Rotherham Doncaster and South Humber NHS Foundation Trust

Depression Formulary Guidance [v3.0]

(Adapted from NICE guidelines NG222, NG215 CG28 and CG90)

1. Introduction

These Guidelines are intended for routine use. However, there will be instances where they are not suitable for the patient you are managing, where more bespoke treatment will be necessary. In such instances the rationale for prescribing away from formulary must be recorded. They are intended to discuss the pharmacological management only. Full NICE guidance should be consulted for advice around non-pharmacological management.

2. Key Principles

- Discuss with the patient if they have any preferences, including what treatments they found helpful previously.
- Allow adequate time for the initial discussion, involve family members or other supports as agreed with the person.

3. Prescribing and Use of Antidepressants – Key Points

- Prescribing of antidepressants should always be seen as part of a package of care for the treatment of patients with depression and should never be carried out in isolation. See full NICE guidance for the use of psychological treatment options.
- Do not use antidepressants routinely to treat persistent sub-threshold depressive symptoms or mild depression because the risk-benefit ratio is poor, however they should be considered for people with:
    - A past history of moderate or severe depression or
    - Initial presentation of sub-threshold depressive symptoms that have been present for a long period (typically at least 2 years) or
    - Sub-threshold depressive symptoms or mild depression that persist(s) after other interventions
    - Mild depression that complicates the care of a chronic physical health problem
- Antidepressants should be considered for people presenting with moderate depression.
- Antidepressants should be considered for people with a chronic physical health problem and presenting with moderate depression, after other interventions have been attempted or rejected by the person.

- Antidepressants should be considered for people presenting with severe depression.
- Diagnosis should be carried out using ICD10. Trust approved rating scales may be used to monitor treatment outcomes
- **Starting antidepressant medication**
- When offering a person medication for the treatment of depression, discuss and agree a management plan with the person. Include:
    - The reasons for offering medication
    - The choices of medication (if a number of different antidepressants are suitable)
    - 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 and how the medication may help
    - The harms, covering both the possible side effects and withdrawal effects, including any side effects they would particularly like to avoid (for example, weight gain, sedation, effects on sexual function)
    - Any concerns they have about taking or stopping the medication (also see the recommendations on stopping medication).

Make sure they have written information to take away and to review that is appropriate for their needs.

- When prescribing antidepressant medication, ensure people have information about:
    - How they may be affected when they first start taking antidepressant medication, and what these effects might be
    - How long it takes to see an effect (usually, if the antidepressant medication is going to work, within 4 weeks)
    - When their first review will be; this will usually be within 2 weeks to check their symptoms are improving and for side effects, or after 1 week if a new prescription is for a person aged 18 to 25 years or if there is a particular concern for risk of suicide (see recommendations on antidepressant medication for patients at risk of suicide)
    - The importance of following instructions on how to take antidepressant medication (for example, time of day, interactions with other medicines and alcohol)
    - Why regular monitoring is needed, and how often they will need to attend for review
    - How they can self-monitor their symptoms, and how this may help them feel involved in their own recovery
    - That treatment might need to be taken for at least 6 months after the remission of symptoms, but should be reviewed regularly
    - How some side effects may persist throughout treatment

- withdrawal symptoms and how these withdrawal effects can be minimised (see also the recommendations on stopping antidepressant medication). **[2022]**

- There is little evidence of difference in efficacy between different drugs but there are differences in side effect profiles, potential for interactions and safety in overdose. If all of these are equal, then cost should be considered.
- The physical health and comorbid conditions/medication should be taken into account when choosing medication.
- There is a possibility of increased anxiety, agitation, and suicidal ideation in the first few weeks of antidepressant treatment, especially SSRI's and related. If this occurs and is intolerable the judicious use of a benzodiazepine can be considered, as well as increased levels of support, and patient education around this time.
- Patients should be reviewed on a regular basis for continued efficacy and tolerability, ideally no less than 6 monthly.
- For patients with a first episode treatment should be continued for a minimum for 6 months post remission, for those with two or more episodes in a short space of time then 2 years treatment is advised. If patients have multiple relapses, then long term treatment should be considered.

4. Side-effects and Interactions

(See table for comparison of common side effects)

Most side effects are transient in nature, and patients should be encouraged to see if they can work through them until they abate.

