PRIMARY CARE

GUIDE TO

ANTIDEPRESSANTS:

PRESCRIBING, STOPPING & SWAPPING
Nottinghamshire GP guide to antidepressants – Prescribing, swapping and stopping

This document will remain within the confines of the Nottinghamshire Joint Formulary where possible. It will be kept up to date with national guidance and relevant information that has resulted from queries relating to antidepressant treatment across the interface. A full reference list can be found at the end of the document. Resources used include BAP, BNF, CKS, The Maudsley, Martindale: The Complete Drug Reference & NICE as well as a thorough literature review. NICE guidance on depression is due an update in 2022; some of the suggestions to be made there will be explored in this document.

Please do not hesitate to contact me with questions regarding mental health medications, to discuss mental health medications across the interface, or future work you feel would be useful to strengthen prescribing across primary and secondary care.

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Treatment summary of current NICE Guidance (CG90)

Diagnosis of depression is based on DSM-V criteria (CKS advice).

First line treatment for recent onset/mild depression is not medication; rather active monitoring, sleep hygiene, exercise, guided self-help and CBT.

Sleep Hygiene

Choice and Medication Fact Sheet – Insomnia and Sleep Hygiene

The charity MIND has a really useful webpage on how to cope with sleep problems. This includes an explanation of sleep and mental health, practical suggestions and where to get support.

MIND - how to cope with sleep problems
Antidepressant treatment

Antidepressants are recommended for treatment of moderate or severe depression, subthreshold symptoms present for over 2 years, or mild depression that persists despite other interventions. First line choice of antidepressant is a SSRI.

When discussing antidepressant treatment options with a patient, cover the following:

- Choice of antidepressant
- Reason for prescribing
- The gradual development of full antidepressant effect
- Importance of taking medication as prescribed/the need to continue after remission
- Potential side effects (see Appendix One)
- Potential interactions with other medication/physical health problems (see section 6)
- The risk of discontinuation symptoms (and the most likely symptoms associated with the antidepressant they are prescribed) when they stop the antidepressant (see section 5)
Monitoring antidepressant treatment

When initiating an antidepressant a review period should be discussed with the patient.

For those not considered to be at increased risk of suicide:
- Review after two weeks
- Review regularly in the first three months (e.g. every 2-4 weeks)
- Thereafter review at longer intervals if the response is good

For those considered to present an increased risk of suicide / are younger than 30 years:
- Review after one week
- Review regularly thereafter until the risk is no longer considered clinically important

During a review with a patient using antidepressants the following should be discussed:
- Tolerability of the medication (directly ask about known side effects that may not be reported- e.g. adverse effect on sexual function with SSRIs).
- Adherence to the medication.
- Thoughts of hopelessness or suicide; including any specific intent or plans (particularly during the early stage of treatment or treatment changes).
- The person’s depressive symptoms (i.e. response to treatment?) – the PHQ-9 (patient completion) or 6-item Hamilton (Bech; clinician completion) are good ways of monitoring change.
- Any ongoing stresses that may contribute to depression.
- The impact of any current psychological interventions or the potential benefit of this type of treatment if not undertaken so far.
- The benefits of exercise and structured activity (where possible) to the outcome of antidepressant treatment.
- Ask about alcohol and recreational drug use
- Any hypomanic symptoms

If a patient suffers a side effect multiple strategies can be implemented. Symptoms can be monitored closely where side effects are mild and acceptable to the patient or the antidepressant treatment can be stopped and switched to another if the patient prefers.

Continuation of antidepressant treatment and relapse prevention

The following are current NICE guidelines (CG90):

| Support and encourage a person who has benefited from taking an antidepressant to continue medication for at least six months after remission of an episode of depression. (This greatly reduces the risk of relapse. Antidepressants are not associated with addiction). |

| Review with the person with depression the need to continue antidepressant treatment beyond six months after remission, taking into account: |
| - The number of previous episodes of depression |
| - The presence of residual symptoms |
| - Risk associated with previous episodes, including suicide, neglect, relationships and work |
| - Concurrent physical health problems and psychosocial difficulties |

| Advise the person with depression to continue antidepressants for at least two years if they are at higher risk of relapse. Maintain the dose at the level at which acute treatment was effective (unless there is good reason to reduce the dose, such an unacceptable adverse effects) if: |
- They have had two or more episodes of depression in the recent past, during which they experienced significant functional impairment.
- They have other risk factors for relapse such as residual symptoms, multiple previous episodes or a history of severe or prolonged episodes or of inadequate response.
- The consequences of relapse are likely to be severe (for example suicide attempts, loss of functioning, severe life disruption and inability to work).

