NICE National Institute for Health and Care Excellence

Royal College of Physicians

NICE guideline

Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults

NICE guideline
Published: 20 April 2022

www.nice.org.uk/guidance/ng215

Your responsibility

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.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

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.

Contents

This guideline is the basis of QS8.

Overview

This guideline covers general principles for prescribing and managing withdrawal from opioids, benzodiazepines, gabapentinoids, Z-drugs and antidepressants in primary and secondary care.

It does not cover gabapentinoids prescribed for epilepsy, nor opioids prescribed for acute or cancer pain, or at the end of life, nor management of illicit drug dependence.

Who is it for?

- Healthcare professionals
- Commissioners of NHS and local authority services
- People using services, their families and carers, and the public

This guideline was commissioned by NICE and developed at the National Guideline Centre, which is hosted by the Royal College of Physicians.

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Supporting people taking a dependence-forming medicine or antidepressant

1.1.1 Aim to foster collaborative, trusting and supportive relationships with people considering taking, and at all stages of prescribing and withdrawal management of, an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant. Follow the recommendations in the NICE guideline on patient experience in adult NHS services, particularly those relating to:

- continuity of care and relationships
- enabling patients to actively participate in their care
- tailoring healthcare services to each person.

1.1.2 Ask people whether they would like to have support during appointments from a family member, carer, advocate or other person close to them.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on supporting people taking a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review A: patient information and support.

1.2 Making decisions about prescribing and taking a dependence-forming medicine or antidepressant

1.2.1 Before starting or continuing treatment with an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant, ensure that all suitable management options, including non-pharmacological approaches and watchful waiting, have been discussed with and offered to the person.

1.2.2 When making decisions about prescribing medicines, determine whether there are any factors that might increase the person's risk of developing problems associated with dependence, but do not withhold the medicine solely on the basis of one of these factors. Explain and discuss the risk with the person. Factors that might increase risk include:

- a comorbid mental health diagnosis
- a history of drug or alcohol misuse
- not having a clear, defined diagnosis to support the prescription
- taking an opioid together with a benzodiazepine.

1.2.3 During the first discussion about prescribing, give the person information and advice (in their preferred format) to help them balance the potential benefit of the medicine and other treatment options with the risk of long-term consequences. Use the NICE guidelines on shared decision making and decision making and mental capacity to support people when making decisions.

1.2.4 Recognise and acknowledge that decisions about medicines can be difficult for a

person who is in distress.

1.2.5 Acknowledge that these decisions are also difficult for the prescriber particularly when supporting a person who is distressed, and in the presence of risk factors for developing problems associated with dependence, and that additional time may be required to consider options and consult with colleagues.

1.2.6 Consider delaying prescribing if the person needs more time to think about their options or the prescriber needs to consult with other members of the healthcare team. If prescribing is delayed, ensure that a follow-up appointment is arranged.

1.2.7 If a prescriber thinks that a medicine is not in the person's best interests but a shared decision about starting or continuing a medicine cannot be reached with the person, the prescriber should follow the advice on 'handling patient requests for medicines you don't think will benefit them' in the General Medical Council guidance: good practice in prescribing and managing medicines and devices. The prescriber should:

- not prescribe a medicine if they believe it is not in the person's best interests
- explain the reasons for their decision to the person
- document all discussions carefully and give a copy to the person
- offer the person a second opinion.

1.2.8 For people who find it difficult to communicate their symptoms, for example people with a learning disability or cognitive impairment:

- explore a range of methods to understand the person's symptoms, including discussion with family members, carers or an advocate if appropriate
- make necessary reasonable adjustments, for example increasing the appointment length, using short clear sentences or alternative methods of communication and visual aids during consultations, to help the person understand their options for treatment and the associated risks and benefits of each, and to express their view
- ensure that family members or carers are aware of the properties of any medicine prescribed, if appropriate.

For more information, see the NICE guidelines on shared decision making, care and support of people growing older with learning disabilities and dementia.

1.2.9 Ensure that people with a learning disability or mental health problem have had a full assessment before prescribing a dependence-forming medicine or antidepressant, to ensure that they do not have other unmet needs and that prescribing is the appropriate option. Consider involving the relevant specialist teams.

For more information, see the NICE guideline on challenging behaviour and learning disabilities.