SSRIs are better tolerated and safer in overdose than other antidepressants.

Common side effects of SSRIs:

- Headache, nausea, and anxiety/agitation, especially when starting treatment, this usually settles within the first week or so.
- Other side effects are insomnia, tremor, akathisia, sweating, parathesia, sexual dysfunction, (including reduced libido, and difficulty with erection and orgasm) muscle/joint pain, weight gain (mild), and rarely manic or psychotic symptoms. Citalopram and escitalopram have dose related QTc changes. The SPC for Lustral states caution in patients with prolonged QTc or on other agents that prolong QTc, however the BNF states that caution is advised when prescribing all SSRI's in patients with cardiac disease, and an appropriate history taken

Common side effects of Tricyclic antidepressants:

- Common side effects tricyclics include anxiety, drowsiness, dizziness, agitation, confusion, anticholinergic effects (dry mouth, constipation, urinary retention, blurred vision); cardiovascular effects (hypotension, tachycardia, arrhythmias, and other ECG changes – baseline ECG advised, where appropriate); hepatic effects, changes in blood sugar, increased appetite, weight gain and sexual dysfunction can occur.

- TCAs have similar efficacy to SSRIs but are more likely to be discontinued because of side effects and are toxic in overdose.

Mirtazapine has few antimuscarinic effects, but causes sedation during initial treatment and is associated with weight gain and blood dyscrasias

Venlafaxine and Duloxetine have similar side effects to SSRI's but can also increase heart rate and blood pressure, as such it is important to identify risk factors prior to prescribing, e.g., uncontrolled hypertension

5. Warnings

- Antidepressants are associated with an initial worsening of anxiety/agitation and an increase of suicidal thinking and behaviour. Monitor closely, at a minimum of two weekly intervals, especially at the start of treatment and when the dose is changed. Consider increased levels of support, and patient education around this time.
- Use antidepressants with care in glaucoma, bipolar, prostate hypertrophy, bleeding disorders and seizures.
- Hyponatremia has been associated with all antidepressants and should be considered in all those who develop drowsiness, confusion, or convulsions whilst taking antidepressants. SSRI's are particularly well known for this and Mirtazapine may be a reasonable alternative should this occur, although continued monitoring is advised.
- SSRIs can increase risk of bleeding. Caution is required in older adults and when used in combination with NSAIDS, aspirin, valproate, or anticoagulants. See also side effects.
- SSRIs can increase risk of falls and osteoporotic fractures in people over 50 years.
- Serotonin syndrome can occur with serotonergic drugs, especially when combined together
- It can present as:
    - Agitation
    - Confusion
    - Tremor
    - Hyperflexia
    - Myoclonus
    - Hyperthermia
- Examples of other serotonergic drugs include Tramadol, Triptans, Lithium, be mindful of co-prescribing these agents.
- Although no specific ongoing physical health monitoring is required for prescribing antidepressants, this should form part of the overall management of the patient.

6. Stopping Antidepressants

- Advise people wishing to stop their medication to talk to the person prescribing it, explain that in most cases it will be necessary to taper the dose, but that most people successfully stop them.
- Advise them if they stop the medication abruptly or miss doses may experience withdrawal features, these may include:
    - Unsteadiness, vertigo, or dizziness
    - Altered sensations e.g., electric shock feelings
    - Altered feelings such as irritability, anxiety, low mood, panic attacks, confusion, or rarely suicidal thoughts
    - Restlessness or agitation
    - Problems sleeping
    - Sweating
    - Abdominal symptoms e.g., nausea
    - Palpitations
- Explain that they can be mild and fade within 1-2 weeks
- Can be more severe lasting weeks or months
- Take in to account the pharmacokinetics
- Consider stepwise reductions, initially 50% of the previous dose, but reducing to 25% at lower doses, take into account available preparations, if withdrawal appears consider stepping back to the previous dose and slow the reduction
- Monitor the person for withdrawal symptoms, relapse, the frequency being based on clinical and support needs
- Explain the difference between withdrawal and relapse, tell them who to contact in the event of problems
- The Royal College has produced guidance to aid id discussion with patients.

