

CLINICAL GUIDELINE

Depression Treatment, for Adults, in Primary Care

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

Version Number:	5
Are there changes to the clinical advice in this version?:	Yes
Date Approved:	17 th December 2020
Date of Next Review:	17 th December 2023
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Approval Group:	Prescribing Management Group – Primary Care

Important Note:

The Intranet version of this document is the only version that is maintained. Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Holistic Assessment

- Symptoms present for 2 weeks or more (as per ICD-10 classification).
- Patient centred biopsychosocial assessment.
- Consider: [PHQ-9 \(see accompanying notes\)](#), CORE 10 or other suitable assessment tool.
- Consider: alcohol (FAST tool), substance misuse, significant life events (e.g. bereavement, etc) exclude organic disease, etc.
- **Assess risk of self-harm, suicide and risk to others.**

Consider Bipolar Disorder: Assessment and Management - [NICE 185](#). Please consider:

- Past history of manic symptoms: over activity; decreased need for sleep; euphoria/elation; inflated self-esteem/grandiosity; pressured speech/racing thoughts, distractibility, social disinhibition, excessive spending.
- Strong family history of bipolar disorder or psychosis.
- Referral: Community Mental Health Team (CMHT).
- Antidepressant monotherapy is not recommended for bipolar illness.

Consider Anxiety Disorders – [NICE 113](#)

Diagnosis Depression¹

- Read Code depressive episode.
- If severe depression (including psychotic symptoms) or suicide risk, consider CMHT referral or out of hours review at CMHT hub; referral either by practitioner or patient by contacting 0845 650 1730.
- Depressive symptoms in adolescents refer for specialist assessment.

Treatment

- **Mild:** Self-help, stress and wellbeing education, psychoeducation groups and classes, Computerised CBT (via SCI gateway), Websites: [Wellbeing](#), [Lifelink](#). Watch, Wait and Review.
- **Recurrence:** Start previous effective antidepressant (increasing to previously effective dose) & self help.
- **Moderate/Severe:** Antidepressant & self-help +/- referral (psychological therapy or further assessment).

Frequency of review will vary with individuals needs, for example every 2–4 weeks (or more frequently if self-harm or suicide risk) within the first 3 months and then at longer intervals if good response.

For the first episode of depression the majority of patients will remit within 6 to 12 months.

Low mood due to adjustment and reactive effects; social factors and life events associated with symptoms, consider: [Lifelink](#); [Citizens Advice](#); [Glasgow Help on Wellbeing menu bar](#)

Self-help and Non-pharmacological Therapy

Consider a range of approaches for all forms of depression

- **Life-style:** Structured day, exercise, alcohol and/or drug use, diet, sleep hygiene; caffeine intake, etc.
- **Exercise:** Structured exercise programme: Live Active.
- **Self-help:** [Information websites & telephone numbers](#) (Appendix 2)
 - Health reading section in libraries.
 - Computerised Cognitive Behavioural Therapy (CBT), refer via SCI gateway.
 - Websites [Wellbeing-Glasgow](#) information and downloadable resources. Other useful sites: [Choose Life](#), [Living Life to the Full](#) and apps [Headspace](#)
- Signposting to support services [Wellbeing-Glasgow-Help](#)
- **Support** patients to problem solve: [Information websites & telephone numbers](#). (Appendix 2)
- **Primary Care Mental Health Team (PCMHT):** consider referral if: symptoms meet diagnostic criteria, individual is motivated and able to engage in structured psychological therapy e.g. CBT

Review Regularly to Support Patients and Improve Outcomes

Self-help and Non-pharmacological Therapy plus Antidepressant

- Spontaneous remission: about 50% of patients recover from first episode within 3 months.²
- All antidepressants are equally efficacious when treatment doses are taken regularly.
- Consider: co-morbidities, pregnancy, interacting medicines, etc.
- Consider: limit antidepressant supply where risk of suicide.
- There is a slight increased risk of suicide when initiating antidepressants (see below).

Information which may be of use to patients, carers and family

- Have realistic expectations. You will still have bad days and setbacks.
- Antidepressants are not addictive. But may cause withdrawal/discontinuation symptoms for some.
- Any thoughts of self-harm please contact your practice, out of hours service (NHS 24, Tel: 111), friend or a family member.
- You may feel benefit when first starting an antidepressant but it can take 2 to 4 weeks to provide its full effect.
- If symptoms are not improving the antidepressant or antidepressant dose might have to be changed.
- You should take your antidepressant for at least 6 months after you feel better. If you have had 2 or more episodes in the recent past the antidepressant may be continued for up to 2 years.
- Side effects can be short lived; reducing within a few weeks of starting an antidepressant.
 - SSRIs: nausea, vomiting, diarrhoea, anxiety, weight loss/gain, headache, insomnia
Agitation is a common side effect associated with starting and increasing SSRIs doses which normally resolves within 7-10 days, but can contribute to suicidal ideation. If this occurs please contact your practice.
 - TCAs: dry mouth, constipation, drowsiness, dizziness, increased appetite, weight gain, confusion.
 - Mirtazapine: sedation (especially at lower doses: 15mg daily), increased appetite, weight gain.
 - Trazodone: sedation, headache, nausea, vomiting, hypotension, priapism.
 - Venlafaxine: constipation, nausea, vomiting, weight loss, palpitations, hypertension.If side effects continue or are troublesome please discuss alternative treatment options with your GP.
- Discontinuation symptoms may occur on stopping, missing doses or when reducing the dose; these are usually mild and self-limiting but can be severe when antidepressants are stopped abruptly.
- More medicines information is available at [NHS Choices Antidepressants](#)
- Avoid alcohol and recreational drugs.
- Self-help: [Information websites & telephone numbers](#) (Appendix 2) Healthy reading section in local libraries.
- For the first episode of depression the majority of patients will remit within 6 to 12 months.
- Have realistic expectations. You will still have bad days and setbacks.

**Check – Do they want to take an antidepressant?
Discuss starting and stopping treatment**

Mild depression

**Watch,
Wait & Review**

Antidepressants demonstrate poor benefit.

Non-pharmacological therapy and self-help: sign-posting, psychoeducation.

**Recurrence
Mild, moderate or
severe**

Start previous effective antidepressant. Increase to previously effective dose

Plus non-pharmacological therapy and self-help.

Moderate/Severe depression

**Sertraline or fluoxetine or
citalopram or mirtazapine**

Trial therapeutic dose: 50mg sertraline, 20mg fluoxetine/citalopram or mirtazapine 30mg daily. Assess efficacy at 2-4 weeks.

