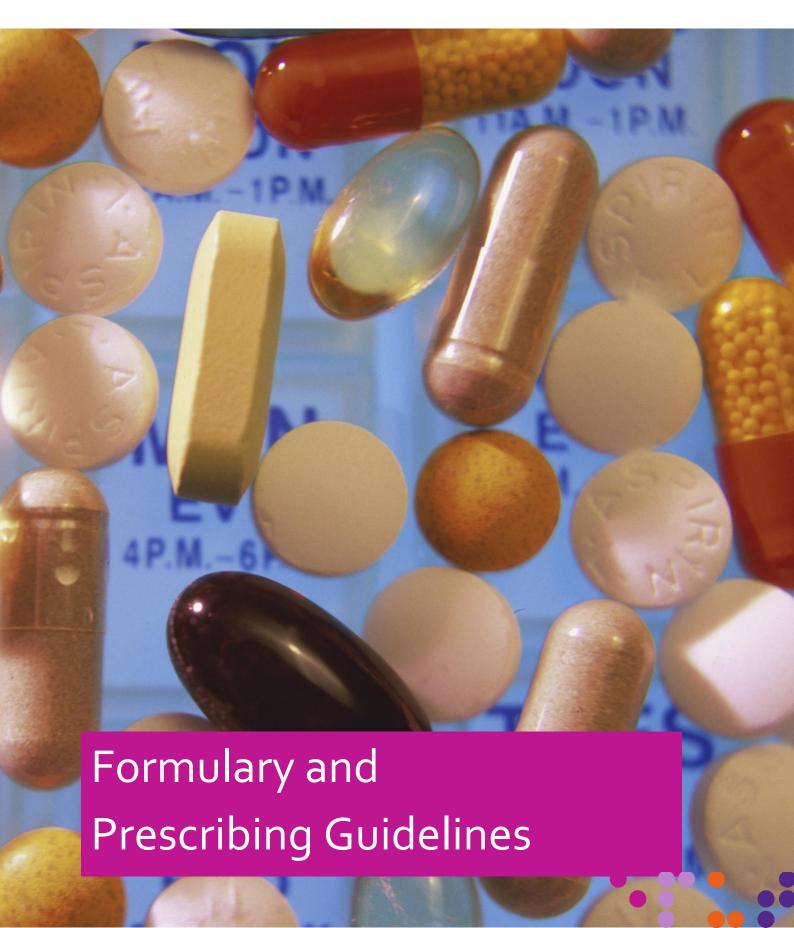


# **SECTION 1: THE TREATMENT OF DEPRESSION**



#### 1.1 Introduction

This guidance should be considered as part of a stepped care approach in the management of depressive disorders. Antidepressants are not routinely recommended for persistent sub-threshold depressive symptoms or mild depression but can be considered in these categories where there is a past history of moderate or severe depression, initial presentation of sub-threshold depressive symptoms for at least 2 years, and persistence of either mild or sub-threshold depression after other interventions<sup>1</sup> have failed. The most current NICE guidance should be consulted wherever possible to obtain the most up to date information.

For individuals with moderate or severe depression, a combination of antidepressant medication and a high intensity psychological intervention (CBT or IPT) is recommended.

When depression is accompanied by symptoms of anxiety, usually treat the depression first. If the person has an anxiety disorder and co-morbid depression or depressive symptoms, consider treating the anxiety first. Also consider offering advice on sleep hygiene, by way of establishing regular sleep and wake times; avoiding excess eating, avoiding smoking and drinking alcohol before sleep; and taking regular physical exercise if possible.

Consider tests for thyroid dysfunction for patients with depression or unexplained anxiety.<sup>7</sup>

If used in pregnancy, refer to the MHRA warning <sup>9</sup> for SSRI and SNRIs, about the small increased risk of postpartum haemorrhage when used in the month before delivery. See formulary section 20 (Antenatal and postnatal prescribing).

Detailed information on the treatment of depression in children and adolescents can be found in <u>section 12</u>. Further guidance on prescribing for older adults and for antenatal/postnatal service users can be found in <u>section 11</u> and <u>section 20</u>, respectively.