7. Use of Lithium to augment Antidepressants (see Lithium Clinic Policy for specific guidance)

- For people with depression taking lithium, assess weight, renal and thyroid function and calcium levels before treatment and then monitor at least every 6 months during treatment, or more often if there is evidence of significant renal impairment.
- For women of reproductive age, in particular if they are planning a pregnancy, discuss the risks and benefits of lithium, preconception planning and the need for additional monitoring
- Monitor serum lithium levels 12 hours post dose, 1 week after starting treatment and 1 week after each dose change, and then weekly until levels are stable. Adjust the dose according to serum levels until the target level is reached.

- When the dose is stable, monitor every 3 months for the first year, after the first year, measure plasma lithium levels every 6 months, or every 3 months for people in any of the following groups:
    - Older people
    - People taking medicines that interact with lithium
    - People who are at risk of impaired renal or thyroid function, raised calcium levels or other complications
    - People who have poor symptom control
    - People with poor adherence
    - People whose last plasma lithium level was 0.8 mmol per litre or higher.
- Determine the dose of lithium according to response and tolerability:
    - Plasma lithium levels should not exceed 1.0 mmol/L (therapeutic levels for augmentation of antidepressant medication are usually at or above 0.4 mmol/L; consider levels 0.4 to 0.6 mmol/L for older people aged 65 or above)
    - Do not start repeat prescriptions until lithium levels and renal function are stable
    - Take into account a person's overall physical health when reviewing test results (including possible dehydration or infection)
    - Take into account any changes to concomitant medication (for example, angiotensin-converting enzyme inhibitors, angiotensin 2 receptor blockers, diuretics and non-steroidal anti-inflammatory drugs [NSAIDs], or over-the-counter preparations) which may affect lithium levels, and seek specialist advice if necessary
    - Monitor at each review for signs of lithium toxicity, including diarrhoea, vomiting, coarse tremor, ataxia, confusion, and convulsions
    - Seek specialist advice if there is uncertainty about the interpretation of any test results.
    - Consider electrocardiogram (ECG) monitoring in people taking lithium who have a high risk of, or existing, cardiovascular disease.
    - Provide people taking lithium with information on how to do so safely, including the NHS lithium treatment pack.
    - Only stop lithium in specialist mental health services, or with their advice. When stopping lithium, whenever possible reduce doses gradually over 1 to 3 months.

8. Use of oral antipsychotics as augmentation

- The use of antipsychotics for the treatment of depression was an off-label use for some antipsychotics. See NICE's information on prescribing medicines.
- Before starting an antipsychotic, check the person's baseline pulse and blood pressure, weight, nutritional status, diet, level of physical activity, fasting blood glucose or HbA1c and fasting lipids. [2022]

- Carry out monitoring as indicated in the summary of product characteristics for individual medicines, for people who take an antipsychotic for the treatment of their depression. This may include:
    - Monitoring full blood count, urea and electrolytes, liver function tests and prolactin
    - Monitoring their weight weekly for the first 6 weeks, then at 12 weeks, 1 year and annually
    - Monitoring their fasting blood glucose or HbA1c and fasting lipids at 12 weeks, 1 year, and then annually
    - ECG monitoring (at baseline and when final dose is reached) for people with established cardiovascular disease or a specific cardiovascular risk (such as diagnosis of high blood pressure) and for those taking other medicines known to prolong the cardiac QT interval (for example, citalopram or escitalopram)
    - At each review, monitoring for adverse effects, including extrapyramidal effects (for example, tremor, parkinsonism) and prolactin-related side effects (for example, sexual or menstrual disturbances) and reducing the dose if necessary
    - Being aware of any possible drug interactions which may increase the levels of some antipsychotics, and monitoring and adjusting doses if necessary
    - If there is rapid or excessive weight gain, or abnormal lipid or blood glucose levels, investigating and managing as needed.
- For people with depression who are taking an antipsychotic, consider at each review whether to continue the antipsychotic based on their current physical and mental health risks.
- Only stop antipsychotics in specialist mental health services, or with their advice. When stopping antipsychotics, reduce doses gradually over at least 4 weeks and in proportion to the length of treatment

9. Special Populations

9.1 Children (under 18 years)

The NICE clinical guideline 28 covers using antidepressants in children and young people in the management of depression

This guideline covers children and young people up to their 18th birthday.

The major points are

- Medication should not be prescribed for mild depression.
- First line treatment for moderate to severe depression in children and young people is psychological therapies including:
    - Information and advice on self-help materials or strategies, exercise, sleep hygiene, anxiety management and nutrition
- Do not offer antidepressant medication except in combination with a concurrent psychological therapy.