SSRIs demonstrate a flat dose response curve for the treatment of depression²⁻⁴
Plus non-pharmacological therapy & self-help.

Review Regularly to Support Patients and Improve Outcomes

Review biopsychosocial assessment and progress ([PHQ-9](#), CORE-10). Review treatment efficacy.

Watch & Wait: Assess response and severity. A large proportion of patients will spontaneously remit.

No response at 4 weeks with therapeutic dose taken regularly.

- Check concordance. Review diagnosis: exclude organic cause, bipolar illness, etc.
- A lack of significant improvement in concordant patients after 2-4 weeks of treatment reduces the probability of an eventual response.
- Consider increasing to therapeutic daily dose: **'50's enough'** for sertraline, **'20's plenty'** for fluoxetine/citalopram, or 30mg of mirtazapine where night-time sedation is required. Higher doses increases avoidable adverse drug effects with little clinical benefit²⁻⁵.
- Consider switch to alternative SSRI or mirtazapine. **Lofepramine** increasing to 140mg daily may also be an appropriate [Formulary](#) option.
- Consider referring to PCMHT, if symptoms meet diagnostic criteria, individual is motivated and able to engage in structured psychological therapy e.g. CBT, and antidepressant and dose are stable.

Partial response at 4 weeks with therapeutic dose taken regularly.

- Check concordance.
- Consider switching antidepressant or increasing current antidepressant dose (evidence is lacking to support increasing SSRI doses³) and review efficacy 2-4 weeks.
- If residual symptoms persist after increasing the dose consider switch to an alternative antidepressant, see [NHSGGC Formulary](#).
- Consider referring to PCMHT as outlined above.

Do NOT combine antidepressants unless directed by consultant psychiatrist.

Full response: Maintain current antidepressant and dose after remission achieved.

- First episode: continue for **6 months** after remission achieved; reviewing according to need.
- Recurrent episodes: consider number of relapses and tailor treatment to patients needs with regular review: at least **1 year** of treatment after full remission for those at increased risk and at least **2 years** in higher risk patients (i.e. >5 lifetime episodes and/or 2 episodes in the last few years^{3,7}).
- Long-term use: review regularly every 6-12 months; consider adding review date to prescription.
- **Review ongoing need.** Consider reducing and stopping after patient has completed the course.

Third line choices: **venlafaxine** is restricted to use as third line agent for depression. The MR preparation is restricted to initiation on the advice of a consultant only, as MR/XL preparations lack clear clinical advantages over standard release. Increase to 225mg if appropriate, and tolerated, for dual effect. Regularly monitor BP as clinically appropriate.

Duloxetine restricted to psychiatrist initiation as third line therapy for major depressive episodes.

Avoid St John's wort (Hypericum). Due to drug-interactions and lack of standardised dose.

Depression with anxiety

- Consider relaxation resources [Wellbeing](#)
- Consider referral to PCMHT, if co-morbid anxiety disorder.
- Agitation is a common side effect associated with starting and increasing SSRIs doses which normally resolves within 10 days, but can contribute to suicidal ideation.
- If a patient is very anxious or agitated, consider the use of benzodiazepines as an adjunct for a maximum of 2 weeks. Use lowest possible dose.
- Avoid long-term (>4 weeks) benzodiazepines or z-hypnotics as they can increase anxiety and worsen depressive symptoms.

General antidepressant information:

- **Switching antidepressants:** When changing antidepressants a wash out period may be required [Clinical Knowledge Summaries \(CKS\), See Prescribing Information, Switching](#). When switching, including within class, response rates vary widely from 12–70% in different studies.
- **Stopping:** All classes of antidepressants can cause discontinuation/withdrawal symptoms, when abruptly stopped or after missing or reducing doses. Encourage patients to discuss stopping before doing so. Discontinuation symptoms more commonly occur with higher doses and longer duration of treatment. Symptoms begin within a few days of stopping and generally subside within 7-10 days, but a minority of patients may experience severe or prolonged symptoms (flu-like, electric shocks, vivid dreams, insomnia, etc). The optimum rate of taper to prevent withdrawals is unknown. Withdrawal reactions may be mistaken for relapse. Slow reduction over ≥4 weeks, or months may be needed. Speed of reduction should be guided by the patient's wishes and needs. ([Reducing and stopping schedules and advice](#) – Appendix 3).
- **Dose response:** Evidence is lacking for better SSRI and mirtazapine efficacy with higher daily doses: **'20's plenty'**, citalopram/fluoxetine/paroxetine, **'50's enough'** for sertraline and 30mg of mirtazapine.³⁻⁶ Higher TCA and venlafaxine doses can be more effective.³⁻⁶
- **Fluoxetine preparations:** Fluoxetine 20mg capsules are the preferred presentation in NHS GGC. Other strengths (e.g. 10mg, 60mg capsules) should not be prescribed routinely, as these are commonly 40-50 times more expensive. Where 10mg daily doses are needed, 20mg dispersible tablets can be halved or alternate day dosing with 20mg capsules can be used.

Co-morbidity and special groups.

- **Cardiovascular disease:**
 - Arrhythmias: Avoid TCAs. Citalopram is contraindicated in people with known QT prolongation or in combination with drugs known to prolong QT: [QT prolongation more information](#). Venlafaxine is contraindicated in people with an identified high risk of serious cardiac ventricular arrhythmia
 - Hypertension: venlafaxine and duloxetine are contraindicated for people with uncontrolled hypertension. For people who experience a sustained increase in blood pressure while receiving venlafaxine, either dose reduction or discontinuation should be considered.
 - Left ventricular systolic dysfunction (LVSD): avoid TCAs, venlafaxine, trazodone. Sertraline or mirtazapine likely to be safe⁸
 - Post MI: use sertraline post recent MI or unstable angina. Mirtazapine and other SSRIs are also likely to be safe.⁴
 - **Anticoagulants:** Warfarin: monitor INR when antidepressants are initiated, doses changed and after discontinuing. Increased bleeding risk with SSRIs and all anticoagulants, due to SSRI antiplatelet effects.
- **Dementia:** Although depression may be a common feature in early dementia, with antidepressants having moderate effect³, patients should be routinely reviewed to assess ongoing need.
- **Diabetes:** SSRI first line choice³. Mirtazapine may be considered as an alternative but is associated with weight gain. Avoid TCAs and MAOIs. Monitor blood glucose carefully when antidepressants are initiated, doses are changed and after discontinuation.
- **Elderly:** May require lower starting dose increasing to therapeutic dose. Avoid TCAs where possible due to anticholinergic, cardiovascular and sedative effects.
- **Epilepsy:** Sertraline or mirtazapine may be appropriate for less complex cases. However seek specialist advice for more complex individuals. Medicines Information Tel:0141 211 4407

- **Post stroke:** consider fluoxetine or citalopram or mirtazapine in ischaemic stroke; avoid SSRIs in haemorrhagic stroke due to increased bleeding risk.⁴
- **Pregnant or breast feeding:** Seek specialist advice for individual cases: Perinatal Mental Health Service: 0141 211 6500. Background information available at [CKS – Antenatal and Postnatal Management of perinatal mood disorders – SIGN 127](#).