When deciding whether to continue maintenance treatment beyond two years, re-evaluate with the person with depression taking into account age, comorbid conditions and other risk factors.

People with depression on long term maintenance treatment should be regularly re-evaluated with frequency of contact determined by: comorbid conditions, risk factors for relapse, severity and frequency of episodes of depression.

New NICE guidance (currently in draft, to publish May 2022) is set to strengthen these positions with the following:

Discuss the likelihood of having a relapse with people who have recovered from depression. Explain:
- That a history of previous relapse increases the chance of further relapses
- That further episodes may be more severe
- That antidepressants significantly reduce the risk of relapse; at least within the first two years but maybe longer

Take into account that the following may increase the risk of relapse:
- How often a person has had episodes of depression and how recently
- Any other chronic physical health or mental health problems
- Any residual symptoms and unhelpful coping styles (for example avoidance and rumination)
- How severe their symptoms were, risk to self and if they had functional impairment in previous episodes of depression
- The effectiveness of previous interventions for treatment and relapse prevention
- Personal, social and environmental factors

For people continuing with medication to prevent relapse, hold reviews at 3, 6 and 12 months after maintenance treatment has started. At each review:
- Monitor mood state using a formal validated rating scale, for example the PHQ-9
- Review side effects
- Review any personal, social and environmental factors that may impact on the risk of relapse
- Agree the timescale for further review (no more than 12 months)

Amending antidepressant treatment

It is important to manage the expectations of the patient from the outset of treatment. Once a medication has been initiated, all antidepressants show a pattern of response where improvement is usually seen by the patient by week two. If this is not the case:

- Check that the medication has been taken regularly and in the prescribed dose

Those that show no discernible response at 4-6 weeks having taken the medication appropriately and at a therapeutic dose may never respond to that medication. Conversely those that show even small improvement at three weeks may go on to respond fully.
In individuals where no antidepressant effect is evident after 4-6 weeks at a therapeutic dose, an increase in dose or switching to another antidepressant may be indicated (there is more support for increasing the dose of some medications, such as venlafaxine or tricyclics than for SSRIs).

If the person’s depression shows some improvement by four weeks, continue treatment for another 2 to 4 weeks. Consider switching to another antidepressant if the response is still not adequate, if there are side effects or if the person prefers to change treatment.

NICE suggests evidence for switching from one antidepressant to another is more favourable than increasing the dose of an antidepressant. Generally switching with another SSRI before considering an alternative class is the best course of action – many patients who cannot tolerate one SSRI will tolerate another.

The choice of medication beyond the first SSRI should be individual and patient based. It should be informed by several factors that are unique to each patient:

- Response to current medication/historical success
- Secondary characteristics of the depression (e.g. insomnia, anxiety)
- Side effects/issues the patient would wish to avoid (e.g. weight gain with mirtazapine)
- Other medications (potential drug-drug interactions) or any contraindications/cautions for use.
- Additional medical or psychiatric diagnoses
- For women of childbearing potential avoid paroxetine where possible (due to some indications of excess foetal heart malformation and the higher level of discontinuation effects - meaning any decision to stop may be more difficult)

Do not switch to/start dosulepin or amitriptyline because evidence supporting tolerability relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose. All patients currently prescribed dosulepin in primary care should be reviewed for deprescribing. See Dosulepin Deprescribing Information Sheet here.

The preferred tricyclic for prescribing in primary care is lofepramine (due to a consistently low toxicity index), though nortriptyline may be an alternative following discussion with Secondary Care. If a patient with depression is taking amitriptyline (or another tricyclic) for pain or other medical conditions, assess the need for this given risk in overdose.

The time it takes to switch between antidepressants is informed by: half-life of medications (generally five half-lives until a medication reaches steady state or is excreted below therapeutic range), interactions between the medications, risk of serotonin syndrome and the reduction of potential discontinuation symptoms. Methods of swapping include cross tapering, taper to stop & start and direct switch. Switching antidepressants is covered in a table in Appendix Two.