## 1.2 Approved Drugs for the treatment of Depression in Adults

For licensing indications, see Annex 1

Drug <sup>5</sup>	Formulation <sup>5</sup>	Comments <sup>2,3,4</sup>
Amitriptyline	Tabs 10mg, 25mg, 50mg Liquid 50mg/5ml	TCA Tricyclic Antidepressant
Citalopram	Tabs 10mg, 20mg, 40mg Drops 40mg/ml (1drop=2mg) 4 drops (8 mg) ≡ 10mg tablet	SSRI Selective Serotonin Reuptake Inhibitor Bioequivalence varies between tablets and liquid
Clomipramine	Caps 10mg, 25mg, 50mg	TCA
Dosulepin	Caps 25mg Tabs 75mg	TCA For existing patients only, if no contra-indication.
Duloxetine	Caps 30mg, 60mg	4 <sup>th</sup> line for depression. 3 <sup>rd</sup> line for adults over 65.
Fluoxetine	Caps 20mg, Liquid 20mg/5ml	SSRI 1st line (based on acquisition cost)

Drug⁵	Formulation <sup>5</sup>	Comments <sup>2,3,4</sup>
Flupentixol	Tabs 500mcg, 1mg	'Other' antidepressant
Imipramine	Tabs 10mg, 25mg Liquid 25mg/5ml	TCA
Lofepramine	Tabs 70mg Liquid 70mg/5ml	TCA
Mirtazapine	Tabs 15mg, 30mg, 45mg Orodispersible Tabs 15mg, 30mg, 45mg Liquid 15mg/ml	NaSSa Noradrenaline and Specific Serotonin antidepressant
Moclobemide	Tabs 150mg, 300mg	RIMA Reversible Inhibitor of Monoamine A
Paroxetine	Tabs 20mg, 30mg Liquid 10mg/5ml	SSRI
Phenelzine	Tabs 15mg	MAOI
Sertraline	Tabs 50mg, 100mg	SSRI
Trazodone	Caps 50mg, 100mg Tabs 150mg Liquid 50mg/5ml	Tricyclic-related antidepressant
Venlafaxine	Tabs 37.5mg, 75mg M/R Caps 75mg, 150mg	Doses above 300mg monitoring required. Cardiac risk. Consultant supervision.
Vortioxetine	Tabs 5mg, 10mg, 20mg	Serotonin Modulator and Stimulator 3 <sup>rd</sup> line – see note below**

<sup>\*</sup>Agomelatine is non formulary based on the guidance provided by NICE in relation to the termination of <u>TA 231</u>, July 2011 (due to the lack of evidence to support use).

Trimipramine is non formulary as it does not represent a cost-effective choice of TCA.

### 1.2 NICE Clinical Guidelines

NICE CG90: Depression in adults: recognition and management (October 2009) <sup>4</sup>
NICE CG91: Depression in adults with a chronic physical health problem: recognition and management (October 2009) <sup>8</sup>

## 1.2.1 Choice of antidepressant

 Consider using a baseline assessment for severity of depression and regularly review symptoms both clinically and using standard severity rating

<sup>\*\*</sup>Vortioxetine is the subject of a NICE Technology Appraisal (<u>TA 367</u>) and is approved for treatment of major depressive episodes in adults which have been unresponsive to two previous antidepressants.

scales. Initially, normally **choose a generic SSRI** whilst taking the following into account:

- Fluoxetine, fluvoxamine and paroxetine have a higher propensity for drug interactions (<u>see current BNF</u>). 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 problems (see table below)
- Paroxetine has a higher incidence of discontinuation symptoms (consider half-lives). See section 1.3
- SSRIs 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
- The risk of suicide attempted suicide or self-harm. Mirtazapine, venlafaxine and trazadone have been associated with the highest absolute risk.
- Acquisition cost (Fluoxetine is currently lowest)
- Discuss choice of antidepressant, covering:
  - Patient choice the patient's perception of the efficacy and tolerability<sup>4</sup>
  - Existing co-morbid psychiatric disorders such as obsessive compulsive disorder, anxiety spectrum disorder etc., through accurate history taking (<u>Annex 1</u>)
  - Anticipated adverse events for example, agitation, nausea and vomiting (with SSRI antidepressants), and discontinuation symptoms (see <u>Annex 2</u>)
  - Potential interactions with concomitant medication or physical illness (there is currently no evidence to support using specific antidepressants in particular physical health problems)

Medication for physical health problem	Recommended antidepressant(s) <sup>4</sup>
NSAIDs (non-steroidal anti-inflammatory drugs)	Do not normally offer SSRIs – but if no suitable alternatives can be identified, offer gastro-protective medicines (for example, proton pump inhibitors) together with the SSRI. Consider mirtazapine, moclobemide or trazodone
Warfarin or heparin	Do not normally offer SSRIs. Consider mirtazapine.
Theophylline, clozapine, or methadone	Do not normally offer fluvoxamine – offer sertraline or citalopram
'Triptan' drugs for migraine	Do not offer SSRIs – offer mirtazapine or trazodone.