Antidepressant Adverse Effects: Some effects mimic signs and symptoms of depression e.g. SSRIs: insomnia, hypersomnia or anxiety; venlafaxine: anxiety, palpitations and weight loss.

- **Bleeding and SSRIs (see anticoagulants above):** SSRIs are associated with an increased risk of GI bleed. Concomitant NSAID and/or antiplatelets significantly increasing bleed risk, therefore consider patients risk factors (age, previous GI history, current medicines) and if gastro-protection is required^{3,7} Omeprazole and lansoprazole capsules are NHS GGC formulary preferred PPIs.
- **Falls risk:** Increased risk for elderly: TCAs having the highest risk followed by SSRIs and mirtazapine. Higher SSRI doses are associated with a three-fold increase in falls risk.
- **Hyponatraemia** is a potentially serious adverse effect (dizziness, nausea, lethargy, confusion, cramps, seizures) associated with most antidepressants; onset with 30 days of starting treatment. Higher risk with one or more of the following: previous hyponatraemia, elderly (>80 years), female, reduced renal function (GFR <50ml/min), co-morbidities (hypothyroid, diabetes, COPD, hypertension, CVA, etc) and other medicines (diuretics, carbamazepine, NSAIDs, tramadol, omeprazole or trimethoprim). Consider monitoring at baseline, 2 and 4 weeks, and then 3 monthly.⁴
- **Sexual dysfunction:** Consider asking patients if this is problematic as this is usually under reported ([More information](#) – Appendix 4) Both depression and antidepressants can cause disorders of desire, arousal and orgasm. Antidepressant induced sexual dysfunction spontaneously remits for 10% and partially remits for 11%. If problematic consider dose reduction, switching ([CKS - see menu, Prescribing Information](#)), or stopping ([Reducing and stopping schedules and advice](#)).
- **Suicide and antidepressants:** There is a slight increased risk of suicide when initiating antidepressants, especially in ≤30 year old. The benefits of antidepressant use outweigh the risk for their licensed indications ([More information](#) – Appendix 4) .
- **Weight changes** may be experienced by patients with antidepressant use ([More information](#) – Appendix 4) .

Managing adverse effects:

- Where appropriate give patient permission to stop the drug causing side effects e.g. akathisia, aggression, etc.
- Dose reduction may help where tolerance to the adverse effect does not develop e.g. sexual dysfunction, insomnia or hypersomnia.
- Switching antidepressant to one with potentially less side effects.
- Drug holidays or cessation may also be considered as an option.

Other links which may be useful

[Choice and Medication](#)

[British Association for Psychopharmacology www.bap.org.uk](#)

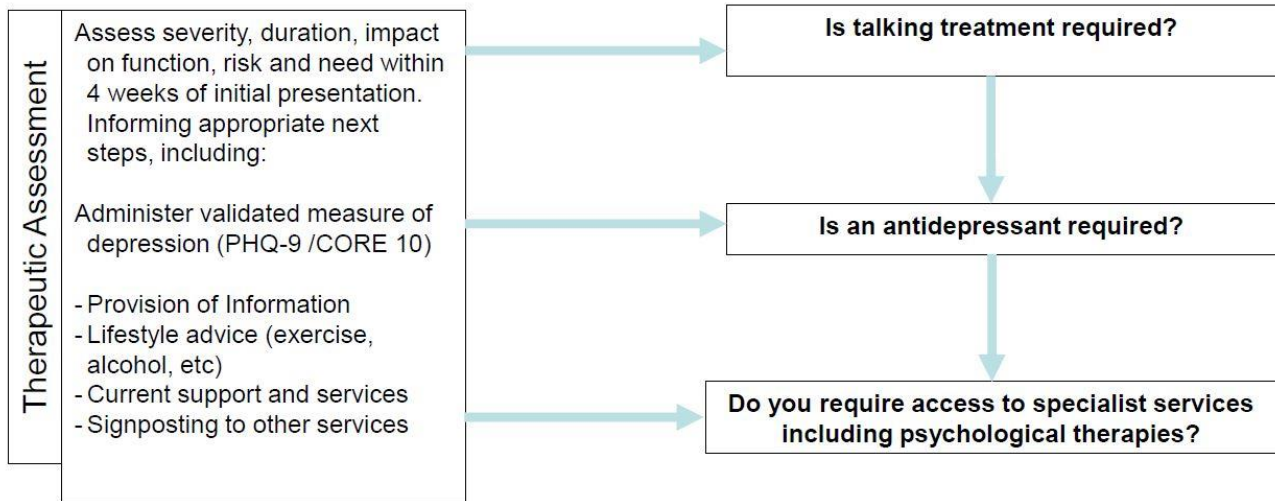
[NICE 90 Depression in Adults www.nice.org](#)

[NICE 91 Depression in Adults with a Chronic Physical Health Problem www.nice.org](#)

References

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2. Spijker J, et al. Duration of major depressive episodes in the general population. *Brit J Psych* 2002;181:208-213.
3. Cleare A, Pariante CM, Young AH, et al. Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2008 British Association for Psychopharmacology guidelines. *J Psychopharmacol* 2015;29(5):459-525.
4. Taylor D, Paton C, Kapur S. *The Maudsley Prescribing Guidelines* 13th ed. Wiley-Blackwell; 2018.
5. Adli M, Baethge C, Heinz A, et al. Is dose escalation of antidepressants a rational strategy after a medium-dose treatment has failed? A systematic review. *Eur Arch Psychiatry Clin Neurosci* 2005;255(6):387-400.
6. Furukawa TA, Cipriani A, Cowen PJ, Leucht S, Egger M, Salanti G. Optimal dose of selective serotonin reuptake inhibitors, venlafaxine, and mirtazapine in major depression: a systematic review and dose-response meta-analysis. *Lancet Psychiatry* 2019;6(7):601-609.
7. NICE. Treatment and management of depression in Adults. Clinical Guideline 90. 2009
8. NICE. Depression in adults with chronic physical health problems. CG 91. 2009

Appendix 1



Issues / Barriers	Outcomes
View All Detail	

Appendix 2 - Mental Health Support Resources and Information

Other services may be available in your area.

