

Antidepressant Treatment Guidelines (Adults 18 years and over)

NICE (NG222) guideline has defined new episodes of depression as [less severe or more severe](#) depression. Less severe depression encompasses subthreshold and mild depression, and more severe depression encompasses moderate and severe depression. Using thresholds on validated scales, scores less than 16 on the PHQ-9 scale are defined as less severe depression, and scores of 16 or more are defined as more severe depression.

For all people with depression having treatment:

- review how well the treatment is working with the person between 2 and 4 weeks after starting treatment
- monitor and evaluate treatment concordance
- discuss the benefits and monitor for side effects and harms of treatment
- monitor suicidal ideation, particularly in the early weeks of treatment (see [recommendations on antidepressant medication for people at risk of suicide](#) and [recommendations on risk assessment](#))
- consider [routine outcome monitoring](#) (using appropriate validated sessional outcome measures, for example PHQ-9) and follow up.
- For preventing relapse, see [visual summary on preventing relapse](#)

Treatment for a new episode of less severe depression. Discuss treatment options and match treatment to clinical needs and preferences, reaching a shared decision on a treatment choice appropriate to the person's clinical needs. Use table 1 and the [visual summary](#) for **first line non-pharmacological treatment options** and to guide and inform the conversation and take into account that all treatments in table 1 can be used as first-line treatments, but consider the least intrusive and least resource intensive treatment first (guided self-help). **Do not routinely offer antidepressant medication as first-line treatment for less severe depression unless that is the person's preference.** **Active monitoring in people who do not want treatment:** arrange a further assessment, normally within 2 to 4 weeks and make contact (with repeated attempts if necessary) if the person does not attend follow-up appointments.

Treatment for a new episode of more severe depression. Discuss treatment options and match treatment to clinical needs and preferences, reaching a shared decision on a treatment choice appropriate to the person's clinical needs. Use table 2 and the [visual summary](#) to guide and inform the conversation and take into account that all treatments in table 2 can be used as first-line treatments.

Pharmacological treatments

- Treatment choice will depend on preference for specific medication effects such as sedation, concomitant illnesses or medications, suicide risk and previous history of response to antidepressant medicines
- SSRIs are generally well tolerated, have a good safety profile and should be considered as the first choice for most people, although can be serotonin–norepinephrine reuptake inhibitor (SNRI), or other antidepressant if indicated based on previous clinical and treatment history.
- Medication will usually work within 4 weeks and might need to be taken for at least 6 months after remission of symptoms, but should be reviewed regularly
- Discuss benefits, side effects, withdrawal effects and address any concerns about taking or stopping medication. Advise patients that antidepressant withdrawal should be tapered, not stopped abruptly [NICE recommendations on stopping medication](#).
- For further advice on safe prescribing of antidepressants, see the [NICE guideline on medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults](#). For further advice on the safe and effective use of medicines for people taking 1 or more medicines, see the [NICE guideline on medicines optimisation](#).
- The first review will usually be within 2 weeks to check their symptoms are improving and for side effects, or after 1 week if a new prescription is for a person aged 18 to 25 years or if there is a particular concern for risk of suicide (see [recommendations on antidepressant medication for people at risk of suicide](#))
- Be aware of the possible increased prevalence of suicidal thoughts, self-harm and suicide in the early stages of antidepressant treatment, and ensure a risk management strategy is in place (see [section on risk assessment and management](#)). Review at 1 week after starting medication or increasing the dose, and review again as often as needed, but no later than 4 weeks after medication initiation.
- For people with depression taking lithium as augmentation, see [rationale and impact section on use of lithium as augmentation](#)
- For use of antipsychotics for the treatment of depression, see [rationale and impact section on use of oral antipsychotics as augmentation](#)

Further – line treatment - See [visual summary on further-line treatment](#). If there is limited or no response to treatment with antidepressant medication alone, and no obvious cause can be found and resolved, consider adding group exercise intervention, switching to a psychological therapy, or increasing the dose or changing the drug.

- Switching to another medication in the same class (e.g., another SSRI). Cross-tapering may be needed; see the [NICE clinical knowledge summary on switching antidepressants](#) and [Maudsley Prescribing Guidelines in Psychiatry](#) (accessed June 2021).
- Switching to a medication in a different class (e.g., SSRI, SNRI or in, or with advice from secondary care, a TCA or MAOI).
- If there is no or limited response, switch to another psychological therapy or increase the dose or switch to another antidepressant or add in another medication.
- Consider vortioxetine when there has been an unsatisfactory response to at least 2 previous antidepressants. See the [NICE technology appraisal guidance on the use of vortioxetine](#).
- Further treatment options include adding an additional antidepressant medication from a different class (for example, adding mirtazapine or trazodone to an SSRI) or
- combining an antidepressant medication with a second-generation antipsychotic (for example, aripiprazole, olanzapine, quetiapine or risperidone) or lithium or augmenting antidepressants with electroconvulsive therapy (see the [recommendations on electroconvulsive therapy for depression](#)), or off label use of lamotrigine, or triiodothyronine (liothyronine).

