Antidepressant review and deprescribing guidance

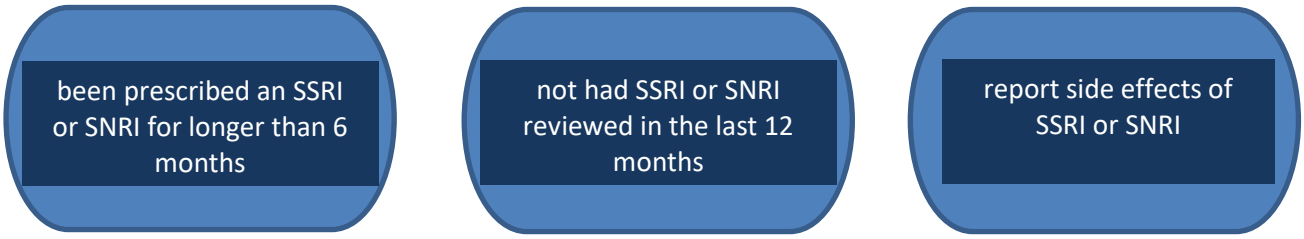
This guidance should be read in conjunction with NICE CG90 – Depression in adults: recognition and management [1]. The guidance has been designed to advise primary are clinicians as a framework on how to identify, contact, engage and manage patients in reviewing and deprescribing antidepressants.

Abbreviations

CBT	Cognitive Behavioral Therapy
GP	General Practitioner
GAD	Generalised Anxiety Disorder
IAPT	Improving Access to Psychological Therapies
OCD	Obsessive Compulsive Disorder
TCAs	Tricyclic Antidepressant
SNRIs	Serotonin and Noradrenaline Reuptake Inhibitors
SSRIs	Serotonin Selective Reuptake Inhibitors

Patients with depression who benefit from treatment with antidepressants are advised to continue with treatment for at least six months after remission, extending to at least two years for patients who are at risk of relapse. At this point, deprescribing should be considered.

Which patients are suitable for review?



At each review, the ongoing severity of depression should be assessed.

PHQ9 [2] is the most appropriate tool for assessing severity of depression in primary care and can apply to both new presentations and those already undergoing treatment.

STEP 1: SHOULD I DEPRESCRIBE? (PATIENT ASSESSMENT)

Deprescribing triggers

Inappropriate indication, no current indication, presence or risk of adverse events, drug interaction, drug-disease interaction, high drug burden index (DBI),[3] poor adherence, or patient preference.

1a. Is there a documented indication or symptoms supporting continued use?

Inappropriate indication for continued use:
No current depression >6 months.
Consult/review with treating psychiatrist.

Do not deprescribe if:
Recurrent or severe depression or other psychiatric condition such as OCD or GAD.

If there remains significant risk of relapse, particularly if there are residual depressive symptoms

Discuss with the treating psychiatrist.

1b. Are there adverse effects?

Consider potential adverse effects:

Falls, dizziness, agitation, headaches, nausea, diarrhoea, insomnia, tremor, dry mouth, sweating, weakness, sexual dysfunction, rhinitis, myalgia, rash, palpitations, tachycardia, hypotension, hyponatraemia, confusion, anxiety, drowsiness, or sedation.[4]

1c. Is this medication likely to cause more harm than benefit?

See Evidence-based advice in the appendix for additional information on risks of harm and benefits of continued use.

Does the patient/carer agree with the recommendation to deprescribe?

Over 90% of people would be willing to stop their medicines if recommended by their physician.[5]

Following provision of information, discussion and shared decision making, the patient or carer has communicated that they would like to proceed with or decline the deprescribing recommendation.

To prevent long-term prescribing, engage the patient when discussing an antidepressant as to what the medication is being used for; how long to continue taking the medication for with an indicative review date as appropriate, and mention the long-term effects of antidepressant use which can include:

- Sexual problems (72%), including the inability to reach orgasm (65%)
- Weight gain (65%)
- Feeling emotionally numb (65%)
- Not feeling like themselves (54%)
- Reduced positive feelings (46%)
- Feeling as if they're addicted (43%)
- Caring less about other people (36%)

STEP 2: HOW DO I DEPRESCRIBE? (RECOMMENDATION AND MANAGEMENT)

2a. How to wean (Based on recommendations: NSW Therapeutic Advisory Group – Deprescribing Tools)

Initiation

- Establish a supportive and trusting relationship with the patient to engage in complex/sensitive discussions. See bottom of appendix 1 for an example weaning template you may wish to consider.
- Accompany weaning with commencement of relevant non-pharmacological therapy. See Alternative management recommendations.
- Reduce dose slowly by 25-50% of the daily dose every 2-4 weeks.
  In patients prescribed high doses for longer periods a more gradual reduction plan may be more appropriate. Certain antidepressants with a higher risk of withdrawal symptoms require a more cautious reduction (see appendix 2).
- Organise GP follow up appointment (frequency determined by rate of weaning)
- Consider weaning faster if deprescribing reason due to adverse effects
- Provide advice to patient/carer on self-monitoring and what to do if symptoms re-occur.
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Adjust dose according to response (see monitoring recommendations)

- If no withdrawal symptoms occur, continue to wean and stop.
- Consider slower weaning (e.g. 12.5%) when reducing to the final lowest dose.
- End treatment 2 weeks after administering the lowest dose.
- Consider alternate day dosing to aid with weaning if dosage forms are limited.