Helplines	NHS 24	111	24 hour
	Samaritans	116 123	24 hour
	Child Line	0800 11 11	24 hour
	Scottish Domestic Abuse Helpline (For anyone affected by domestic abuse)	0800 027 1234	24 hour
	Breathing Space	0800 83 85 87	Mon to Thurs 6pm-2am, Fri 6pm to Mon 6am
	Saneline	0300 304 7000	4.30pm-10.30pm Daily
	Rape Crisis Scotland (For anyone affected by sexual violence)	08088 010203	6pm-Midnight
	Parent line Scotland (For anyone caring for or concerned about a child)	0800 028 22 33	Mon-Fri 9am-9pm, Sat-Sun, 9am to 12pm
	Renfrew Association for Mental Health (RAMH) (Residents of Renfrewshire only)	0800 221 8929 0141 848 9090	Crisis contact Mon- Fri 9am-8pm Sat-Sun 9am- 5pm

Other Support	Scottish Association for Mental Health (SAMH)	0141 530 1000	www.samh.org.uk	Mon-Fri 9am to 5pm
	Glasgow Association for Mental Health (GAMH)	0141 552 5592	www.gamh.org.uk/	Mon-Thurs 9am-5pm, Fri 9am-4:30pm
	Renfrew Association for Mental Health (RAMH) (Residents of Renfrewshire only)	0141 847 8900	https://ramh.org/	Mon- Fri 9am-5pm
	Lifelink (Counselling & Resources)	0141 552 4434	www.lifelink.org.uk/	Mon - Fri 8:30am -5pm
	Living Life : Guided self- help and Cognitive Behavioural Therapy (CBT) telephone service	0800 328 9655	www.breathingspace.scot/living-life	Mon-Fri 1pm -9pm
	Scottish Care and Information on Miscarriage	0141 552 5070	www.miscarriagesupport.org.uk	Sometimes answer machine - can leave contact detail for a phone back
	Relationship Scotland	0345 119 2020	www.relationships-scotland.org.uk	Mon-Fri 9.30am to 4.30pm
	Glasgow Council on Alcohol	0800 802 9000	www.glasgowcouncilonalcohol.org	Mon-Wed 9am-9pm, Thur-Fri 9am-5pm, Sat 9am-1pm
	Al-Anon (For anyone affected by someone else's drinking)	0800 0086 811	www.al-anonuk.org.uk	10am- 10pm daily
	Cruse Bereavement Care Scotland	0845 600 2227	www.crusescotland.org.uk	Mon-Thurs 10am-8pm Fri 10am- 4pm
	Gamblers Anonymous Scotland	0370 050 8881	www.gascotland.org/	24 hour
	Know the Score (Drug use and addiction)	0333 230 9468	www.knowthescore.info/	Mon-Fri 9am-11pm & Sat-Sun 11am-4pm

Online Support

Self-help	Action on Depression	Support Information	http://www.elament.org.uk/finding-a-service/action-on-depression/
	Living Life to the Full	Support Information	www.lltff.com
	Beating the Blues	Online programme of Cognitive Behavioural Therapy	www.beatingtheblues.co.uk
	Wellbeing Glasgow	Support Information	www.wellbeing-glasgow.org.uk
	NHS Inform Mental Health and Wellbeing	Support information	https://www.nhsinform.scot/illnesses-and-conditions/mental-health
Other support	Wellbeing-Glasgow-Help	Provides contact details and information on mental health and non-mental health services	http://wellbeing-glasgow.org.uk/help/
	NHS Choices	Support Information	www.nhs.uk/pages/home.aspx
	Citizens Advice	Information and advice to resolve money, legal and other problem	www.cas.org.uk
Apps	Headspace	Guided meditation and Mindfulness. Advice, tips and tools to let go of stress, to help relaxation and improve sleep.	www.headspace.com
	WellMind	Advice, tips and tools to improve your mental health and boost your wellbeing	WellMind – available on App Store and Google Play

Antidepressants: Information which may be of use to patients, carers and family

- Have realistic expectations. You will still have bad days and setbacks
- Antidepressants are not addictive.
- Any thoughts of self harm please contact your practice, out of hours service (NHS 24, Tel: 111), friend or a family member.
- You may feel benefit when first starting an antidepressant but it can take 2 to 4 weeks to provide its full effect.
- If symptoms are not improving, the antidepressant or antidepressant dose might have to be changed.
- You should take your antidepressant for at least 6 months after you feel better. If you have had 2 or more depressive episodes in the recent past, the antidepressant may be continued for up to 2 years.
- Side effects can be short lived and reduce within a few weeks of starting an antidepressant.
 - Selective serotonin re-uptake inhibitors (SSRIs) such as citalopram, fluoxetine, sertraline: nausea, vomiting, diarrhoea, anxiety, weight loss/gain, headache, insomnia. Agitation is a common side effect associated with starting and increasing SSRIs doses which normally resolves within 7-10 days, but can contribute to suicidal ideation. If this occurs please contact your practice.
 - Tricyclic antidepressants (lofepramine, amitriptyline, etc): dry mouth, constipation, drowsiness, dizziness, increased appetite, weight gain, confusion.
 - Mirtazapine: sedation (especially at lower doses: 15mg daily), increased appetite, weight gain.
 - Trazodone: sedation, headache, nausea, vomiting, hypotension, priapism.
 - Venlafaxine: constipation, nausea, vomiting, weight loss, palpitations, hypertension.

If side effects continue or are troublesome please discuss alternative treatment options with your GP.

- Discontinuation symptoms may occur on stopping, missing doses or when reducing the dose; these are usually mild and self-limiting but can be severe when antidepressants are stopped abruptly. When considering stopping antidepressants please discuss with your GP or other healthcare professional to ensure appropriate managed reduction and stopping.
- More medicines information is available at [NHS Choices Antidepressants \(http://www.nhs.uk/conditions/Antidepressant-drugs/pages/introduction.aspx \)](http://www.nhs.uk/conditions/Antidepressant-drugs/pages/introduction.aspx)
- Avoid alcohol and recreational drugs.
- Self-help: as outlined above and healthy reading section in local libraries.
- For the first episode of depression, the majority of people will experience remission within 6 to 12 months.
- Have realistic expectations. You will still have bad days and setbacks.