Exercise particular caution when switching:

- From fluoxetine to other antidepressants, because fluoxetine has a long half-life (approximately one week).
- From fluoxetine or paroxetine to a tricyclic; both of these medications inhibit the metabolism of tricyclics. A lower starting dose of the tricyclic will be required, particularly if switching from fluoxetine.
- To a new serotonergic medication or MAOI, risk of serotonin syndrome (see below).

From a non-reversible MAOI (e.g. phenelzine, isocarboxazid); a two week washout period is required. Other antidepressants should not routinely be prescribed during this time (a single dose of an SSRI medication may cause a severe and life-threatening Serotonin Syndrome if given with an MAOI). Some general medical treatments (such as opiates) also release serotonin and there should be caution in using these with MAOIs, or within the two week
washout period.

Reducing doses and discontinuation symptoms

How to reduce/stop antidepressants

A general rule is that antidepressants taken for months should be withdrawn over weeks, and if taken for years withdrawn over months. However, individual circumstances and preferences should be taken into account. For example, if there is persistent depression (and an alternative treatment is required) or significant side effects or if an adverse event has occurred it may be necessary to withdraw antidepressant treatment more quickly.

New NICE guidance (currently in draft, to publish May 2022) advises the following:

When stopping an antidepressant medication, as a general rule, slowly reduce the dose based on how long the person has been taking it. For example:

- Over several days if the person has been taking it for 2–8 weeks
- Over several weeks if the person has been taking it for 2–12 months
- Over several months if the person has been taking it for 12 months or more

Reduce the rate of discontinuation as the dose gets lower (‘as you go lower, go slower’) – and this will help minimise discontinuation effects, which are reported as severe by some people.

Discontinuation symptoms

- Although antidepressants are not addictive, they can cause discontinuation symptoms if stopped too quickly (due to CNS adaptation).
- This can begin within days of discontinuation or dose reduction.
- Tend to be more severe when the medication half-life is relatively short (e.g. venlafaxine, paroxetine) and/or where the medication inhibits its own metabolism (e.g. paroxetine). Discontinuation of these medications should be planned with particular care.
- Tend to be less severe when the medication half-life is relatively long (e.g. fluoxetine); more rapid reductions may be possible.
- Discontinuation symptoms can be mild and self-limiting. However, there is substantial variation in people’s experiences. For some patients, symptoms can last much longer and be more severe.
- The symptoms are varied, and may at times present as similar to depression itself (e.g. anxiety, restlessness, insomnia), or with more overtly physical symptoms (e.g. sweating, GI symptoms including nausea or altered sensations, such as ‘brain zaps”).
- Treatment of discontinuation symptoms is pragmatic.
- If symptoms are mild, it may be enough to monitor the symptoms and provide reassurances that these symptoms are common.
- If symptoms are severe consider: returning to the previous dose (prior to symptom onset) or reintroducing the original antidepressant at a dose that controls symptoms and reduce more gradually whilst monitoring symptoms.
- Remember by discontinuing slowly and by educating the patient on what to expect, the symptoms (and a patient’s perception of their severity) may be lessened or avoided entirely.
The charity MIND have some useful counselling points on withdrawal of antidepressants for patients:

https://www.mind.org.uk/information-support/drugs-and-treatments/antidepressants/withdrawal-effects-of-antidepressants

**SSRI discontinuation** (commonly associated with, but not limited to paroxetine):

**Commonly** – Flu-like symptoms (chills, myalgia, excessive sweating, headache, nausea, goose-bumps), ‘shock-like’ symptoms, dizziness exacerbated by movement, insomnia, excessive dreaming, irritability, crying spells, nausea, vomiting, diarrhoea

**Less commonly** – Movement disorders, problems with concentration and memory

**TCA discontinuation** (commonly associated with, but not limited to amitriptyline and imipramine):

**Commonly** – Anxiety, flu like symptoms (chills, myalgia, excessive sweating, headache, nausea, goose-bumps), insomnia, excessive dreaming, restlessness

**Less commonly** - fast/irregular heartbeat, movement disorders, mania

**MAOI discontinuation** (all carry a high risk)

**Commonly** – Agitation, irritability, difficulty thinking, ataxia, movement disorders, insomnia, somnolence, vivid dreams, cognitive impairment, slowed speech,

**Less commonly** – Hallucinations, paranoid delusions

**SNRI discontinuation** (venlafaxine, duloxetine)

**Commonly** – Dizziness, sensory disturbances, sleep disturbances, agitation or anxiety, nausea and vomiting, tremor, vertigo, headache, flu symptoms.