1.2.10 Prescribers must understand and take into account the principles set out in the Mental Capacity Act 2005 when working with individuals who may lack capacity to make decisions.

For more information, see the NICE guideline on decision making and mental capacity.

1.2.11 Prescribers should use the Royal Pharmaceutical Society's Competency framework for all prescribers to support safe and effective prescribing and improve prescribing practice.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on making decisions about prescribing and taking a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in:

- evidence review A: patient information and support
- evidence review B: prescribing strategies
- evidence review E: risk factors.

1.3 Starting a dependence-forming medicine or antidepressant

Information and support for people starting a medicine

See the Medicines and Healthcare products Regulatory Agency's (MHRA's) safety advice on improving information supplied with gabapentinoids (pregabalin/gabapentin), benzodiazepines and Z-drugs and opioids: risk of dependence and addiction, including for details of discussions to have with people before starting these medicines. See also the MHRA's patient leaflets on the risks of addiction, dependence and withdrawal when using benzodiazepines, gabapentinoids and Z-drugs.

1.3.1 Before starting treatment with an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant, give the person verbal and written information (in their preferred format) about the medicine. Ensure that the information is evidence-based and understandable by the person. Explain to the person:

- the potential side effects of the medicine, whether these are likely to be temporary or permanent and whether they might improve or worsen over time
- any additional implications of taking the medicine if the person is pregnant or planning pregnancy
- what the options might be if the medicine does not work
- how difficult it might be to stop the medicine later and how that might be managed (see the section on withdrawing a dependence-forming medicine or antidepressant)
- that missing doses may lead to symptoms of withdrawal
- how to store medicines safely (for more information, see the NICE guideline on controlled drugs).

1.3.2 Before starting treatment with an opioid, benzodiazepine, gabapentinoid or Z-drug, explain and discuss with the person:

- that dependence is an expected effect of these medicines and is not a reason in itself to avoid the medicine
- the potential for developing problems associated with dependence
- the symptoms that suggest the development of problems associated with dependence and, if appropriate, the importance of making family members, carers or other people close to them aware of these symptoms.

1.3.3 Before starting treatment with an antidepressant or gabapentinoid, explain and discuss with the person:

- that any beneficial effect of the medicine may occur slowly, and they might experience side effects before noticing any benefit
- that many side effects are likely to ease over time.

1.3.4 Consider supplementing verbal and written information with details of peer support networks or online forums suitable for the person.

Management planning

1.3.5 Discuss and agree a management plan with the person. Document the plan in the person's medical record and give them a copy in their preferred format. Include:

- what the medicine has been prescribed for, the intended outcomes of treatment and how these might be assessed
- the starting dose and intervals between dose adjustments or titrations
- who to contact if problems occur
- information about how long the medicine will take to work and how long they might be taking it for
- the duration of each prescription that will be issued
- the risks of taking more than the prescribed dose

- the symptoms and signs of an overdose and what they should do if this happens
- the plans for reviewing the medicine (including where and by whom this will be done) and the date of their next review.

1.3.6 Think about a strategy for regular reviews and include these in the management plan. Use regular reviews to:

- ensure that the benefits of the medicine continue to outweigh the potential harms
- check whether the dose needs to be adjusted and, if so, how to do this safely.

Prescribing strategies

1.3.7 Take steps to reduce the risk of developing problems associated with dependence, for example starting at a low dose, and consider avoiding modified-release opioids. Explain the importance of these steps to the person.

1.3.8 Discuss with the person the range of doses likely to be safe and effective. Start with a low dose and agree frequent, regular reviews to ensure that timely adjustments can be made to test effectiveness, safety and acceptability and to find the lowest effective dose. Once an effective dose has been established, avoid automatically increasing the dose if the response is not sustained.

1.3.9 If the person's individual circumstances or the setting (for example, a secure setting) mean that usual prescribing practices are not suitable, adjust the prescription to ensure that:

- the medicine can be administered safely as part of the setting's routine
- the medicine does not pose a risk to the person or to others living in that setting.

For more information, see the NICE guideline on physical health of people in

prison.

1.3.10 The duration of each individual prescription:

- should reflect the management plan (see recommendation 1.3.5)
- should comply with best practice in controlled drugs prescribing
- must comply with relevant legislation (for more information, see the NICE guideline on controlled drugs).