Appendix 3

Antidepressant Reduction Advice

Background

All classes of antidepressants can cause discontinuation/withdrawal symptoms, especially when stopped abruptly. Withdrawals may also occur to a lesser extent when doses are missed or reduced. Some people may be more sensitive to withdrawals than others, and unfortunately it is difficult to know who will or will not experience withdrawal effects.

The optimum rate of taper to prevent withdrawals is also unknown. Therefore, the prescriber and individual should discuss and agree the most appropriate approach to reducing the dose and reviewing progress. Reducing over 4-6 weeks may be appropriate for people receiving antidepressant treatment for 9 months or less, whereas slower reduction over a period of months may be required due to longer term (>9 months) use, or for people that are anxious/distressed about reducing and/or stopping. Where people experience significant or unbearable withdrawal effects, increasing back to the previous dose that did not cause withdrawals, and stabilising, and then considering a slower rate of reduction may help.

Current evidence indicates that withdrawals more commonly occur with paroxetine and venlafaxine, as well as higher antidepressant doses and longer duration of treatment with other antidepressants. Therefore, this advice is intended to provide prescribers and patients with a range of options to appropriately support and enable successful antidepressant reduction and discontinuation.

Quick Links (use Ctrl+click)

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4 Difficulty withdrawing SSRI/SNRI or fearful	8
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1. Considerations for reducing and/or stop antidepressants ([Return to top](#))

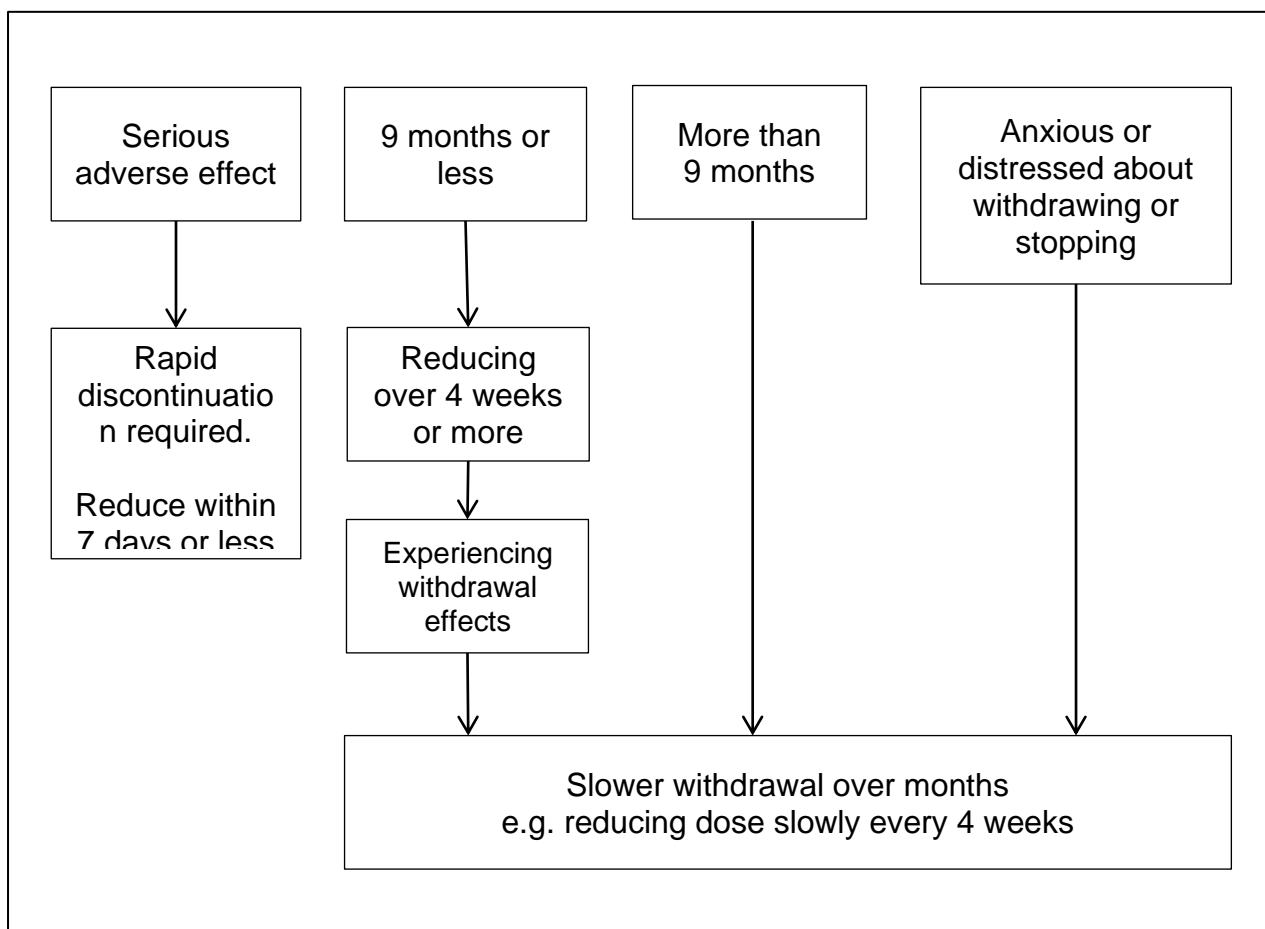


Figure 1, Reducing and stopping antidepressants

Consider the clinical situation when reviewing and discussing reducing/stopping antidepressants, and encourage individuals' to discuss stopping with their prescriber before doing so. By discussing and planning withdrawals the most appropriate rate of reduction can be agreed and planned with the individual according to their preferences and needs:

- Experiencing serious adverse effects; may require rapid discontinuation within 7 days or less (Table 1).
- Completed a 6-9 month course of antidepressant treatment e.g. first episode of moderate to severe depression – reduce over a minimum of 4 weeks, but some individuals may need a slower reduction.
- Completed a longer course (9 months or more) of antidepressant treatment, and/or a history of recurrent depression or anxiety. Reducing and tapering the dose at a slower rate over months may be more appropriate.
- Anxious about reducing/withdrawing antidepressant or history of experiencing discontinuation effects. Reducing and tapering the dose at a slower rate over months may be more appropriate.

The strategy for reducing/stopping antidepressants should be guided and informed by the individual's preferences and needs.