**Less commonly** - symptoms may be more severe or prolonged

**Mirtazapine discontinuation** (may happen after long term use, majority mild and self-limiting)

**Commonly** – Dizziness, orthostatic hypotension, headache, increased appetite

**Less commonly** – Lethargy, nausea, agitation, anxiety

The following Choice and Medication fact sheets are designed to support patients with decision making around stopping antidepressants:

Coming off Mental Health Medicines

Stopping Antidepressants

**Drug interactions and Serotonin Syndrome**

This section is not exhaustive. For a full list of drug interactions with antidepressants please consult the individual product literature.

Common drug interactions to be aware of:

- **SSRIs**: risk of gastrointestinal side effects when concomitantly administered with NSAIDs
- **SSRIs**: risk of bleeding when concomitantly administered with medicines that have an effect on platelet function (e.g. anticoagulants and NSAIDs)
- Fluoxetine is a strong inhibitor of CYP2D6 enzyme, concomitant therapy with medications also metabolised by this enzyme system may lead to drug interactions (e.g. increased serum levels of some antipsychotic medications).
• Risk of QTc interval prolongation if some antidepressants are administered concomitantly with other agents known to cause this effect (see MHRA alert linked below regarding citalopram and escitalopram).
• Additive CNS depressant effects when classes of antidepressants are prescribed for separate indications (e.g. a tricyclic for neuropathic pain and a SNRI for depressive illness).
• SSRIs: reports of increased lamotrigine concentration and toxicity when concomitantly administered with sertraline. Bear the possibility of an interaction in mind if a patient presents with troublesome adverse effects or skin rash/blistering/fever.

Serotonin syndrome can occur with the use of high dose serotonergic agents – usually after the introduction of a second agent. Some serotonergic agents are not associated with the treatment of depression and include opioids, Parkinson’s disease treatments and anticonvulsants amongst others. See the UKMi link below for an extensive summary.

Serotonin syndrome is caused by excessive central and peripheral serotonergic activity. Onset of symptoms can occur within hours or days of increase in serotonergic medication. Causative agents should be stopped, and decisions leading up to the choice of medication re-assessed.

It is classed as poisoning, and severe symptoms will need urgent management in an acute care setting. Symptoms generally have three forms, outlined well by UKMi:

<table>
<thead>
<tr>
<th>Alteration of mental status</th>
<th>Neuromuscular abnormalities</th>
<th>Autonomic hyperactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>agitation</td>
<td>tremors</td>
<td>hypertension</td>
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<tr>
<td>anxiety</td>
<td>clonus</td>
<td>tachycardia</td>
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<td>disorientation</td>
<td>hyperreflexia</td>
<td>tachypnea</td>
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<tr>
<td>restlessness</td>
<td>muscle rigidity</td>
<td>hyperthermia</td>
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<tr>
<td>excitement</td>
<td>bilateral Babinski signs</td>
<td>mydriasis</td>
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<td></td>
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<td>diaphoresis</td>
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<td></td>
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<td>dry mucous membranes</td>
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<td></td>
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<td>flushed skin</td>
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<td></td>
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<td>shivering</td>
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<td></td>
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<td>vomiting</td>
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<td></td>
<td></td>
<td>diarrhoea</td>
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<tr>
<td></td>
<td></td>
<td>hyperactive bowel sounds</td>
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<tr>
<td></td>
<td></td>
<td>arrhythmias</td>
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</tbody>
</table>

UKMi have a very good summary of serotonin syndrome: [https://www.sps.nhs.uk/articles/what-is-serotonin-syndrome-and-which-medicines-cause-it-2/](https://www.sps.nhs.uk/articles/what-is-serotonin-syndrome-and-which-medicines-cause-it-2/)

Useful resources

For information on mental health medications, take a look at: [https://www.choiceandmedication.org/nottinghamshirehealthcare/](https://www.choiceandmedication.org/nottinghamshirehealthcare/)

The charity MIND have useful patient-facing information: [https://www.mind.org.uk/information-support/drugs-and-treatments/antidepressants/about-antidepressants/N.XFs_KBpTMA](https://www.mind.org.uk/information-support/drugs-and-treatments/antidepressants/about-antidepressants/N.XFs_KBpTMA)

Nottinghamshire Healthcare Trust has access to Recap, which allows the sharing of useful information for patients. Email digital.health@nottshc.nhs.uk for details.

