NICE National Institute for Health and Care Excellence

NICE Pathways

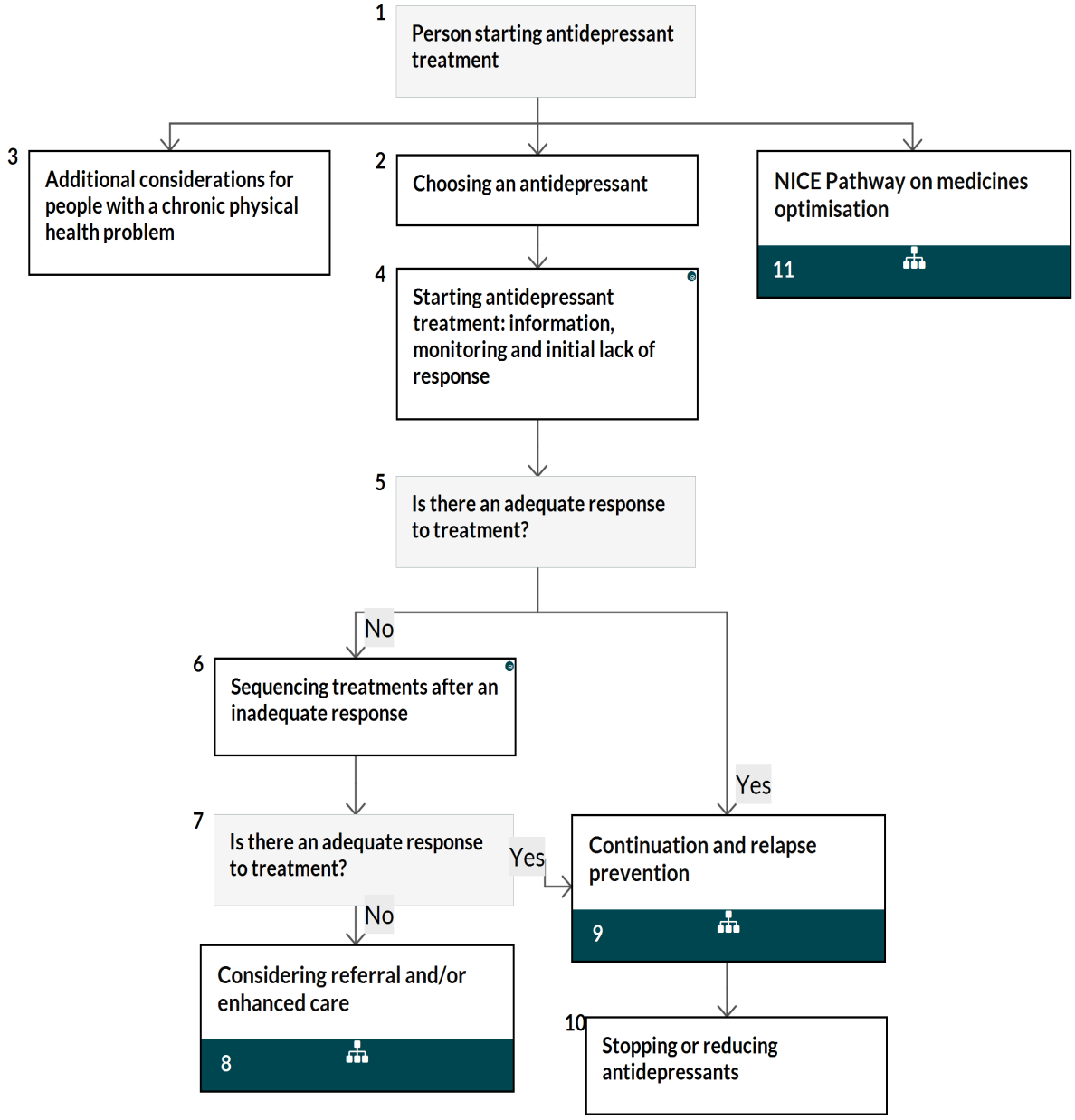
Antidepressant treatment in adults

NICE Pathways bring together everything NICE says on a topic in an interactive flowchart. NICE Pathways are interactive and designed to be used online.