Be aware that some combinations of classes of antidepressants are potentially dangerous and should be avoided (for example, a SSRI, SNRI or TCA with a MAOI).

Chronic depressive symptoms. People presenting with chronic depressive symptoms that significantly impair personal and social functioning and who have not received previous treatment for depression offer CBT, SSRIs, SNRIs, TCA or combination therapy with CBT and an SSRI or TCA. For those who have not responded to SSRIs or SNRIs, consider alternative medication in specialist settings, or after consulting a specialist. Alternatives include TCAs, moclobemide, irreversible MAOIs such as phenelzine, off label low dose amisulpride.

First line - all choices GREEN

Restart a previously effective antidepressant if appropriate or choose from options below, considering any factors that might affect SSRI choice

- Sertraline
- Citalopram
- Mirtazapine [where SSRI contraindicated e.g., medications such as NSAIDs, SSRI related adverse effects, or where insomnia is impacting function where improvement is paramount]

The first review will usually be within 2 weeks to check their symptoms are improving and for side effects, or after 1 week if a new prescription is for a person aged 18 to 25 years or if there is a particular concern for risk of suicide

Second line - all choices GREEN

Switch to a different antidepressant from the list below, considering any factors that might affect choice

- Sertraline
- Citalopram
- Escitalopram
- Fluoxetine
- Mirtazapine [criteria as above]

Third line

Switch, augment or combine, considering any factors that might affect choice

- Vortioxetine GREEN according to [NICE TA367 Vortioxetine for treating major depression](#)
- Duloxetine GREEN • Augment with lithium A SC
- Venlafaxine GREEN • Augment a second-generation antipsychotic (aripiprazole, quetiapine, olanzapine, or risperidone) A SC
- Mirtazapine GREEN
- Trazodone GREEN
- Combine an SSRI or SNRI with mirtazapine or trazodone A SC

Fourth line

Use antidepressants or augmentation strategies listed under previous steps. The following may also be considered with Specialist input

- Agomelatine A SC
- Moclobemide A SC
- MAOI (preferred MAOI = phenelzine) A SC
- TCA (lofepramine, imipramine, or clomipramine) N.B. avoid in elderly GREEN
- Bupropion A SC
- SSRI or SNRI plus bupropion A SC
- Add liothyronine RED

When considering treatments for people with depression:

- carry out an assessment of need
- develop a treatment plan, taking into account any previous treatment history
- take into account any physical health problems and any coexisting mental health problems
- discuss what factors would make the person most likely to engage with treatment
- address any barriers to the delivery of treatments because of any disabilities, language or communication difficulties
- ensure regular liaison between healthcare professionals in specialist / non-specialist settings if the person is receiving specialist support or treatment.
- depression questionnaires can be helpful in detecting depression and in assessing severity but should not be used in isolation

For assessment and treatment options, refer to the appropriate guideline(s)

For depression in adults, see [NICE guidance for the treatment and management of depression in adults](#) and for depression in children and young people, see [NICE guidance for the identification and management of depression in children and young people](#). For people with depression who also have learning disabilities, see [NICE guideline on mental health problems in people with learning disabilities](#). For people with depression who also have autism, see [NICE guideline on autism spectrum disorder](#). For people with depression in pregnancy or the postnatal period, or who are breastfeeding, see [NICE guideline on antenatal and postnatal mental health](#). For people with depression who are menopausal, see [NICE guideline on menopause](#). For people with depression and physical health problems, see [NICE guideline on depression in adults with a chronic physical health problem](#). and the recommendations on collaborative care in the full guideline. For people with stressful or traumatic life events see [NICE guideline on post-traumatic stress disorder](#). If a person with depression is assessed to be at risk of suicide, see [NICE guideline on self-harm and recommendations on antidepressant medication for people at risk of suicide](#). For people with depression who also have dementia, see the [section on depression and anxiety in the NICE guideline on dementia](#). For people with depression and a diagnosis of personality disorder, see [NICE guideline on borderline personality disorder](#). For people with depression with psychotic symptoms see [visual summary on treatment of psychotic depression](#).