- If psychological therapies are declined medication may still be offered but monitor regularly and focus on adverse drug reactions.
- Fluoxetine is the only antidepressant for which trials in young people show that benefit outweighs risk.
    - The effectiveness in children is not established.
    - It should only be prescribed after full assessment and diagnosis and MDT review.
    - Ensure weekly contact for at least the first four weeks. Assess for the emergence of adverse side effects such as anxiety, irritability, hostility, suicidal thoughts, or self-harm.
    - Inform the patient and their parents/carers of these potential adverse effects and urge them to contact the prescribing doctor if they emerge.
    - Written and verbal information should be provided. This should also include details of delay in onset of effect, time course of treatment, the need to take medication as prescribed and the need to discontinue gradually at the end of treatment
    - Start with 10mg per day as liquid Fluoxetine. This comes as 20mg/5ml. Then increase the dose after one week to 20mg capsules.
- If fluoxetine is unsuccessful after an adequate trial at adequate doses and the depression is sufficiently severe to justify the trial of another antidepressant, NICE recommends citalopram or sertraline as second line treatment options.
- Starting doses should be low.
- Prozac brand of fluoxetine is the only licensed product for the treatment in over 8 years old. No other treatment is licensed under the age of 18. Patients and parents/carers should be informed of the implications of this, and formal consent obtained.
- Do not use paroxetine or venlafaxine, tricyclic antidepressants, or St John's Wort.
- Other antidepressants should start with half the daily adult starting dose. Increase, if necessary, over 2-4 weeks to the usual daily adult dose.
- There is little evidence regarding the effectiveness of doses above 20mg daily for fluoxetine or upper adult daily doses for other antidepressants.
- Higher doses should only be considered in older children of higher body weight and young people when the severity of the illness makes an early clinical response a priority.

9.2 Pregnancy

- The risks of medicine should be balanced against the risks of symptom relapse. Uncontrolled symptoms may affect the mother child relationship directly or via an increase in risk taking, such as co-morbid alcohol, drug, and nicotine use.
- Risks associated with use of medicine to treat depression during pregnancy include teratogenicity and neonatal side effects. The latter may be toxicity or

withdrawal effects (usually mild and self-limiting). Little is known about the developmental effects of foetal exposure to antidepressants.

- With all women of childbearing potential discuss contraception and the risks of symptom relapse and the use of medication in pregnancy.
- Most of the danger for organ damage is in weeks 3 to 8 post conception. This may be before a woman is aware she is pregnant. All woman of childbearing age should be advised of the importance of effective contraception. The woman should be encouraged to plan any pregnancies with the psychiatrist or other clinician.
- Treatment options will depend on the patient's previous history and the patient and clinician's preferences. These may include non-pharmacological treatments such as cognitive behavioural therapy, treatment break during the first trimester, continuing current effective treatment with monitoring or reducing or stopping treatment before delivery. Consult tests such as NICE, Drugs in Pregnancy, Maudsley prescribing guidelines. You can also contact the Trust Pharmacy Services (03000 211308) and/or the National Teratology information Service (0191 2321525).
- It is important to ensure all healthcare professionals involved in the pregnancy and delivery, are aware of any prescribed medicines.
- Exposure to SSRIs and SNRIs in late pregnancy may increase the risk of persistent pulmonary hypertension of the newborn.
- NICE recommends that paroxetine is stopped if a woman is planning a pregnancy or has an unplanned pregnancy.
- Venlafaxine may be associated with increased risk of high blood pressure at high doses.
- The choice of antidepressant may also be influenced by the woman's intention to or not to breast feed.

9.3 Elderly

When prescribing antidepressant medication for older people:

- Take into account the person's general physical health, comorbidities and possible interactions with any other medicines they may be taking
- Carefully monitor the person for side effects
- Be alert to an increased risk of falls and fractures
- Be alert to the risks of hyponatraemia (particularly in those with other risk factors for hyponatraemia, such as concomitant use of diuretics).