Trazodone, Trimipramine and Dosulepin deprescribing documents can be found [here](https://www.choiceandmedication.org/nottinghamshirehealthcare/).
# Primary Care Guide to Antidepressants

V1.2  |  Last reviewed: September 2020  |  Review date: May 2022

## MHRA ALERTS


## FAQs

This section will be updated with further useful information as a result of developments, or queries related to antidepressants.

### September 2019 – Dispersible fluoxetine

Currently fluoxetine 10mg capsules and tablets are very expensive; use is not recommended.

There are two alternative preparations
- Dispersible fluoxetine (Olena®): 20mg tablets can be halved to give a 10mg dose
- Liquid: fluoxetine 20mg/5ml (70ml), but not the sugar-free version as this is much more expensive

### August 2020 – Phenelzine supply issues

Ongoing supply problems with phenelzine. No UK licensed product available since July 2019 and no end date to this. Most patient’s supply had been continued with imported US-licensed product but supplies of this are currently unstable due to global supply issues. Some patients may be switched to alternatives (e.g. isocarboxazid). See the [Nottinghamshire Joint Formulary](https://nps.org.au/australian-prescribe/articles/oral-and-dental-effects-of-antidepressants) for further information.

## References

- Literature review carried out 7/11/2018 on PubMed, EMBASE and Medline using the terms “depression” & “primary care”.
- NICE depression in adults: treatment and management (In development [GID-CGWAVE0725], expected publication date: May 2022) ([link](https://www.gov.uk/drug-safety-update/citalopram-and-escitalopram-qt-interval-prolongation)), last accessed 06/08/2020
- Clinical Knowledge Summaries (CKS), Depression ([link](https://nps.org.au/australian-prescribe/articles/oral-and-dental-effects-of-antidepressants)), last accessed 26/08/2020
- Patient Health Questionnaire – PHQ-9, available from [http://www.psycho-oncology.info/PHQ9_depression.pdf](http://www.psycho-oncology.info/PHQ9_depression.pdf), last accessed 26/08/2020
## Appendix One: Info on medications

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<thead>
<tr>
<th>Medication</th>
<th>Traffic Light Status: Depression</th>
<th>Class</th>
<th>Relative common adverse effect (Maudsley)</th>
<th>Minimum effective dose (BNF, Maudsley)</th>
<th>Common side effects (most common first, not a comprehensive list (SPCs))</th>
<th>How to respond</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>Grey</td>
<td>TCA</td>
<td>+++ +++ +++ +++ ++ ++ ++</td>
<td>50mg/day (10mg initially &gt;65 years old)</td>
<td>Sedation (w/hangover), Postural hypotension, tachycardia, anticholinergic effects</td>
<td>Take at bedtime, exercise good dental hygiene</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Green</td>
<td>SSRI</td>
<td>- - + - ++ +++</td>
<td>20mg/day (20mg/day max dose &gt;65years old)</td>
<td>GI disturbances, rash, sweating, agitation</td>
<td>Take with food, in the morning.</td>
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<tr>
<td>Clomipramine</td>
<td>Green</td>
<td>TCA</td>
<td>++ +++ +++ ++ ++ ++</td>
<td>10mg/day</td>
<td>“amitriptyline”</td>
<td>Take at bedtime, exercise good dental hygiene</td>
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<tr>
<td>Doxepin</td>
<td>Grey</td>
<td>TCA</td>
<td>+++ ++ +++ +++ ++ ++ +</td>
<td>75mg/day</td>
<td>“amitriptyline”</td>
<td>Take at bedtime, exercise good dental hygiene</td>
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<tr>
<td>Duloxetine</td>
<td>Amb2</td>
<td>SNRI</td>
<td>- - - - - ++ ++</td>
<td>60mg/day</td>
<td>Nausea, insomnia, headache, dizziness, dry mouth</td>
<td>Exercise good dental hygiene</td>
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<td>Escitalopram</td>
<td>Green</td>
<td>SSRI</td>
<td>- - + - ++ +++</td>
<td>10mg/day (5mg &gt;65years old)</td>
<td>GI disturbances, rash, sweating, agitation</td>
<td>Take with food, in the morning.</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Green</td>
<td>SSRI</td>
<td>- - - - - ++ +++</td>
<td>20mg/day</td>
<td>Insomnia, agitation, rash, GI disturbances</td>
<td>Take with food, in the morning.</td>
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<tr>
<td>Imipramine</td>
<td>Green</td>
<td>TCA</td>
<td>++ +++ +++ +++ ++ +</td>
<td>75mg/day (10mg/day initially &gt;65 years old, gradually up to 30-50mg/day)</td>
<td>“amitriptyline”, but less sedative</td>
<td>Take at bedtime, exercise good dental hygiene</td>
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<tr>
<td>Isocarboxazid</td>
<td>Amb2</td>
<td>MAOI</td>
<td>+ ++ + ++ + +</td>
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<td>Postural hypotension, dizziness, drowsiness, insomnia, dry mouth</td>
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<td>TCA</td>
<td>+ + + ++ + +</td>
<td>140mg/day (lower for elderly)</td>
<td>“amitriptyline”, less sedative, less anticholinergic, less</td>
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</table>
# Primary Care Guide to Antidepressants