Table 1 Serious adverse effects which may require rapid discontinuation

Adverse effect	Drugs	Symptoms/Signs
Serotonin syndrome (very rarely occurs)	SSRI, SNRI, clomipramine, moclobemide, and other medicines e.g. triptans, tramadol, fentanyl, etc.	<p>Mild (patient may/may not be concerned): insomnia, anxiety, nausea, diarrhoea, hypertension, tachycardia, hyper-reflexia.</p> <p>Moderate (causes distress): agitation, myoclonus, tremor, mydriasis, flushing, diaphoresis, low fever (<38.5°C)</p> <p>Severe (medical emergency): severe hyperthermia, confusion, rigidity, respiratory, coma, death</p>
QTc interval prolongation	Citalopram, escitalopram, TCAs, and other medicines e.g. quinine, methadone, antipsychotics, antibiotics etc.	ECG changes in QTc interval

Note: Serotonin syndrome, for more detail see Buckley et al 2014 and Isbister 2007, QTc prolongation is of concern as it is associated with ventricular tachycardia and sudden cardiac death, see Kallergis et al 2012.

2. Discontinuation/withdrawal symptoms ([Return to top](#))

These may begin within a few days of stopping an antidepressant and generally subside within 7-10 days, but a minority of people may experience severe or prolonged symptoms (Table 2).

Table 2. Antidepressant discontinuation/withdrawal symptoms

Antidepressant class	Most commonly associated ^a	Symptoms ^b	
		Common	Occasional
SSRI, Clomipramine (TCA)	Paroxetine	Flu-like symptoms (chills, myalgia, excess sweating, nausea, headache), 'shock like' sensations, dizziness exacerbated by movement, insomnia, excess (vivid) dreaming, irritability, crying spells	Movement disorders, concentration, memory difficulties
SNRIs	Venlafaxine	Same as above, due to serotonin effects	Same as above
TCAs	Amitriptyline, Imipramine	Flu-like symptoms, insomnia, excess dreaming. <i>Anticholinergic rebound</i> – more common in the elderly: headache, restlessness, diarrhoea, nausea and vomiting	Movement disorders, mania, cardiac arrhythmias.
Other	Mirtazapine ^c	Anxiety, panic attacks, insomnia, irritability, nausea	
	Agomelatine		No discontinuation symptoms have been reported ^d
	Trazodone		Rarely SSRI type withdrawals ^e
	Vortioxetine		No discontinuation symptoms have been reported ^f

- Although most commonly associated with the listed medicines, other medicines in the group may cause similar symptoms.
- Symptoms: As individuals may or may not experience discontinuation/withdrawal symptom, and the intensity and range of symptoms may vary by individual, people may experience or identify symptoms not listed above.
- Limited data: mirtazapine case studies, see Cosci et al 2017.
- Agomelatine and vortioxetine are rarely used. At time of writing no case reports in literature.
- See Haddad et al 2001. and Otani et al 1994. for more detail.
- Adapted from and informed by Maudsley and Psychotropic Drug Directory.

3. Standard reduction approaches ([Return to top](#))

Appropriate for patients taking antidepressants that have no past history of distressing withdrawal, and no particular fear of withdrawing and/or stopping antidepressants over 4 to 6 weeks.

Review and reduce dose every 1 to 4 weeks or as guided by the individual's needs and/or preferences. However reducing every 4 weeks may be more practical for individuals due to their carer, family and work commitments, as well as for collecting prescriptions and enabling appropriate face-to-face or phone review follow up.

3.1 Selective serotonin reuptake inhibitors (SSRI) ([Return to top](#))

Due to the long half-life, the following can be stopped at standard daily doses: citalopram 20mg, escitalopram 10mg, fluoxetine 20mg and sertraline 50mg per day. However, individuals may prefer or require a slower reduction with lower doses.

SSRIs	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Citalopram	40mg	30mg	20mg	10mg	Stop	
Escitalopram	20mg	15mg	10mg	5mg	Stop	
Fluoxetine	40mg	30mg*	20mg	10mg**	Stop	
Fluvoxamine	300mg	200mg	100mg	50mg	Stop	
Sertraline	200mg	150mg	100mg	50mg	25mg***	Stop
Paroxetine†	40mg	30mg	20mg	10mg	5mg	Stop

Steps: the rate of withdrawal will vary with individual's needs e.g. weekly to 4 weekly reductions for some.

All doses are single daily doses

*Alternate day dosing 40mg/20mg

**Alternate day dosing with 20mg capsule, or consider using fluoxetine liquid

***Alternate day dosing with 50mg tablet

† Some people may require to be switched to an alternative SSRI if experiencing significant withdrawals, see below.

3.2 Serotonin and noradrenaline reuptake inhibitors (SNRI) ([Return to top](#))

Most individuals will be able to slowly withdraw and discontinue duloxetine and venlafaxine without any adverse effects. Where individuals experience discontinuation/withdrawal effects after stopping, it may be appropriate to restart the antidepressant at the previous dose and frequency for 7 days then switch to a long acting SSRI, interactions and contra-indications allowing ([section 4](#)).

SNRI	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Duloxetine ^a	120mg	90mg	60mg	30mg	Stop	
Venlafaxine MR ^b	300mg	225mg	150mg	75mg	37.5mg	Stop
Venlafaxine ^c	150mg twice daily	150mg morning 75mg night	75mg twice daily	37.5mg twice daily	Stop ^d	

Steps: the rate of withdrawal will vary with individual's needs e.g. weekly to 4 weekly reductions for some.

Note: Venlafaxine 300mg daily used as example, as individuals on higher doses are usually under the care of community mental health teams who should be involved in decisions to reduce or withdraw.

- BNF only has 60mg dose listed for treatment of major depressive disorder, but duloxetine SmPC (data sheet) quotes up to 120mg daily.
- If receiving modified release (MR) preparations as split dose e.g. twice daily, please consider that MR preparations are intended as once daily preparations.
- Some individuals may have a preference for reducing the night-time or morning dose first.
- Ordinary release. If needed the 37.5mg MR daily could be used for another step before stopping.

3.3 Tricyclic antidepressants (TCAs) ([Return to top](#))

Older adults and more frail individuals may require and need slower reduction to minimise the risk of cholinergic rebound (nausea, vomiting, headache, restlessness). Therefore slow reduction over longer than 6 weeks, or months, may be needed for some individuals depending on their preference and/or needs.