Aspirin	Use SSRIs 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.
Monamine oxidase B inhibitors (for example, selegiline or rasagiline)	Do not normally offer SSRIs – offer mirtazapine or trazodone.
Flecainide or propafenone	Offer sertraline as the preferred antidepressant – mirtazapine or moclobemide may also be used.

- When prescribing antidepressants for older adults (see <u>section 11</u> for further information)
  - Prescribe at an age-appropriate dose taking into account physical health, and existing medication (see table above)
  - Monitor carefully for side-effects (see <u>Annex 2</u>)
- When prescribing drugs other than SSRIs, take into account:
  - The increased likelihood of the person stopping treatment because of side effects, and the consequent need to increase the dose gradually, as for example with venlafaxine and tricyclic antidepressants (TCAs)
  - That dosulepin should not be prescribed
  - That irreversible Monoamine oxidase inhibitors MAOIs (such as phenelzine) should only normally be prescribed by a Consultant Psychiatrist
- Take into account toxicity in overdose for people at significant risk of suicide.
  When initiating antidepressants, especially SSRIs, actively monitor suicidal
  ideations, self-harming thoughts and changes in both. If changes are
  noticed, increase review frequency. Be aware that:
  - Compared with other equally effective antidepressants recommended in primary care (such as SSRIs), venlafaxine is associated with a greater risk of death from overdose, but the greatest risk in overdose is with TCAs, except for lofepramine
  - For people who are not considered to be at increased risk of suicide, normally review after 2 weeks, then regularly every 2–4 weeks in the first 3 months for example, and then at longer intervals if response is good
  - For people who are considered to be at increased risk of suicide or are younger than 30 years, normally see them after 1 week and then frequently until the risk is no longer clinically significant, particularly if they have been commenced on a SSRI. Review periods should be based on individual assessments

#### General Issues

- Explore any concerns that the person may have about taking an antidepressant and provide information about:
- The gradual development of the full antidepressant effect
- The importance of taking the medication as prescribed and the need to continue beyond remission
- Potential side effects and drug interactions and strategies for minimisation
- The risk and nature of discontinuation symptoms (particularly with drugs with a shorter half-life, such as paroxetine and venlafaxine)
- The fact that addiction does not occur.
- Do not prescribe or advise use of St John's Wort for depression
  - Explain the different potencies of the preparations available and the potential serious interactions of St John's Wort with other drugs (including oral contraceptives, anticoagulants and anticonvulsants)
- Patients receiving ECT can be prescribed antidepressants simultaneously and there is evidence that there is a synergistic effect when antidepressants are used.

In every instance, choice of antidepressant should be based on the circumstances of the individual being treated and their individual preferences. If after consultation a range of choices are available taking into consideration safety and concordance profiles, the drug of lowest acquisition cost should be selected.

## 1.2.2 Early treatment with an antidepressant<sup>4</sup>

If increased anxiety or agitation develops early in treatment with an SSRI, a short period of concomitant therapy (usually no longer than 2 weeks) with a benzodiazepine may be considered<sup>4</sup>. (This consideration does <u>not</u> apply to patients with chronic anxiety and benzodiazepines should only be used with caution in patients at risk of falls<sup>4</sup>.) The patient should be informed that this is usually a transient effect and should last no longer than a few weeks. If the anxiety or agitation is unacceptable to the patient, consider changing to a different antidepressant (see Annex 3).