They are updated regularly as new NICE guidance is published. To view the latest version of this NICE Pathway see:

http://pathways.nice.org.uk/pathways/depression
NICE Pathway last updated: 10 September 2020

This document contains a single flowchart and uses numbering to link the boxes to the associated recommendations.



1 Person starting antidepressant treatment

No additional information

2 Choosing an antidepressant

For additional considerations on using antidepressants and other medications (including the assessment of the relative risks and benefits) for women who may become pregnant, please refer to the BNF and individual drug summary of product characteristics. For women in the antenatal and postnatal periods, see also the NICE Pathway on pharmacological treatments for antenatal and postnatal mental health problems.

Discuss choice of antidepressant, covering:

- anticipated adverse events – for example, side effects and discontinuation symptoms (see stopping or reducing antidepressants [See page 10]).
- potential interactions with concomitant medication or physical illness
- the person's perception of the efficacy and tolerability of any antidepressants they have previously taken.

Normally choose an SSRI in generic form. Take the following into account:

- SSRIs are associated with an increased risk of bleeding. Consider prescribing a gastroprotective drug in older people who are taking NSAIDs or aspirin.
- Fluoxetine, fluvoxamine and paroxetine have a higher propensity for drug interactions.
- For people who also have a chronic physical health problem, consider using citalopram or sertraline as these have a lower propensity for interactions.
- Paroxetine is associated with a higher incidence of discontinuation symptoms.

Take into account toxicity in overdose for people at significant risk of suicide. Be aware that:

- compared with other equally effective antidepressants recommended in primary care, venlafaxine is associated with a greater risk of death from overdose
- the greatest risk in overdose is with TCAs, except for lofepramine.

When prescribing drugs other than SSRIs, take into account:

- the increased likelihood of the person stopping treatment because of side effects, and the consequent need to increase the dose gradually, with venlafaxine, duloxetine and TCAs

- the specific cautions, contraindications and monitoring requirements for some drugs
- that non-reversible MAOIs, such as phenelzine, combined antidepressants and lithium augmentation of antidepressants should normally be prescribed only by specialist mental health professionals (for more information see sequencing treatments [See page 7]).
- that dosulepin should not be prescribed.

When prescribing antidepressants for older adults:

- prescribe at an age-appropriate dose taking into account physical health and concomitant medication
- monitor carefully for side effects.

Agomelatine

The appraisal of agomelatine for the treatment of major depressive episodes (NICE technology appraisal 231) was terminated because no evidence submission was received from the manufacturer or sponsor of the technology. Therefore NICE is **unable to make a recommendation** about the use in the NHS of agomelatine for the treatment of major depressive episodes.

3 Additional considerations for people with a chronic physical health problem

When prescribing antidepressants, be aware of drug interactions and seek specialist advice if uncertain. If needed, refer the person to specialist mental health services for continued prescribing.

Do not prescribe subtherapeutic doses of antidepressants.

Take into account:

- additional physical health problems
- side effects of antidepressants that may impact on the underlying physical disease
- that there is currently no evidence to support using specific antidepressants for particular physical health problems.

Interactions of SSRIs with other medications

Medication for chronic physical health problem	Recommended antidepressant(s)
NSAIDs	• **Do not normally offer** SSRIs – but if no suitable alternatives can be identified, offer gastroprotective medicines (for example, proton pump inhibitors) together with the SSRI • Consider mianserin, mirtazapine, moclobemide, reboxetine or trazodone
Warfarin or heparin	• **Do not normally offer** SSRIs • Consider mirtazapine (note that when taken with warfarin, the international normalised ratio [INR] may increase slightly)
Aspirin	• Use SSRIs with caution – if no suitable alternatives can be identified, offer gastroprotective medicines together with the SSRI • Consider trazodone, mianserin or reboxetine when aspirin is used as a single agent • Consider mirtazapine
'Triptan' drugs for migraine	• **Do not offer** SSRIs • Offer mirtazapine, trazodone, mianserin or reboxetine
Monoamine oxidase B inhibitors (for example, selegiline and rasagiline)	• **Do not normally offer** SSRIs • Offer mirtazapine, trazodone, mianserin or reboxetine
Theophylline, clozapine, methadone or tizamidine	• **Do not normally offer** fluvoxamine • Offer sertraline or citalopram
Flecainide or propafenone	• Offer sertraline as the preferred antidepressant • Mirtazapine and moclobemide may also be used