TCAs	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6	Step 7	Step 8
Amitriptyline ^a	150mg	100mg	50mg	Stop				
Amitriptyline ^{a,b}	150mg	125mg	100mg	75mg	50mg	25mg	10mg ^c	Stop
Lofepamine ^d	210mg	140mg	70mg	35mg ^e	Stop			

- The same reduction schedule would be advised for:

Clomipramine	Dosulepin (dotheipin)	Doxepin
Imipramine	Nortriptyline	Trimipramine
- Older adults and some individuals may require reductions using smaller dose increments to minimise the risk of adverse withdrawal effects.
- Dosulepin and doxepin not available as 10mg dose, therefore consider if necessary using 25mg capsules on alternate days, then stop.
- If dose is split morning and night, consider reducing and stopping morning dose first, and then continuing reduction with night time dose.
- Tablets are less suitable for halving as they have a film coating. If necessary, a 35mg dose can be given using lofepramine 70mg/5ml oral suspension.

3.4 Other antidepressants and monoamine oxidase inhibitors (MAOIs) ([Return to top](#))

Other		Step 1	Step 2	Step 3	Step 4	Step 5	Step 6	Step 7
Agomelatine		50mg	25mg	Stop				
Mirtazapine		45mg	30mg	15mg ^a	Stop			
Trazodone		300mg ^b	250mg	200mg	150mg	100mg	50mg	Stop
Vortioxetine		20mg	10mg	Stop				
Isocarboxazid ^c	Morning	60mg	50mg	40mg	30mg	20mg	10mg	Stop
Moclobemide ^d	Morning	300mg	300mg	150mg	150mg	Stop		
	Night	300mg	150mg	150mg	Stop			
Phenelzine ^c	Morning	30mg	30mg	30mg	15mg	15mg	15mg	Stop
	Afternoon	30mg	15mg	15mg	15mg	Stop	Stop	
	Night	30mg	30mg	15mg	15mg	15mg	Stop	
Tranylcypromine ^c	Morning	30mg	20mg	10mg	Stop			

Steps: the rate of withdrawal will vary with individual's needs e.g. weekly to 4 weekly reductions for some.

- Some people may find the 15mg dose more sedating than higher doses due more antihistamine effects.
- For higher doses consider reducing at each step by 50mg. However, clinical need and/or individual's preferences may require larger reduction steps e.g. 100mg.
- Isocarboxazid, phenelzine and tranylcypromine inhibit monoamine oxidase A and B for up to 2 weeks after stopping. Consider risk of interactions for 2 weeks after stopping.
- Moclobemide is a reversible inhibitor of monoamine oxidase A.

4. Difficulty withdrawing SSRI/SNRI or fearful ([Return to top](#))

For individuals who have had or are having difficulty withdrawing and stopping short half-life antidepressants: paroxetine, venlafaxine or duloxetine. Switching to a longer half-life SSRI may enable reduction and stopping, as venlafaxine and duloxetine act as SSRIs at low doses.

Convert to long acting SSRI and stop

Reduce the total daily dose in a stepwise fashion to: paroxetine 20mg, venlafaxine 75mg, duloxetine 30mg daily (see [3.1 SSRIs](#) and [3.2 SNRI](#)). Then convert to an approximate dose equivalent* of fluoxetine, citalopram or sertraline (Step 1), using standard capsules, tablets or liquid, and stabilise on that dose for 3-7 days then stop.

For example, duloxetine 30mg daily changed to fluoxetine 20mg daily and continued for 3-7 days then stopped.

Convert to long acting SSRI and reduce slowly

As some individuals may prefer or need slower reductions.

Daily dose		Step 1*	Step 2	Step 3	Step 4	Step 5	Step 6
Duloxetine 30mg	To any of these SSRIs	Fluoxetine 20mg	20mg alternate days	20mg every third day	Stop		
Or		Citalopram 20mg	10mg	10mg alternate days	Stop		
Paroxetine 20mg		Sertraline 50mg	50mg alternate days	50mg every third day	Stop		
Or		Fluoxetine liquid ^{a,b,c} (20mg in 5ml)	16mg (4ml)	12mg (3ml)	8mg (2ml)	4mg (1ml)	Stop
Venlafaxine MR 75mg (37.5mg twice daily)							

Steps: the rate of withdrawal will vary with individual's needs e.g. weekly to 4 weekly reductions for some.

* Approximate dose equivalents

- Some community pharmacies may not stock 1ml graduated 5ml oral syringes, but they can order these if given some warning.
- Citalopram 40mg/ml and escitalopram 20mg/ml liquid are not recommended due to the difficulty with accurately measuring small doses.
- Sertraline liquid is not recommended as it is unlicensed in the UK, and individuals may experience oral numbness on their tongue and mouth due to the anaesthetic effects of non-tablet formulations.

*Approximate dose equivalents and switching considerations:

- Due to inter-patient variability and differing half-lives, this means that these are approximate dose equivalents, not exact equivalence.
- The drug and dose equivalents can never be exact, and should be interpreted considering your clinical knowledge and the individual patient's needs.
- Drug interactions and drug-disease interactions.

Fluoxetine liquid may be required for a few individuals that require or prefer a slower reduction at weekly to 4 weekly intervals.

5. Significant difficulty or fears withdrawing SSRI/SNRI ([Return to top](#))

For a very small minority of individuals, slower graduated reduction may be appropriate:

- Where standard reduction ([SSRI section 3.1](#) or [SNRI section 3.2](#)) and/or
- Difficulty discontinuing/withdrawing SSRI/SNRI ([section 4](#)), have been tried and are unsuccessful. This approach will help flatten the reductions in plasma drug concentrations at lower doses ([Figure 2](#)).

First, reduce current antidepressant to standard dose as per [SSRI 3.1](#) or [SNRI 3.2](#). Then convert to an approximate dose equivalent of fluoxetine 20mg/5ml liquid.

Fluoxetine 20mg is approximately dose equivalent* to:

- Citalopram 20mg
- Escitalopram 10mg
- Fluvoxamine 50mg
- Paroxetine 20mg
- Sertraline 50mg
- Duloxetine 30mg
- Venlafaxine 75mg

***Approximate dose equivalents and switching considerations:**

- Due to inter-patient variability and differing half-lives, this means that these are approximate dose equivalents, not exact equivalence.
- The drug and dose equivalents can never be exact, and should be interpreted considering your clinical knowledge and the individual patient’s needs.
- Drug interactions and drug-disease interactions.