## 1.2.3 Lack of response to initial antidepressant<sup>4</sup>

- If improvement is not reported within 2-4 weeks, <u>check</u> that the drug has been taken as prescribed and enquire about side-effects experienced (see Annex 2 for side effect profile).
- If response is absent or minimal after 3–4 weeks of treatment with a therapeutic dose of an antidepressant, increase support and consider increasing the dose in line with the summary of product characteristics (SPC) if there are no significant side effects. If there are side effects or if the patient prefers, consider switching to another antidepressant. (*Information relating to stopping/switching can be found in Annex 3*)

- If there is some improvement by week 4, continue treatment for another 2-4
  weeks at an increased dose. Consider switching to another antidepressant if
  response is still not adequate; there are side effects; or if the patient prefers
  to change medication
- If considering switching antidepressant, consider a different SSRI or Mirtazapine if the patient has significant loss of appetite or severe insomnia.
- Subsequently, if the second SSRI or Mirtazapine is not effective/welltolerated, consider switching to one of the better tolerated newer generation antidepressants such as duloxetine or vortioxetine, considering the various factors mentioned above
- Subsequently, consider substituting with an antidepressant of a different class that may be less well tolerated (such as venlafaxine, or a reversible MAOI such as moclobemide, or a TCA)

## 1.2.4 Guidance for Prescribing Venlafaxine:

- Do not prescribe venlafaxine for patients with:
  - 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

### 1.2.5 Guidance for prescribing Tricyclic Antidepressants:

Tricyclic antidepressants are cardiotoxic (defined as causing a 25% increase in baseline QTc interval) – even at therapeutic doses. Therefore, it is advisable to perform an ECG and to monitor BP prior to initiating treatment. NICE does specify that people who start on low dose TCAs, and have a clear clinical response can be maintained on that dose with careful monitoring. Dosulepin is the most cardiotoxic, and NICE specifies 'Do not switch or start, dosulepin'.

- Do not routinely augment an antidepressant with:
  - A benzodiazepine for more than 2 weeks
  - Buspirone, carbamazepine, lamotrigine, valproate or thyroid hormones.
- If a person's depression has not responded to either pharmacological or psychological interventions, consider combining antidepressants with CBT.

## 1.2.6 Guidance for prescribing Vortioxetine:

Vortioxetine is recommended as an option for treating major depressive episodes in adults whose condition has responded inadequately to two antidepressants within the current episode<sup>6</sup>.

- The starting and recommended dose of Vortioxetine is 10 mg once daily in adults less than 65 years of age.
- Depending on individual patient response, the dose may be increased to a maximum of 20 mg vortioxetine once daily, or decreased to a minimum of 5 mg vortioxetine once daily.

## 1.2.7 Pharmacological management of depression with psychotic symptoms<sup>4</sup>

For individuals with depression who have psychotic symptoms consider augmenting their treatment plan with an antipsychotic medication.

- Should augmentation (with lithium, an antipsychotic such as quetiapine, or another antidepressant such as mirtazapine) be considered necessary, then advice from a Consultant Psychiatrist should be sought; especially if the patient is based in primary care. (see sections 2 and 3 for further information relating to monitoring required for these drugs)
- When prescribing Lithium (for augmentation of the primary antidepressant) monitor:
  - Renal and thyroid function before treatment and every 6 months during treatment (more often if there is evidence of renal impairment)
  - Consider ECG monitoring in people at high risk of cardiovascular disease
  - Monitor serum Lithium levels 1 week after treatment starts and after every dose change, and then every 3 months (see <u>section 3</u> for full details)
- When prescribing an antipsychotic, monitor weight, fasting lipid and glucose levels, and other relevant side effects (see section 2 for full monitoring requirements of antipsychotics)

## 1.2.8 Maintenance treatment with antidepressents<sup>4</sup>

- Patients who have responded to antidepressants should continue on said medication for at least 6 months after remission of a single episode. Thereafter, the need to continue should be discussed with the patient taking into consideration such factors as residual symptoms and concurrent physical health and psychosocial problems. Patients with 2 prior episodes and functional impairment should be treated for at least 2 years.
- People who have had multiple episodes of depression and who have a good response to augmentation should remain on this treatment. If one medication is stopped, it should be the augmenting agent.

## 1.3 Stopping or reducing antidepressants <sup>4</sup>

## 1.3.1 Warn the patient about withdrawal/ discontinuation symptoms

Advise people taking antidepressant medication that, before stopping it, they should discuss this with their practitioner.

Advise people that if they stop taking antidepressant medication abruptly, miss doses or do not take a full dose, they may have discontinuation symptoms such as:

- restlessness
- problems sleeping
- unsteadiness
- sweating
- abdominal symptoms
- altered sensations (for example electric shock sensations in the head)
- altered feelings (for example irritability, anxiety or confusion).