9.4 Patients at risk of suicide

Antidepressant medication for people at risk of suicide

When prescribing antidepressant medication for people with depression thought to be at increased risk of suicide, this should include when doses are changed:

- Assess their mental state and mood before starting the prescription, ideally in person (or by video call or by telephone call if in-person assessment is not possible, or not preferred)
- Be aware of the possible increased prevalence of suicidal thoughts, self-harm, and suicide in the early stages of antidepressant treatment and ensure that a risk management strategy is in place.
- Review them 1 week after starting the antidepressant medication or increasing the dose for suicidality (ideally in person, or by video call, or by telephone if these options are not possible or not preferred)
- Review them again after this as often as needed, but no later than 4 weeks after the appointment at which the antidepressant was started
- Base the frequency and method of ongoing review on their circumstances (for example, the availability of support, unstable housing, new life events such as bereavement, break-up of a relationship, loss of employment), and any changes in suicidal ideation or assessed risk of suicide.

Take into account toxicity in overdose when prescribing an antidepressant medication for people at significant risk of suicide. Do not routinely start treatment with TCAs, except lofepramine, as they are associated with the greatest risk in overdose.

Patients should have access to a personal crisis plan, a copy of which can be found on SystmOne under RDaSH MH Crisis Plan

10. Antidepressants and driving

- Section 4 of the Road Traffic Act 1988 does not differentiate between illicit or prescribed drugs. Therefore, any person who is driving or attempting to drive on the public highway or other public places whilst unfit due to any drug is liable for prosecution.
- All drugs action on the central nervous system can impair alertness, concentration and driving performance. This is particularly so at initiation of treatment, or soon after and when dosage is being increased. Driving must cease if adversely affected.
- The older tricyclic antidepressants can have pronounced anticholinergic and antihistaminic effects, which may impair driving. The more modern antidepressants may have fewer adverse effects. **These considerations need to be taken into account when planning the treatment of a patient who is a professional driver.**
- Anti-psychotic drugs, including the depot preparations, can cause motor or extrapyramidal effects as well as sedation or poor concentration, which may either alone or in combination be sufficient to impair driving. Careful clinical assessment is required.
- The epileptogenic potential of psychotropic medication should be considered particularly when patients are professional drivers.

- Benzodiazepines are the most likely psychotropic medication to impair driving performance, particularly the long-acting compounds. **Alcohol will potentiate the effects.**
- Doctors have a duty of care to advise their patients of the potential dangers of adverse effects from medication and interactions with other substances, especially alcohol.

11. References

1. NICE Clinical Guideline (CG90) Depression: the treatment and management of depression in adults (update). http://guidance.nice.org.uk/CG90/Guidance/pdf/English
2. Depression in adults: treatment and management https://www.nice.org.uk/guidance/ng222
3. Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults https://www.nice.org.uk/guidance/ng215
4. NICE Clinical Guideline (CG91) Depression in adults with a chronic physical health problem: Treatment and management. http://guidance.nice.org.uk/CG91/Guidance
5. BAP Consensus Guidelines. Evidence based guidelines for treating depressive disorder with Antidepressants. www.bap.org.uk/pdfs/BAP_Guidelines-Antidepressants.pdf
6. BNF online (British Medical Association and the Royal Pharmaceutical Society of Great Britain). Online BNF at: www.bnf.org
7. Martindale – The complete drug reference online at: http://www.medicinescomplete.com/mc/ [subscription required]
8. SPC for all the drugs referred to in this guideline can be found in the Electronic Medicines Compendium (http://emc.medicines.org.uk/).
9. Psychotropic Drug Directory Bazire 2012
10. The Maudsley Guidelines 13th edition and online at http://www.library.nhs.uk/booksandjournals/ebooks/
11. DVLA For medical practitioners at a glance guide to the current medical standards of fitness to drive Nov 2014 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/390134/aagv1.pdf
12. NICE Clinical guideline (CG 192) Antenatal and postnatal mental health: clinical management and service guidance https://www.nice.org.uk/guidance/cg192
13. NICE Clinical Guideline (CG28) Depression in children and young people: Identification and management in primary, community, and secondary care http://www.nice.org.uk/guidance/cg28