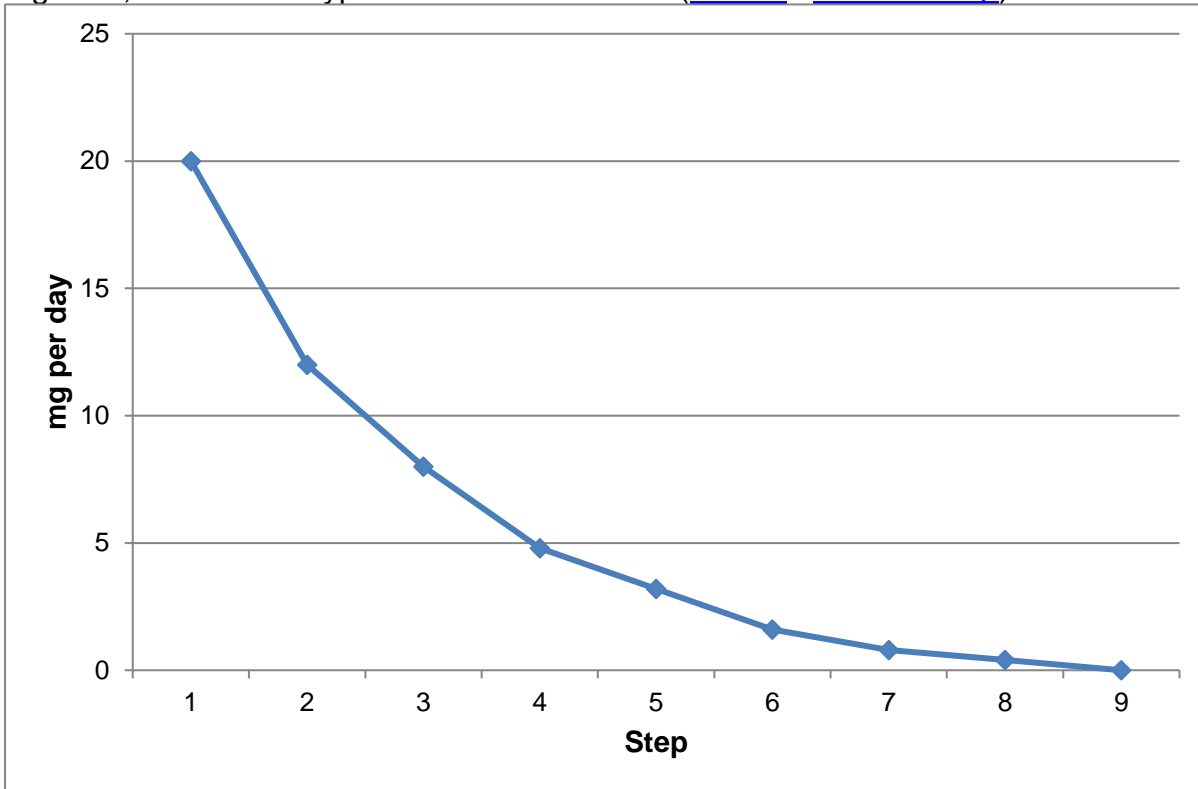
For example: paroxetine 20mg daily to fluoxetine 20mg daily, or paroxetine 10mg daily to fluoxetine 8mg daily (Step 3 below). Switch by taking last dose of paroxetine today and starting new dose of fluoxetine tomorrow at the same time of day. Agree an appropriate rate of reduction e.g. weekly or monthly, agree face-to-face or phone review follow up.

Note:

Fluoxetine liquid 20mg/5ml			
Step	mg/d	ml/d	Step down Difference (mg)
1	20	5	
2	12	3	8
3	8	2	4
4	4.8	1.2	3.2
5	3.2	0.8	1.6
6	1.6	0.4	1.6
7	0.8	0.2	0.8
8	0.4	0.1	0.4
9	Then stop	0	0.4

- Steps: the rate of withdrawal will vary with individual’s needs e.g. weekly to 4 weekly reductions for some.
- Citalopram 40mg/ml and escitalopram 20mg/ml liquid are not recommended due to the difficulty with accurately measuring small doses.
- Sertraline liquid is not recommended as it is unlicensed in the UK, and individual’s may experience oral numbness on their tongue and mouth due to the anaesthetic effects of non-tablet formulations

Figure 2, Fluoxetine hyperbolic dose reduction ([Return](#). [Return to top](#))



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Appendix 4 – Antidepressant side effects

Sexual dysfunction

Severity of sexual dysfunction increases with severity of depression. Antidepressant induced sexual dysfunction is commonly under reported (3-8% of patients spontaneously reporting such side effects and 34-75% reporting side effects on direct questioning¹) with patient presenting with a variety of side effects: reduced libido, arousal dysfunction and orgasmic disorders.¹⁻³ Antidepressant induced sexual dysfunction spontaneously remits in approximately 10% of cases with partial remission in a further 11%.³ All effects are reversible.

Antidepressant	Approximate prevalence of sexual dysfunction
Venlafaxine	70%
SSRIs	60-70%
Duloxetine	46%
Tricyclic antidepressants	30%
Mirtazapine	25%
Placebo	14%
Trazodone	Unknown

Adapted from Maudsley 2015³ and Serretti & Chiesa 2009.¹

Consider other causes such as alcohol, benzodiazepines, beta-blockers, co-morbidity, relationship difficulties, etc. Spontaneously remits for 10% and partially remits for 11%. If this does not occur consider dose reduction, switching or discontinuing antidepressant where appropriate.

Suicide, akathisia and aggression.

Akathisia or restless over activity experienced by some patients when initiating or increasing SSRI doses is usually short lived (settles within the first 10 days) but can contribute to suicidal ideation,^{4,5} with under 30's being at higher risk of suicidality associated with a variety of antidepressants.⁶ Aggressive behaviours are also associated with antidepressant use with greatest associated risk being observed for children and adolescents (<18 years old).⁷ If this occurs please ask the patient to contact the practice for advice or consider giving advice to stop and attend for review if appropriate. TCAs (excluding lofepramine) and venlafaxine have greatest risk of death in overdose.

Weight changes

Patients may experience weight changes during antidepressant treatment. Weight gain may be associated with depression recovery and improved appetite on one hand and undesirable antidepressant effects on the other;⁸ however, many placebo controlled studies report no weight data making it difficult to accurately estimate weight changes.² SSRIs have been seen as weight neutral, or in some cases associated with weight loss in the short-term (≤ 8 wk studies) and weight gain in the long-term.⁸

Antidepressant	% Patient with Weight gain
Amitriptyline	22%
Imipramine	13.3%
Mirtazapine	12.7%
Fluoxetine	4.8-6.8%
Sertraline	4.2%
Citalopram	3.9%
Placebo	2.6-6.3%
Venlafaxine	Weight loss.
Weight gain can vary from 0.5-1kg with SSRIs ⁸ to 2.5-3.3kg with mirtazapine ⁹	
Summarised from review articles ^{2,8}	

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