**V1.2 | Last reviewed: September 2020 | Review date: May 2022**

<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>Drug Class</th>
<th>Incidence/Severity</th>
<th>Side Effects</th>
<th>Cardiotoxic</th>
<th>Dosage</th>
<th>Notes</th>
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<td>Mirtazapine</td>
<td>Piperazinoazepine</td>
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<td>-</td>
<td>-</td>
<td>++</td>
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<td>Tranylcypromine</td>
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<td>SNRI</td>
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<td>+</td>
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<td>+++</td>
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<td>Vortioxetine</td>
<td>SSRI</td>
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<td>+</td>
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+++ High incidence/severity

++ Moderate

+ Low

- Very low/none
## Appendix Two: Switching Nottinghamshire Wide Formulary Antidepressants

<table>
<thead>
<tr>
<th>FROM</th>
<th>TO</th>
<th>Trazodone</th>
<th>Venlafaxine</th>
<th>Duloxetine</th>
<th>Clomipramine</th>
<th>Doxepin</th>
<th>Mirtazapine</th>
<th>Moclobemide</th>
<th>MAOIs: Phenelzine</th>
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<th>SSRIs: Sertraline</th>
<th>Citalopram</th>
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<th>Clomipramine</th>
<th>Fluoxetine</th>
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<td><strong>HOW TO STOP</strong></td>
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<td>Reduce over at least 4 weeks</td>
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<tr>
<td>Clomipramine</td>
<td>Taper and stop, then start fluoxetine at 100mg/day (liquid)</td>
<td>Taper and stop, wait for 3 weeks then start mirtazapine</td>
<td>Taper and stop, then start moclobemide</td>
<td>Taper and stop, start MAOI</td>
<td>Taper and stop, then start SSRI</td>
<td>Taper and stop, then start vortioxetine</td>
<td>Taper and stop, then start vortioxetine</td>
<td>Taper and stop, then start vortioxetine</td>
<td>Taper and stop, then start vortioxetine</td>
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<tr>
<td>Doxepin</td>
<td>Cross taper cautiously</td>
<td>Taper slow, then start low doxepin</td>
<td>Cross taper cautiously</td>
<td>Cross taper cautiously</td>
<td>Cross taper cautiously</td>
<td>Taper slow, then start low doxepin</td>
<td>Cross taper cautiously</td>
<td>Taper slow, then start low doxepin</td>
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<tr>
<td>Fluoxetine</td>
<td>Taper and stop fluoxetine. Wait 2 weeks, then start low dose clomipramine (orally 10mg)</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
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<td>Mirtazapine</td>
<td>Cross taper cautiously</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
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<tr>
<td>Moclobemide</td>
<td>Taper and stop, wait for 24 hours then start clomipramine</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
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<td>MAOIs: Phenelzine</td>
<td>Taper and stop, then start clomipramine</td>
<td>Taper and stop, wait for 24 hours then start fluoxetine</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
<td>Taper and stop, wait for 2 weeks then start mirtazapine</td>
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<td>SNRI: Venlafaxine</td>
<td>Taper and stop, then start clomipramine</td>
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<td>SSRIs: Sertraline</td>
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</table>
| Trazodone    | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously | Cross taper cautiously |}
Tricyclics

Lofepramine
Amitriptyline
*Imipramine
Nortriptyline

Taper TCA to half dose, then add fluoxetine 10mg (liquid) and cross taper cautiously.