Adjust in case of recurrent symptoms

If recurrent/withdrawal symptoms occur, restart medication at the lowest effective dose with retrial weaning after 6-12 weeks (e.g. 5-12.5% of daily dose each month) then stop.

Note: In all the steps above, consider recommending the use of non-pharmacological replacement therapy to reduce reliance on antidepressants

STEP 2: HOW DO I DEPRESCRIBE?
(RECOMMENDATION AND MANAGEMENT)

Withdrawal symptoms or relapse indicators

- Withdrawal symptoms normally start soon after medication is reviewed/stopped, potentially within 1 or 2 days.
- Re-emergence of depression or anxiety typically takes longer – weeks or months.
- In the case of emergence of withdrawal symptoms, it should be remembered that this can take longer with some antidepressants with longer half-lives (e.g. fluoxetine). Potentially this may make it more difficult to differentiate between withdrawal symptoms and re-emergence of original symptoms.
- Some symptoms are specific to withdrawal, such as the feeling of electric shocks ('zaps'). The patient may also indicate that symptoms experienced are different to those they experienced from their condition in the past which *may* indicate they are related to withdrawal.
- Withdrawal symptoms also usually respond to re-introduction of the antidepressant far more quickly (hours-days) than symptoms of depression/anxiety (weeks).

It should be noted that the above points are an intended as a guide only and that multiple factors may affect the above and vary between patients.

2b. Alternative management

Non-pharmacological support
Psychological therapy, social support, cognitive behavioural therapy, interpersonal therapy, supportive counselling and problem-solving techniques, physical activity.

For psychological treatment advice, self refer to the South Tyneside Lifecycle Service on 0191 283 2937, following link for more information: https://www.southtynesidelifecyclementalhealth.nhs.uk/

Consider a referral to your practice social prescribing link workers.

Switching within drug class or consider alternative therapy
If there is a current indication, consider dose reduction or consider switching to another antidepressant that may be better tolerated.

Care must be taken when switching between antidepressants to minimise drug interactions and adverse events (including serotonin syndrome).

To consider other options, refer to the Maudsley prescribing guidelines table in appendix 3.

Prescribing of antidepressants in learning disability and autism across Sunderland CCG

Recent NHS digital figures showed an increase in the prescribing of antidepressants in learning disability. This is in line with the findings from the STOMP agenda showing an increased reliance on antidepressant prescribing against a reduction in antipsychotic use.

In autism services, there is also an increased reliance on antidepressant use for anxiety related to autism. This may present in typical or atypical ways with the most common types of anxiety being felt to be GAD, social, agoraphobia and phobias. It can often present as behavioural issues including outbursts, repetitive behaviours, including rocking and stimming, and self-harm.

There is also documented evidence for a link between Asperger's diagnosis and higher rates of depression and suicidality.

Challenging antidepressant prescribing in learning disability and autism

- Ensure appropriate and accessible information is available to help each person to understand the implications of discontinuation
- Consider capacity and best interest requirements before the work is agreed
- Consider a more cautious approach to deprescribing given increased sensitivity to medication in this patient group. This could include smaller reductions or an extended review period.
- Produce a clear monitoring plan based on known anxiety presentation and symptoms
- Ensure behavioural plans are available and relevant to each individual patient with evidence on the positive impact of interventions
- Factor in more atypical presentations in this cohort of patients
- Consider a referral criteria based on individual competency and experience of learning disability and autism

Seek advice from the community learning disability team if any of the above points are unclear.

References

This guidance is primarily adapted from guidance produced by New South Wales Therapeutic Advisory Group, which is available online at https://www.nswtag.org.au/deprescribing-tools/

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Appendix 1.

EVIDENCE-BASED ADVICE [1]

Effectiveness and safety

A Cochrane meta-analysis of studies predominantly lasting 6-8 weeks, estimated that seven patients with depression needed to be treated with a SSRI in order to obtain a benefit in one (number needed to treat [NNT] = 7). Whereas, compared to placebo, 20-90 patients needed to be treated with a SSRI in order to suffer harm (withdrawal due to side effects) (number needed to harm [NNH] = 20-90).[6]

The risk of recurrence after the first episode of depression (after stopping 2 years of maintenance therapy) is approximately 60% over 2 years.[7]

Cognitive therapy has shown to be at least as effective in major depression as antidepressants, with sustained effects.[8,9]

It is uncertain whether continued or maintained pharmacotherapy (or both) with the reviewed antidepressant agents is a robust treatment for preventing relapse and recurrence in adults with persistent depressive disorder. [10]

Overall, there is currently a lack of quality evidence generally exploring the relationship with respect to withdrawal, relapse, and adverse effects. [11]

Recommended duration of use

Limit drug treatment to short-term use. Antidepressants are associated with significant harm (e.g. falls, fractures), and long-term use is not recommended, especially in older adults.