Table 1: PHARMACOLOGICAL TREATMENTS FOR DEPRESSION
1a: FIRST AND SECOND LINE OPTIONS

First Line:	Relative Cost	Notes
Citalopram	**£**	Has less drug/drug interactions, but be aware of MHRA advice regarding dose related QTc prolongation. The BNF states caution in prescribing SSRI's in patients with cardiac disease, however NICE guidance has not altered regarding Sertraline and Mirtazapine being the drugs of choice, unless otherwise contraindicated.
Sertraline	**£**	Sertraline has a superior tolerability and is preferred in cardiac disease, however the SPC for Lustral, states caution in patients with prolonged QTc or on other agents which prolong QTc, or have other cardiac disease. . The BNF states caution in prescribing SSRI's in patients with cardiac disease, however NICE guidance has not altered regarding Sertraline and Mirtazapine being the drugs of choice, unless otherwise contraindicated.
Mirtazapine	**£**	Useful where weight is not a concern and sedation is preferable Lack of anticholinergic side effects, lack of sexual side effects
Fluoxetine Liquid	**£** **££**	Long half life – useful if compliance is an issue, has many drug interactions . The BNF states caution in prescribing SSRI's in patients with cardiac disease, however NICE guidance has not altered regarding Sertraline and Mirtazapine being the drugs of choice, unless otherwise contraindicated.
Second Line:	**Relative Cost**	**Notes consider if first line inappropriate or already tried**
Venlafaxine XL	£- ££	More toxic than SSRIs; risk of discontinuation reaction, avoid in uncontrolled hypertension
Lofepramine	££	Least cardiotoxic of TCAs
Trazodone	£	Useful in anxiety and agitation where sedation is required
Duloxetine	££	Little or no advantages over other antidepressants; Expensive; care needed to use correct dosage regimen; associated with nausea and headache, and can also increase blood pressure. It may however be considered in patients who also have co-morbid neuropathic pain
Reboxetine	**££**	Unlicensed in elderly patients, may be useful in patients who are sensitive to serotenergic side effects
Third Line:	**Reltive Cost**	Notes
Vortioxetine	**££**	Consider as an option if a patient has failed to respond to two different agents within a single episode of depression

1b: FOR SPECIALIST CARE INITIATION

Specialist Care initiation only	Relative Cost	Notes
MAOI's	**£**	Dietary problems. Use for atypical depression when lack of response to other antidepressants
Mianserin	**££**	Regular blood counts needed
Clomipramine	**£**	Useful if OCD symptoms are present as well
Tricyclics (other than those listed above)	**£**	Toxic in overdose, poorly tolerated

1c: NOT RECOMMENDED

Not Recommended		Notes
Dosulepin	£	Avoid due to increased cardiac risk and toxicity in overdose.
Agomelatine	£££	Liver function test required during use; expensive; Use not recommended by Trust. However if patients are admitted to our service on this medication, the prescriber must ensure that the recommended Liver Function Tests are carried out. https://www.gov.uk/drug-safety-update/agomelatine-valdoxan-risk-of-liver-toxicity

TABLE 2: TREATMENT RESISTANT DEPRESSION

For initiation and stabilisation in secondary care

General Guidance on options		
General guidance Assure compliance, and manage ADR's that may impact on this Escalate antidepressant doses for an adequate duration Switch drugs – ensuring that all drug classes have been tried optimally Augment the antidepressant with other drugs or combine two antidepressants Treatment Options Use combination of mirtazapine & venlafaxine – recommended by NICE Add lithium – well established – recommended by NICE High Dose Venlafaxine >225mg/day (up to 375mg, notes increased risk of side effects) Augment with an antipsychotic if evidence of psychosis If the above are unsuccessful, then consult current literature and seek expert opinion where necessary		
Augmentation	**Relative Cost**	**Notes (initiated in secondary care)**
Lithium	£	Use in treatment resistant depression – blood tests needed
Antipsychotic	£-£££	Use in depression with psychotic symptoms or resistant major depression (see Maudsley Guidelines)

