibitors (SSRI's)	Adult max dose mg/d	Elderly max dose mg/d	Anti-cholinergic	Cardiac	Nausea	Sedation	Overdose	Pro-convulsant	Sexual dysfunction
Citalopram	40	20	○	○	●●●	○	●	○	●●
Fluoxetine	60	40 (60)	○	○	●●	○	○	○	●●
Paroxetine	50	40	○	○	●●	○	○	○	●●●
Sertraline	200	200	○	○	●●	○	○	○	●●
Tricyclic Antidepressants (TCA's)	Adult max dose mg/d	Elderly max dose mg/d	Anti-cholinergic	Cardiac	Nausea	Sedation	Overdose	Pro-convulsant	Sexual dysfunction
Amitriptyline	200	75	●●●	●●●	●●	●●●	●●●	●●	●●
Clomipramine	250	75	●●●	●●	●●	●●	●	●●	●●●
Imipramine	300	50	●●	●●	●●	●	●●●	●●	●●
Lofepramine	210	<Ad	●●	●	●	●	○	○	●●
Nortriptyline	150	50	●●	●	●●	●	●●	●	●●
Trimipramine	300	<Ad	●●●	●●	●	●●	●●	●	●●
Monoamine Oxidase Inhibitors (MAOI's)	Adult max dose mg/d	Elderly max dose mg/d	Anti-cholinergic	Cardiac	Nausea	Sedation	Overdose	Pro-convulsant	Sexual dysfunction
Moclobemide	600	600	●	○	●	○	○	?	●
Phenelzine	90	90	●	●	●●	●	●●●	○	●
Others	Adult max dose mg/d	Elderly max dose mg/d	Anti-cholinergic	Cardiac	Nausea	Sedation	Overdose	Pro-convulsant	Sexual dysfunction
Duloxetine	120	Caution	○	○	○	○	○	○	○
Mirtazapine	45	45	○	○	○	●●	○	●●	●●
Reboxetine	12	NR	●	●	●	○	○	○	○
Trazodone	600	+300	●	●	●●●	●●	●	○	●●
Venlafaxine	375	375	○	●●	●●	●	●●	●	●●
Vortioxetine	20	Caution >10	○	○	●●	○	?	?	●●

●●● marked effect ●● moderate effect ● mild/ transient effect ○ little or minimal effect ? no information available or little repor

Appendix 2 - Table of swapping and stopping Antidepressants[5]

The following tables can be used by prescribers to help guide swapping and stopping antidepressant therapy taken directly from The Maudsley Prescribing Guidelines 12th Edition.

From	To Agomelatine	Bupropion	Clomipramine	Fluoxetine	Fluvoxamine	MAOIs Phenelzine Tranylcypromine Selegiline
Agomelatine†		Stop agomelatine then start bupropion	Stop agomelatine then start clomipramine	Stop agomelatine then start fluoxetine	Stop agomelatine then start fluvoxamine	Stop agomelatine then start MAOIs
Bupropion‡	Cross-taper cautiously		Cross-taper cautiously with low dose clomipramine	Cross-taper cautiously	Cross-taper cautiously	Taper and stop then wait for 2 weeks then start MAOIs
Clomipramine	Cross-taper cautiously	Cross-taper cautiously		Taper and stop then start fluoxetine at 10 mg/day	Taper and stop then start low dose fluvoxamine	Taper and stop then wait for 3 weeks then start MAOIs
Fluoxetine§	Cross-taper cautiously	Cross-taper cautiously	Taper and stop fluoxetine. Wait 2 weeks. Start low dose clomipramine		Taper and stop. Wait 2 weeks then start low dose fluvoxamine	Taper and stop then wait for 5–6 weeks then start MAOIs
Fluvoxamine¶	Taper and stop then wait for 1 week	Cross-taper cautiously	Taper and stop then start low dose clomipramine	Taper and stop then start fluoxetine at 10 mg/day		Taper and stop then wait for 1 week then start MAOIs
MAOIs Phenelzine Tranylcypromine Selegiline	Cross-taper cautiously	Taper and stop then wait for 2 weeks	Taper and stop then wait for 3 weeks	Taper and stop then wait for 2 weeks	Taper and stop then wait for 2 weeks	Taper and stop then wait for 2 weeks
Moclobemide	Cross-taper cautiously	Taper and stop then wait 24 hours	Taper and stop then wait 24 hours	Taper and stop then wait 24 hours	Taper and stop then wait 24 hours	Taper and stop, wait 24 hours then start MAOIs
Mirtazapine	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Taper and stop then wait for 2 weeks then start MAOIs
Reboxetine**	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Taper and stop then wait for 1 week then start MAOIs
Trazodone	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously with low dose clomipramine	Cross-taper cautiously	Cross-taper cautiously	Taper and stop then wait for 1 week