Explain that whilst the withdrawal symptoms which arise when stopping or reducing antidepressants can be mild and self-limiting, there is substantial variation in people's experience, with symptoms lasting much longer (sometimes months or more) and being more severe for some patients.

When stopping an antidepressant, gradually reduce the dose, normally over a 4-week period, although some people may require longer periods, particularly with drugs with a shorter half-life (such as paroxetine, venlafaxine and duloxetine), and longer than 4-weeks for MAOIs. This is not required with fluoxetine because of its long half-life.

Inform the person that they should seek advice from their practitioner if they experience significant discontinuation symptoms.

Withdrawal symptoms usually occur within 5 days of stopping treatment, or occasionally during taper or after missed doses (short half-life drugs). The perception of symptom severity may be worse if the patient is not warned of the possibility in advance. Some symptoms are more likely with particular drugs.

Patients prescribed short half-life drugs (e.g. paroxetine); patients who have taken an antidepressant for more than 8 weeks; patients who developed anxiety at the start of antidepressant therapy (particularly SSRI's); patients taking other centrally acting drugs (e.g. antihypertensives, antihistamines, antipsychotics); children and adolescents; patients who have experienced discontinuation symptoms before<sup>1</sup> are most at risk of developing discontinuation symptoms.

## 1.3.2 How to treat discontinuation symptoms?

Mild symptoms – reassure patient, and monitor symptoms.

Severe symptoms – reintroduce the original drug at the effective dose, or prescribe a drug in the same class with a longer half-life (e.g. if patient was using paroxetine, introduce fluoxetine), withdraw slowly and monitor.<sup>1</sup>

	MAOI's	TCA's	SSRI's & related
Symptoms	Common: Agitation, irritability, ataxia, movement disorders, insomnia, somnolence, vivid dreams, cognitive impairment, slowed speech, pressured speech.  Occasionally: Hallucinations, paranoid delusions.	Common: Flu-like symptoms (chills, fever, sweating, headache, nausea), insomnia, vivid dreams.  Occasionally: Movement disorders, mania, cardiac arrhythmia.	Common: Flu-like symptoms, 'shock-like' sensations, dizziness, insomnia, vivid dreams, irritability, crying spells.  Occasionally: Movement disorders, impaired concentration and memory.
Drugs most often associated with discontinuation symptoms	All (Tranylcypromine is partly metabolised to amphetamine and is associated with a true 'withdrawal syndrome')	Amitriptyline Imipramine	Paroxetine (all SSRIs have the propensity to cause discontinuation syndrome) Venlafaxine (↑ risk of NMS), Duloxetine

#### References

- South London & Maudsley NHS Foundation Trust Prescribing Guidelines 12<sup>th</sup> edition, Wiley Blackwell, 2015
- 2. Psychotropic Drug Directory 2014, Bazire S., Page Brothers Ltd
- Summary of Product Characteristics for Individual Drugs [accessed May 2017] http://www.medicines.org.uk/EMC/
- 4. NICE CG90: Depression in adults: recognition and management. Published date: 28 October 2009. Updated April 2016, September 2019 and February 2020. Accessed 6/5/2020.
- 5. BNF 72<sup>nd</sup> current edition, September 2016 to March 2017
- NICE Technical Appraisal (TA 367) (accessed May 2017) Vortioxetine for treating major depressive episodes <a href="http://www.nice.org.uk/guidance/ta367/resources/vortioxetine-for-treating-major-depressive-episodes-82602733813189">http://www.nice.org.uk/guidance/ta367/resources/vortioxetine-for-treating-major-depressive-episodes-82602733813189</a>
- 7. NICE guideline [NG145]: Thyroid disease: assessment and management. Published date: 20 November 2019. Accessed 6/5/2020.
- 8. NICE CG91: Depression in adults with a chronic physical health problem: recognition and management. Published date: 28 October 2009. Accessed 6/5/2020.
- 9. SSRI/SNRI antidepressant medicines: small increased risk of postpartum haemorrhage when used in the month before delivery. Drug Safety Update volume 14, issue 6: January 2021: 5. Accessed 29/4/21.