TABLE 3: USUAL RECOMMENDED TREATMENT OF DEPRESSION IN CHRONIC MEDICAL CONDITIONS

Co-morbidity	Recommended treatment In all chronic conditions any possible drug interactions must be considered as a matter of priority
Post stroke	SSRIs Mirtazapine (small effect on INR – causing an increase to INR)
Diabetes	SSRIs – fluoxetine best supported by data Venlafaxine Mirtazapine
Cardiovascular disease	SSRIs – preferably sertraline especially if also prescribed flecainide, propafenone. – not recommended if also prescribed antiplatelets, aspirin or anticoagulants due to increased risk of bleeding Mirtazapine
Epilepsy	Check choices with Medicines Information before use of any antidepressant
Hepatic	Lofepramine or Paroxetine, monitor closely for increased side effects
Elderly	SSRIs – but be aware of risk of hyponatraemia Mirtazapine In Parkinson's disease do not use SSRIs with MAO-B inhibitors e.g. selegiline
Renal impairment	If unsure check with pharmacy before use of any antidepressant, especially if CKD 3b or worse
Musculoskeletal disease	SSRIs not recommended to be used with NSAIDs. If essential use a gastroprotective agent at the same time
Migraine	In people receiving triptans use mirtazapine / trazodone / mianserin or reboxetine

TABLE 4: RELATIVE SIDE-EFFECT PROFILES OF ANTIDEPRESSANTS

	MAIN SIDE EFFECTS					
Drug	**Drowsiness**	**Weight gain**	**Nausea**	**Anticholinergic effects**	**Sexual problems**	**Cardiac effects**
Citalopram	+	+	+++	+	+++	+
Sertraline	+	+	+++	+	+++	+
Fluoxetine	+	+	+++	+	+++	+
Escitalopram	+	+	+++	+	+++	+
Mirtazapine	+++	+++	o	o	o	+
Venlafaxine	+	+	+++	++	+++	++
Moclobemide	+	+	++	++	+	++
Amitriptyline	+++	++	++	+++	++	+++
Clomipramine	+++	++	++	+++	++	+++
Imipramine	++	++	++	++	++	+++
Nortriptyline	++	++	++	++	++	+++
Lofepramine	++	++	++	+	++	+++
Trazodone	+++	+	++	o	+	+++
Paroxetine	+	+	+++	+	+++	+
Fluvoxamine	+	+	+++	+	+++	+
Reboxetine	o	o	o	+++	+	++
Duloxetine	+	+	+++	++	+++	++
Phenelzine	+	+	++	++	++	+++
Agomelatine	o	o	o	o	o	++
Vortioxetine	+	+	+++	+	+	o
Tryptophan	+	o	+	o	o	+
Lithium	+	++	+	o	o	+

TABLE 5: ADVICE ON SWITCHING ANTIDEPRESSANTS

(Adapted from the Maudsley Prescribing Guidelines)

From	To	Advice
MAOI's	anything	Stop and wait two weeks before initiating
Tricyclic Antidepressants (TCA)	MAOI	Withdraw and wait one week
	Other TCA	Cross taper cautiously
	Mirtazapine	Cross taper cautiously
	SSRI's	Halve dose, add SSRI and withdraw slowly
	Venlafaxine	Cross taper cautiously, start with venlafaxine 37.5mg
	Duloxetine	Cross taper cautiously, start with 60mg alternate days
SSRI's (except fluoxetine)	MAOI's	Withdraw and wait 2 weeks
	TCA	Cross taper cautiously with low dose TCA
	Mirtazapine	Cross taper cautiously
	Other SSRI	Withdraw and start new agent
	Venlafaxine	Cross taper cautiously and start venlafaxine 37.5mg at night
	Duloxetine	Withdraw, start 60mg on alternate days, increase slowly
Fluoxetine	MAOI's	Withdraw and wait 5-6 weeks
	TCA	Withdraw, wait 5-7 days, then slowly titrate cautiously
	Mirtazapine	Cross taper cautiously
	Venlafaxine	Withdraw, start 37.5mg at night an titrate slowly
	Duloxetine	Withdraw, wait 5-7 days, start 60mg on alternate days, increase slowly
Mirtazapine	MAOI	Withdraw, wait one week
	TCA	Withdraw, then start TCA
	SSRI/Venlafaxine	Cross taper cautiously
	Duloxetine	Withdraw, start 60mg on alternate days, increase slowly
Venlafaxine	MAOI	Withdraw and wait at least one week

	TCA/SSRI	Cross taper cautiously starting with low dose
	Mirtazapine	Cross taper cautiously
	Duloxetine	Withdraw, start 60mg on alternate days, increase slowly
Duloxetine	MAOI	Withdraw and wait one week
	TCA	Cross taper cautiously starting with low dose
	SSRI/Venlafaxine and Duloxetine	Withdraw then start new drug