From	Moclobemide	Mirtazapine	Reboxetine	Trazodone	Other SSRIs,†† vortioxetine	SNRIs Duloxetine Venlafaxine Desvenlafaxine	TCAs (except clomipramine)
Agomelatine†	Stop agomelatine then start moclobemide	Stop agomelatine then start mirtazapine	Stop agomelatine then start reboxetine	Stop agomelatine then start trazodone	Stop agomelatine then start SSRI	Stop agomelatine then start SNRI	Stop agomelatine then start TCA
Bupropion‡	Taper and stop then start moclobemide	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously with low dose TCA
Clomipramine	Taper and stop then wait for 1 week then start moclobemide	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously starting with low dose trazodone	Taper and stop then start low dose.	Taper and stop. Start low dose SNRI	Cross-taper cautiously
Fluoxetine§	Taper and stop then wait for 5–6 weeks then start moclobemide	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously starting with low dose trazodone	Taper and stop fluoxetine. Wait 4–7 days then start low dose	Taper and stop. Start low dose SNRI¶¶	Taper and stop fluoxetine. Wait 4–7 days then start low dose
Fluvoxamine¶	Taper and stop then wait for 1 week then start moclobemide	Cross-taper cautiously. Start mirtazapine at 15 mg	Cross-taper cautiously	Cross-taper cautiously starting with low dose trazodone	Taper and stop then start low dose SSRI	Taper and stop then start low dose SNRI¶¶	Cross-taper cautiously with low dose TCA
MAOIs Phenelzine Tranylcypromine Selegiline	Taper and stop then wait for 2 weeks then start moclobemide	Taper and stop then wait for 2 weeks	Taper and stop then wait for 2 weeks	Taper and stop then wait for 2 weeks	Taper and stop then wait for 2 weeks	Taper and stop then wait for 2 weeks	Taper and stop then wait for 2 weeks†††
Moclobemide		Taper and stop then wait 24 hours	Taper and stop then wait 24 hours	Taper and stop then wait 24 hours	Taper and stop then wait 24 hours	Taper and stop then wait 24 hours	Taper and stop then wait 24 hours
Mirtazapine	Taper and stop then wait for 1 week then start moclobemide		Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously
Reboxetine**	Taper and stop then wait for 1 week then start moclobemide	Cross-taper cautiously		Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously
Trazodone	Taper and stop then wait for 1 week then start moclobemide	Cross-taper cautiously	Cross-taper cautiously		Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously with low dose TCA

From	To Agomelatine	Bupropion	Clomipramine	Fluoxetine	Fluvoxamine	MAOIs Phenelzine Tranylcypromine Selegiline
Other SSRIs,† vortioxetine‡‡,‡‡‡	Cross-taper cautiously	Cross-taper cautiously starting with low dose bupropion	Taper and stop then start low dose clomipramine	Taper and stop then start fluoxetine at 10 mg/day	Taper and stop then start low dose fluvoxamine	Taper and stop then wait for 1 week§§
SNRI Duloxetine¶¶ Venlafaxine Desvenlafaxine	Cross-taper cautiously	Cross-taper cautiously starting with low dose bupropion	Taper and stop then start low dose clomipramine	Taper and stop then start fluoxetine at 10 mg/day	Taper and stop then start low dose fluvoxamine	Taper and stop then wait for 1 week
Tricyclics	Cross-taper cautiously	Halve dose and add bupropion and then slow withdrawal	Cross-taper cautiously	Halve dose and add fluoxetine and then slow withdrawal	Cross-taper cautiously	Taper and stop then wait for 2 weeks***
Stopping†††	Can be stopped abruptly	Reduce over 4 weeks	Reduce over 4 weeks	At 20 mg/day just stop. At higher doses reduce over 2 weeks	Reduce over 4 weeks	Reduce over 4 weeks or longer if necessar

Moclobemide	Mirtazapine	Reboxetine	Trazodone	Other SSRIs,†† vortioxetine	SNRIs Duloxetine Venlafaxine Desvenlafaxine	TCAs (except clomipramine)
Taper and stop then wait for 1 week then start moclobemide	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously starting with low dose trazodone	Cross-taper cautiously starting with low dose	Cross-taper cautiously with low dose SNRI¶¶	Cross-taper cautiously with low dose TCA
Taper and stop then wait for 1 week then start moclobemide	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously starting with low dose	Cross-taper cautiously with low dose SNRI¶¶	Cross-taper cautiously with low dose TCA
Taper and stop then wait for 1 week then start moclobemide	Cross-taper cautiously	Cross-taper cautiously	Halve dose and add trazodone and then slow withdrawal	Halve dose and add SSRI then slow withdrawal	Cross-taper cautiously starting with low dose SNRI	Cross-taper cautiously
Reduce over 4 weeks	Reduce over 4 weeks	Reduce over 4 weeks	Reduce over 4 weeks	Reduce over 4 weeks or longer if necessary‡‡‡	Reduce over 4 weeks or longer if necessary	Reduce over 4 weeks

Notes

*Advice given in this table is partly derived from manufacturers' information and available published data and partly theoretical. There are several factors that affect individual drug handling and caution is required in every instance.
†Agomelatine has no effect on monoamine uptake and no affinity for α, β adrenergic, histaminergic, cholinergic, dopaminergic and benzodiazepine receptors. The potential for interactions between agomelatine and other antidepressants is low (except contraindication with concomitant use of fluvoxamine) and it is not expected to mitigate discontinuation reactions of other antidepressants.
§Beware: interactions with fluoxetine may still occur for 5 weeks after stopping fluoxetine because of its long half-life.
¶Fluvoxamine is a potent inhibitor of CYP1A2, and to a lesser extent of CYP2C and CYP3A4, and has a high potential for interactions hence extra caution is required
**Switching to reboxetine as antidepressant monotherapy is no longer recommended.
††Citalopram, escitalopram, paroxetine and sertraline.
‡‡Limited experience with vortioxetine and extra precaution required. Particular care when switching to or from bupropion and other 2D6 inhibitors such as fluoxetine and paroxetine.[11]
§§Wait 3 weeks in the case of vortioxetine.[12]
¶¶Abrupt switch from SSRIs and venlafaxine to duloxetine is possible starting at 60 mg/day.[4]
***Wait 3 weeks in the case of imipramine.
†††See general guidance at the beginning of this section.
‡‡‡Reduce over 1 week to 10 mg/day, then stop.
MAOI, monoamine oxidase inhibitor; SNRI, selective noradrenaline reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

Please note that these tables include treatments that are non-formulary in HPFT.