## Licensed indication(s) for antidepressants

Drug	Depression	Anxiety	OCD	Panic Disorder	Social Anxiety	PTSD	GAD	Bulimia - Nervosa	PMDD
Amitriptyline	✓								
Citalopram	✓			✓					
Clomipramine	✓		✓						
Dosulepin	✓								
Duloxetine	✓						✓		
Fluoxetine	✓		✓					✓	
Flupentixol	✓								
Imipramine	✓								
Lofepramine	✓								
MAOI's	✓								
Mianserin	✓								
Mirtazapine	✓								
Moclobemide	✓				✓				
Paroxetine	✓		✓	✓	✓	✓	✓		
Sertraline	✓		✓	✓	✓	✓			
Trazodone	✓	✓							
Venlafaxine	✓			✓	√§		√§		
Vortioxetine	✓								

Indications correct as of December 2015 – check for changes in the latest SPC.

### **Abbreviations**

OCD = Obsessive Compulsive Disorder

PTSD = Post Traumatic Stress Disorder

GAD = Generalised Anxiety Disorder

PMDD = Pre-Menstrual Dysphoric Disorder

§ Only the XL formulation of Venlafaxine is licensed for these indications

#### References

 Summary of Product Characteristics for Individual Drugs [accessed May 2017] http://www.medicines.org.uk/EMC/

## **Summary of Drug Particulars (relative side effect profile)**

Adult (Licensed)	Max Daily Max Daily Relative Side Effects at Average Doses (most									ostly dose-related)		
Amitriptyline 200 75 +++ +++ ++ ++ ++ ++ ++ ++ ++ ++ ++ ++	Drug <sup>1</sup>	Adult	Elderly		Cardiac	Nausea	Sedation	dose	convul	Sexual Dysfunct ion		
Clomipramine   250   75				Tricycli	Tricyclics (TCAs)							
Dosulepin	Amitriptyline	200	75	+++	+++	++	+++	+++	++	++		
Imipramine	Clomipramine	250	75	+++	++	++	++	+	++	+++		
Citalopramine   210   CAd   ++	Dosulepin	150	75	++	++	0	+++	+++	++	++		
SSRIS	Imipramine		50	++	++	++	+	+++	++	++		
Citalopram²         40         20         0         ++         +++         0         +         0         ++           Fluoxetine         60         60         0         0         ++         0         0         0         ++           Paroxetine         50(depressio n) 60 (others)         40         0         0         ++         0         0         0         +++           Sertraline         200         200         0         0         ++         0         0         0         ++           Tricyclic-Related           Mainserin         200 (usually30-90) <ad< td="">         +         0         0         ++++         0         0         +           Tricyclic-Related           MAOIs           Isoarboxazid         600 (Hosp) 300 (Outpt)         300         +         +         ++++++++++++++++++++++++++++++++++++</ad<>	Lofepramine	210	<ad< td=""><td>++</td><td>+</td><td>+</td><td>+</td><td>0</td><td>0</td><td>++</td></ad<>	++	+	+	+	0	0	++		
Paroxetine   60   60   0   0   ++   0   0   0   ++				S	SRIs							
Paroxetine         50(depression n) 60 (others)         40         0         0         +++         0         0         0         +++           Sertraline         200         200         0         0         +++         0         0         0         ++           Tricyclic-Related           Mianserin         200 (usually30-90) <ad< th="">         +         0         0         ++++         0         0         +           Trazodone         600 (Hosp) 300 (Outpt)         300         +         +         ++++++++++++++++++++++++++++++++++++</ad<>	Citalopram <sup>2</sup>	40	20	0	++	+++	0	+	0	++		