How to wean:

Recommend gradually reducing to _____ **for** _____ **and reassess,**
(drug: e.g. citalopram 15mg daily) (timeframe: e.g. 1 week)

then reduce to _____ **for** _____ **and reassess,**
(e.g. citalopram 10mg daily) (e.g. 1 week)

then reduce to _____ **for** _____ **and reassess,**
(e.g. citalopram 5mg daily) (e.g. 1 week)

then reduce to _____ **for** _____ **and stop.**
(e.g. citalopram 2.5mg daily (e.g. 2 weeks)

Follow up with clinician _____ **after discharge.**
(e.g. fortnightly)

Appendix 2

Table 1: Risk of withdrawal symptoms with individual antidepressant

Highest risk	Moderate risk	Low risk	Lowest risk
Amitriptyline	Citalopram	Bupropion	Agomelatine
Clomipramine	Escitalopram	Fluoxetine	
Paroxetine	Fluvoxamine		
Venlafaxine	Imipramine		
Duloxetine	Lofepramine		
	Nortriptyline		
	Mirtazapine		
	Reboxetine		
	Sertraline		
	Trazodone		
	Vortioxetine		

Table 2: Potential types of withdrawal symptoms

Physical symptoms	Sleep symptoms	Emotional symptoms
Nausea	Insomnia	Anxiety
Headache	Increased dreaming	Depression
Dizziness	Vivid dreams	Panic
Abdominal cramps	Nightmares	Agitation
Diarrhoea		Irritability
Fatigue		Mood changes
Flu-like symptoms		
Electric shock sensations (‘zaps’)		
Loss of appetite		
Visual disturbances (double vision; visual trailing)		
Palpitations		
Missed beats		
Sweating		
Flushing		
Tremor		
Tinnitus		
A feeling of inner restlessness and inability to stay still (akathisia)		

Above tables from: Stopping antidepressants | Royal College of Psychiatrists (rcpsych.ac.uk)

Appendix 4. - Antidepressant use: swapping

The table below has been adapted from the Maudsley prescribing guidelines via the Mid Essex CCG 'Guidance for the treatment of depression in adults'. There are no clear guidelines on switching antidepressants, so caution is required. Also the specific summary of product characteristics for each of the antidepressants involved should be consulted.

To / From	Citalopram	Sertraline	Fluoxetine	Paroxetine	Mirtazapine	Tricyclic Antidepressants (TCA)	Venlafaxine
Citalopram		Withdraw citalopram. Start sertraline at 25mg per day	Withdraw Start Fluoxetine at 10mg OM	Withdraw. Start Paroxetine at 10mg OM	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously 37.5mg OM Increase very slowly
Sertraline	Withdraw then start Citalopram 10mg per day		Withdraw then start Fluoxetine	Withdraw then start Paroxetine 10mg per day	Cross taper cautiously	Cross taper cautiously with very low dose of TCA	Withdraw sertraline then start venlafaxine 37.5mg per day
Fluoxetine	Stop fluoxetine. Wait 4-7 days. Start citalopram at 10mg OM and increase slowly	Stop fluoxetine. Wait 4-7 days. Start sertraline at 25mg per day and increase slowly		Stop fluoxetine. Wait 4-7 days. Start paroxetine at 10mg OM and increase slowly	Cross-taper cautiously, start mirtazapine at 15mg ON	Stop Fluoxetine. Wait 4-7 days. Start TCA at very low dose. Increase dose slowly.	Withdraw. Start venlafaxine 37.5mg OM Increase very slowly.
Paroxetine	Withdraw paroxetine Start citalopram 10mg per day	Withdraw paroxetine. Start sertraline at 25mg per day	Withdraw paroxetine. Start Fluoxetine		Cross taper cautiously	Cross taper cautiously with very low dose of TCA	Cross taper cautiously. Start venlafaxine 37.5mg OM. Increase very slowly
Mirtazapine	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously		Cautious cross tapering. Start TCA using very low starting dose	Cross taper cautiously
TCA	Halve dose. Add Citalopram then slowly withdraw TCA	Halve dose. Add Sertraline then slowly withdraw TCA	Halve dose. Add Fluoxetine then slowly withdraw TCA	Halve dose. Add Paroxetine then slowly withdraw TCA	Cross taper cautiously		Cross taper cautiously, starting venlafaxine 37.5mg OM
Venlafaxine	Cross taper cautiously. Start with citalopram 10mg per day	Cross taper cautiously. Start with sertraline 25mg per day	Cross taper cautiously. Start with 20mg fluoxetine on alternate days.	Cross taper cautiously. Start with paroxetine 10mg per day	Cross taper cautiously	Cautious cross tapering. Start TCA using very low starting dose	