Atomoxetine	• **Do not offer** fluoxetine or paroxetine • Offer a different SSRI

[1]

4 Starting antidepressant treatment: information, monitoring and initial lack of response

Information

Explore any concerns the person has about taking medication and provide information, including:

- the gradual development of the full antidepressant effect
- the importance of taking medication as prescribed and the need to continue beyond remission
- potential side effects and drug interactions
- the risk and nature of discontinuation symptoms (particularly with drugs with a shorter half-life, such as paroxetine and venlafaxine)
- the fact that addiction does not occur.

Monitoring

For people who are not considered to be at increased risk of suicide, normally see them after 2 weeks. See them regularly, for example every 2 to 4 weeks in the first 3 months, and then at longer intervals if response is good.

For people who are considered to be at increased risk of suicide or are younger than 30 years, normally see them after 1 week and then frequently until the risk is no longer clinically important.

If a person experiences side effects early in treatment, provide information and consider:

- monitoring symptoms closely if side effects are mild and acceptable to the person **or**
- stopping or changing to a different antidepressant if the person prefers **or**
- short-term concomitant treatment (usually no longer than 2 weeks) with a benzodiazepine if anxiety, agitation and/or insomnia are problematic, except in people with chronic symptoms of anxiety; use with caution in people at risk of falls.

[1] Refer to appendix 1 of the BNF and appendix 16 of depression in adults with a chronic physical health problem

People who start on low-dose TCAs and have a clear clinical response can be maintained on that dose with careful monitoring.

Initial lack of response

If improvement is not occurring on the first antidepressant after 2 to 4 weeks, check that the drug has been taken as prescribed.

If response is absent or minimal after 3 to 4 weeks of treatment with a therapeutic dose of an antidepressant, increase support and consider:

- increasing the dose in line with the summary of product characteristics (SPC) if there are no significant side effects **or**
- switching to another antidepressant if there are side effects or if the person prefers.

If there is some improvement by 4 weeks, continue treatment for another 2 to 4 weeks. Consider switching antidepressants if:

- response is still not adequate **or**
- there are side effects **or**
- the person prefers to change drug.

Quality standards

The following quality statements are relevant to this part of the interactive flowchart.

Depression in adults

11. Reassessing people prescribed antidepressants

12. Lack of response to initial treatment within 6 to 8 weeks

5 Is there an adequate response to treatment?

No additional information

6 Sequencing treatments after an inadequate response

Also see information on combining psychological and drug treatment.

Switching and combining antidepressants

When reviewing treatment after an inadequate response to initial pharmacological interventions:

- check adherence to, and side effects from, initial treatment
- increase the frequency of appointments
- be aware that using a single antidepressant is usually associated with a lower side-effect burden
- consider reintroducing treatments that have been inadequately delivered or adhered to, including increasing the dose or switching antidepressants.

When switching antidepressants, consider:

- initially, a different SSRI or a better-tolerated newer-generation antidepressant
- subsequently, an antidepressant of a different class that may be less well tolerated (such as venlafaxine, a TCA or an MAOI).

Do not switch to, or start, dosulepin.

Normally switch within 1 week for drugs with a short half-life. Consider interactions and exercise caution when switching:

- from fluoxetine to other antidepressants
- from fluoxetine or paroxetine to a TCA; use a lower starting dose of the TCA (particularly when switching from fluoxetine)
- to a new serotonergic antidepressant or MAOI (features include confusion, delirium, shivering, sweating, changes in blood pressure and myoclonus)
- from a non-reversible MAOI: a 2-week washout period is required (**do not routinely prescribe** other antidepressants during this period).