Paroxetine         n) 60 (others)         40         0         0         ++         0         0         0         +++           Sertraline         200         200         0         0         ++         0         0         0         ++           Tricyclic-Related           Mianserin         200 (usually30-90) <ad< td="">         +         0         0         +++         0         0         +           Trazodone         600 (Hosp) 300 (Outpt)         300         +         +         +++         ++         +         0         ++           Isocarboxazid         60 (4-6) (4-6</ad<>	Fluoxetine	60	60	0	0	++	0	0	0	++		
Mianserin   200	Paroxetine	n)	40	0	0	++	0	0	0	+++		
Mianserin         200 (usually30-90) <ad< th="">         +         0         0         +++         0         0         +++         0         +         +         +         0         +++         ++         0         +++         +++         ++++++         ++++++++++++++++++++++++++++++++++++</ad<>	Sertraline	200	200	0	0	++	0	0	0	++		
Mianserin         (usually30-90) <ad< th="">         +         0         0         +++         0         0         +           Trazodone         600 (Hosp) 300 (Outpt)         300         +         +         +++         ++         ++         +         0         ++           MAOIs           Isocarboxazid         60 (4-6 weeks) then 40         10         ++         ++         ++         0         ++         0         +           Phenelzine         90         (90)         +         ++         ++         ++         0         +           Tranylcy-promine         30         (30)         +         +         ++</ad<>	Tricyclic-Related											
Socarboxazid   60 (4-6   60 (4-6   60 (4-10   60 (4-1	Mianserin	(usually30-	<ad< td=""><td>+</td><td>0</td><td>0</td><td>+++</td><td>0</td><td>0</td><td>+</td></ad<>	+	0	0	+++	0	0	+		
Isocarboxazid   60 (4-6 weeks)	Trazodone	600 (Hosp) 300 (Outpt)	300	+	+	+++	++	+	0	++		
Isocarboxazid   6weeks   10				M	AOIs							
Tranylcy-promine         30         (30)         +	Isocarboxazid	6weeks)	10	++	++	++	0	++	0	+		
SNRIs   SNRI	Phenelzine	90	(90)	+	+	++	+	+++	0	+		
Duloxetine         120         Caution         0         0         ++         +         ?         ++           Venlafaxine         375 (tabs)         375 (tabs)         375 (SR         0         ++ <td></td> <td>30</td> <td>(30)</td> <td>+</td> <td>+</td> <td>++</td> <td>+</td> <td>+++</td> <td>0</td> <td>+</td>		30	(30)	+	+	++	+	+++	0	+		
375 (tabs)     375 (tabs)       Venlafaxine     375 (SR       375 (SR     0       ++     ++ <td colspan="11">SNRIs</td>	SNRIs											
Venlafaxine         375 (SR         375 (SR         0         ++         ++         +         ++ <td>Duloxetine</td> <td>120</td> <td>Caution</td> <td>0</td> <td>0</td> <td>++</td> <td>+</td> <td>?</td> <td>?</td> <td>++</td>	Duloxetine	120	Caution	0	0	++	+	?	?	++		
caps) caps)	Venlafaxine			0	++	++	+	++	+	++		
Others												
Flupentixol 3 1.5 ++ 0 0 + + ? +	Flupentixol	3	1.5	++	0	0	+	+	?	+		
Mirtazapine 45 45 0 0 0 ++ 0 ++ ++	Mirtazapine	45	45	0	0	0	++	0	++	++		
Moclobemide         600         600         +         0         +         0         ?         +           Kev		600	600	+	0	+	0	0	?	+		