Cross taper cautiously, start SNRI at low dose.

Taper TCA to half dose, then add SSRIs and slow withdrawal of TCA.

Taper TCA to half dose, then add trazodone, slow withdrawal of TCA.

Taper TCA to half dose, then add vortioxetine and slow withdrawal of TCA.

Direct switch possible. See information below.

Taper and stop, wait for 4 weeks then start moclobemide.

Cross taper cautiously, start MAOI (wait 3 weeks in case of imipramine).

Cross taper cautiously, start low dose trazodone.

Cross taper cautiously, start low dose TCA.

Direct switch possible. See information below.

Taper and stop, wait for 1 week then start moclobemide.

Taper and stop, wait for 2 weeks then start MAOI (wait 3 weeks in case of imipramine).

Direct switch possible. See information below.

Taper and stop, wait for one week then start moclobemide.

Taper and stop, wait for three weeks then start MAOI.

Taper and stop, wait for 2 weeks then start MAOI.

Cross taper cautiously, start low dose trazodone.

Cross taper cautiously, start with a low dose of clomipramine.

Cross taper cautiously, start with low dose TCA.

Vortioxetine

Taper and stop, then start low dose moclobemide.

Direct switch possible. See information below.

Direct switch possible. See information below.

Direct switch possible. See information below.

Direct switch possible. See information below.

Cross taper cautiously, start low dose trazodone.

Cross taper cautiously, start with low dose TCA.

* Amitriptyline is GREY for depression

“Direct switch possible” In some instances it may be possible to withdraw the current antidepressant and start the new antidepressant on the next day. For example when switching from one SSRI to another SSRI or a SNRI; the exception is fluoxetine. SSRIs overlap in their mechanism of action, and the new SSRI will usually prevent discontinuation symptoms that may occur when the first SSRI is stopped. Substituting a new SSRI at the relatively equivalent dose of the former SSRI is typically well-tolerated, though starting the new SSRI at a lower dose may also be considered since patients occasionally have idiosyncratic side effects to particular SSRIs.

“Cross taper cautiously” This refers to a technique where over the course of several weeks (several months if the patient is established on the current medication), a slow reduction of the dose through four dosing steps. For example where sertraline may have been used at 100mg, reduce to 75mg on step 1, 50mg on step 2, 25mg on step 3 then stop on step 4. The alternative medication should be started during this period. Be cautious of interaction or synergistic side effects between the two medications.

“Cross taper cautiously, start with a low dose” Usually this means the new dose should be started more cautiously. For example, venlafaxine being introduced at a low dose would be introduced at 37.5mg (the lowest dose available).

“Taper and stop, then start with a low dose” Measured reduction of the medication through four dosing steps should be made. Only when the medication has stopped should the new one start. This is usually due to a longer half-life of one of the medications making clearance a slower process.

“Taper and stop, wait x weeks, the start” Again due to a longer half-life of the medications, resulting in a gap between treatments being required in order to safely proceed. You will see this approach for switches incorporating MAOIs, it is a tactic to avoid serotonin syndrome among other issues.

Switching within class (e.g. TCA to TCA) Advice is usually cross taper cautiously, starting at a low dose. The speed of cross-tapering is judged by monitoring patient tolerability. In some cases the pharmacodynamics of a certain medications may allow an immediate switch (i.e. fluoxetine has a long half-life which makes this possible). It is important to remember the potential dangers of simultaneously administering two antidepressants. They could work synergistically to lead to pharmacodynamics issues (serotonin syndrome, hypotension, drowsiness).
### Appendix Three – Current Mental Health Efficiencies Project Documents

<table>
<thead>
<tr>
<th>Medication</th>
<th>De-prescribing information sheet</th>
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</thead>
<tbody>
<tr>
<td>Dosulepin</td>
<td>De-prescribing information sheet</td>
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<tr>
<td>Trazodone</td>
<td>De-prescribing information sheet</td>
</tr>
<tr>
<td>Trimipramine</td>
<td>De-prescribing <a href="#">PrescQIPP</a></td>
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</table>