Do not normally combine antidepressants in primary care without consulting a consultant psychiatrist. Also:

- select medications that are safe to use together – be aware of the increased side-effect burden
- document and discuss the rationale with the person, inform them if off-label medication is offered, and monitor for adverse effects
- ensure familiarity with the primary evidence and consider obtaining a second opinion if the combination is unusual, the evidence for the efficacy of a chosen strategy is limited or the risk-benefit ratio is unclear.

Vortioxetine

The following recommendations are from NICE technology appraisal guidance on vortioxetine for treating major depressive episodes.

Vortioxetine is recommended as an option for treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode.

People whose treatment with vortioxetine is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

NICE has written information for the public explaining its guidance on vortioxetine.

Augmenting antidepressants

If a person is informed about and prepared to tolerate the increased side-effect burden, consider augmenting an antidepressant with:

- lithium
- an antipsychotic such as aripiprazole, olanzapine, quetiapine or risperidone
- another antidepressant, such as mianserin or mirtazapine.

In October 2009, this was an off-label use of aripiprazole, olanzapine, quetiapine and risperidone. See prescribing medicines at NICE website.

When prescribing lithium:

- monitor renal and thyroid function before treatment and every 6 months during treatment (more often if there is evidence of renal impairment)
- consider ECG monitoring in people at high risk of cardiovascular disease
- monitor serum lithium levels 1 week after treatment starts and every dose change, and then every 3 months.

When prescribing an antipsychotic, monitor weight, lipid and glucose levels, and relevant side effects.

Do not routinely augment an antidepressant with:

- a benzodiazepine for more than 2 weeks as there is a risk of dependence
- buspirone, carbamazepine, lamotrigine or valproate as there is insufficient evidence for their

- use (valproate must not be used in women or girls of childbearing potential, including young girls who are likely to need treatment into their childbearing years; see the MHRA safety advice on risks of using valproate during pregnancy)
- pindolol or thyroid hormones as there is inconsistent evidence of effectiveness.

In October 2009, this was an off-label use of buspirone, carbamazepine, lamotrigine, valproate, pindolol, and thyroid hormones. See prescribing medicines at NICE website.

Quality standards

The following quality statement is relevant to this part of the interactive flowchart.

Depression in adults

12. Lack of response to initial treatment within 6 to 8 weeks

7 Is there an adequate response to treatment?

No additional information

8 Considering referral and/or enhanced care

See Depression / Step 3: Persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial interventions, and moderate and severe depression in adults / enhanced care

9 Continuation and relapse prevention

See Depression / Continuation and relapse prevention for adults with depression

10 Stopping or reducing antidepressants

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

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

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

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

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

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

- monitor symptoms and reassure the person if symptoms are mild
- consider reintroducing the original antidepressant at the dose that was effective (or another antidepressant with a longer half-life from the same class) if symptoms are severe, and reduce the dose gradually while monitoring symptoms.

11 NICE Pathway on medicines optimisation

See medicines optimisation

Glossary

MAOI

monoamine oxidase inhibitor

NSAID

non-steroidal anti-inflammatory drug

SSRI

selective serotonin reuptake inhibitor

TCA

tricyclic antidepressant

Sources

Depression in adults with a chronic physical health problem: recognition and management (2009) NICE guideline CG91

Depression in adults: recognition and management (2009) NICE guideline CG90

Vortioxetine for treating major depressive episodes (2015) NICE technology appraisal guidance 367

Agomelatine for the treatment of major depressive episodes (terminated appraisal) (2011) NICE technology appraisal 231

Your responsibility

Guidelines

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and

practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Technology appraisals

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take these recommendations fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this interactive flowchart is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Commissioners and/or providers have a responsibility to provide the funding required to enable the recommendations to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Medical technologies guidance, diagnostics guidance and interventional procedures guidance

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take these recommendations fully into account. However, the interactive flowchart does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Commissioners and/or providers have a responsibility to implement the recommendations, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this interactive flowchart should be interpreted in a way that would be inconsistent with compliance with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.