#### Key

+++ = Marked effect ++ = Moderate effect += Mild effect 0 = Little effect

? = Unknown <Ad = Less than Adult dose NR = Not Recommended

### References

- 1. Psychotropic Drug Directory 2014, Bazire S., Page Bros Ltd
- 2. MHRA Drug Safety Update, Volume 5, No 5, December 2011

## **Switching Antidepressants**<sup>1</sup>

TO:	Citalopram/ Escitalopram	Duloxetine	Fluoxetine	MAOI - Phenelzine	Mirtazapine	Moclobemide	Paroxetine	Reboxetine	Sertraline	Tricyclics	Trazodone	Venlafaxine
FROM:												
Citalopram/ Escitalopram		Withdraw - start at 60mg	Withdraw - Start fluoxetine at 10mg	Withdraw. Wait 1 week	Cross-taper	Withdraw. Wait 2 weeks	Withdraw. Start paroxetine at 10mg	Cross-taper	Withdraw. Start sertraline at 25 mg	Cross-taper	Withdraw before starting titration	Withdraw. Start at 37.5mg/day. Increase slowly
Duloxetine	Withdraw and start		Withdraw and start	Withdraw. Wait 1 week	Withdraw and start	Withdraw. Wait 1 week	Withdraw and start	Cross-taper	Withdraw and start	Cross-taper	Withdraw starting titration	Withdraw then start venlafaxine
Fluoxetine	Withdraw. Wait for 4 – 7 days. Start citalopram	Stop. Wait for 4 - 7 days. Start duloxetine		Withdraw. Wait 5 - 6 weeks	Withdraw. Wait for 4 – 7 days. Start mirtazapine	Withdraw. Wait 5 weeks	Withdraw. Wait for 7 days. Start paroxetine	Withdraw. Start reboxetine 2mg b.d.	Withdraw. Wait for 4 – 7 days. Start sertraline 25mg	Withdraw. Wait for 4 – 7 days. Start	Withdraw. Wait for 4 – 7 days. Start low dose	Withdraw. Wait 4 - 7 days then start at 37.5mg/ day. Increase. slowly
MAOI - Phenelzine	Withdraw. Wait for 2 weeks	Withdraw. Wait for 2 weeks	Withdraw. Wait for 2 weeks		Withdraw. Wait for 2 weeks	Withdraw. Wait for 2 weeks	Withdraw. Wait for 2 weeks	Withdraw. Wait for 2 weeks	Withdraw. Wait for 2 weeks	Withdraw. Wait for 2 weeks	Withdraw. Wait for 2 weeks	Withdraw. Wait for 2 weeks
Mirtazapine	Withdraw and start	Withdraw and start at 60 mg	Withdraw and start	Withdraw. Wait 1 week		Withdraw. Wait 1 week	Withdraw and start	Withdraw. Wait for 24 hours	Withdraw and start	Withdraw and start	Withdraw and start	Withdraw then start venlafaxine
Moclobemide	Withdraw. Wait for 24 hours	Withdraw. Wait for 24 hours	Withdraw. Wait for 24 hours	Withdraw. Wait for 24 hours	Withdraw. Wait for 24 hours		Withdraw. Wait for 24 hours	Withdraw. Wait for 24 hours	Withdraw. Wait for 24 hours	Withdraw. Wait for 24 hours	Withdraw. Wait for 24 hours	Withdraw. Wait for 24 hours
Paroxetine	Withdraw and start	Withdraw and start at 60mg	Withdraw and start	Withdraw. Wait for 2 weeks	Cross-taper	Withdraw. Wait for 2 weeks		Cross-taper	Withdraw and start	Cross-taper	Withdraw starting titration	Withdraw. Start at 37.5mg/day. Increase slowly
Reboxetine	Cross-taper	Cross-taper	Withdraw. Wait for 1 week	Withdraw. Wait for 1 week	Cross-taper	Withdraw. Wait for 1 week	Withdraw. Wait for 1 week		Cross-taper	Cross-taper	Cross-taper	Cross-taper cautiously
Sertraline	Withdraw and start	Withdraw and start at 60mg	Withdraw and start	Withdraw. Wait for 2 weeks	Cross-taper	Withdraw. Wait for 2 weeks	Withdraw and start	Cross-taper		Cross-taper	Withdraw starting titration	Withdraw. Start venlafaxine at 37.5mg/day.
Tricyclics	halve dose and start citalopram then slow withdrawal	Cross-taper	halve dose and start fluoxetine then slow withdrawal	Withdraw. Wait for 1 week	Cross-taper	Withdraw. Wait for 1 week	halve dose and start paroxetine then slow withdrawal	Cross-taper	halve dose and start sertraline then slow withdrawal		halve dose and start trazadone then slow withdrawal	Cross-taper cautiously. Start venlafaxine at 37.5mg/day
Trazodone	Withdraw and start	Withdraw and start at 60mg	Withdraw and start	Withdraw. Wait for 1 week	Cross-taper	Withdraw. Wait for 1 week	Withdraw and start	Withdraw. Start Reboxetine 2mg b.d.	Withdraw and start	Cross-taper		Withdraw. Start venlafaxine at 37.5mg/day.
Venlafaxine	Cross-taper cautiously. Start at 10mg/day	Withdraw. Start at 60mg on alternate days. Increase slowly	Cross-taper cautiously. Start at 20mg on alternate days	Withdraw. Wait at least 1 week	Cross-taper cautiously	Withdraw. Wait at least 1 week	Cross-taper cautiously. Start at 10mg/day	Cross-taper cautiously	Cross-taper cautiously. Start at 25mg/day	Cross-taper cautiously. Start at very low dose	Cross-taper cautiously	

## References

1. South London & Maudsley NHS Foundation Trust Prescribing Guidelines 12<sup>th</sup> edition, Wiley Blackwell, 2015