Working with other healthcare professionals

1.3.11 When starting a prescription suggested by another healthcare professional, taking over a person's care, or deciding whether to continue a prescription made by another healthcare professional:

- take the same level of care you would take if you were starting the prescription
- follow the section on supporting people taking a dependence-forming medicine or antidepressant to help establish the new relationship
- ensure that you have sufficient knowledge of the person's health and preferences to determine whether continued prescribing is in their best interests or whether careful withdrawal (in discussion with the person) would be more beneficial for them.

1.3.12 Healthcare professionals in secondary care who recommend a dependence-forming medicine or antidepressant to be started or continued in primary care should explain to the person that:

- the medicine will be prescribed by their primary care team
- the primary care team will need to review the medicine
- if the primary care team declines to prescribe the medicine, or wishes to delay it, the secondary and primary care teams will discuss the medicine and involve the person in these discussions, explaining the reasons for any delay

- the secondary care team might not continue to manage and provide the medicine if this is agreed after discussions.

1.3.13 When transferring responsibility for prescribing from secondary to primary care, ensure that all relevant healthcare professionals have access to the management plan in the person's medical record.

1.3.14 If possible, ensure that 1 person has overall responsibility for a prescription. If the initial prescriber is unable to review the medicine, ensure there are arrangements for review by another healthcare professional and that effective communication, including sharing the person's records and management plan as needed, is in place to support this.

Pharmacists working in primary care may play a key role in supporting prescribing. See the section on medication review in the NICE guideline on medicines optimisation.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on starting a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in:

- evidence review A: patient information and support
- evidence review B: prescribing strategies
- evidence review E: risk factors
- evidence review F: monitoring.

1.4 Reviewing a dependence-forming medicine or antidepressant

Frequency of reviews

1.4.1 Offer regular reviews (by phone, video or face to face) to people taking an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant. Base the frequency of reviews on:

- the person's preferences and circumstances
- the type of medicine they are taking and the dose
- factors that might indicate a need for frequent reviews, for example if:
  - the person has additional care needs (such as people with a learning disability or cognitive impairment)
  - the person is taking the medicine for the first time
  - there are potential adverse effects or problems associated with dependence
  - the medicine is being used outside its licensed indications
  - there is potential for misuse of the medicine.

  For more information on antidepressants, see the NICE guidelines on depression in adults and depression in adults with a chronic physical health problem.

1.4.2 Consider increasing the frequency of reviews during dose adjustment. Take into account the person's clinical and support needs when agreeing review frequency.

1.4.3 Offer extra, unscheduled reviews when needed, for example if the person:

- reports adverse effects from the medicine
- becomes pregnant or is planning pregnancy

- has a change in their physical or mental health condition, or social circumstances
- starts taking medicines from a different prescriber
- requests a change in dose.

1.4.4 For guidance on reviewing medicines, see the section on medication review in the NICE guideline on medicines optimisation and the section on reviewing medicines in the NICE guideline on medicines adherence.

Content of reviews

1.4.5 During the review, discuss with the person the benefits and risks of continuing the current dose, adjusting the dose or stopping the medicine. Base decisions on this discussion, taking into account, for example:

- the benefits or harms the person is experiencing from continuing the medicine
- any signs that the person is developing problems associated with dependence (such as running out of a medicine early, making frequent requests for dose increases or reporting loss of efficacy of a medicine that was previously working well)
- the person's preferences.

1.4.6 Agree and update the management plan with the person after each review, and give them a copy (see recommendation 1.3.5). Check that they know who to contact if they have problems or concerns.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on reviewing a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review F: monitoring.

1.5 Withdrawing a dependence-forming medicine or antidepressant

Making shared decisions about withdrawing medicines

1.5.1 Discuss withdrawing an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant with the person if:

- it is no longer benefiting the person
- problems associated with dependence have developed
- the condition for which the medicine was prescribed has resolved
- the harms of the medicine outweigh the benefits
- the person wants to stop taking the medicine.

1.5.2 Explain the benefits the person can expect from reducing the medicine and aim to reach agreement using a shared decision-making approach. Allow enough time to explore the person's circumstances and preferences.

1.5.3 Understand that the person might be reluctant or anxious about discussing problems associated with dependence. Reassure them that dependence is an expected effect of these medicines and that problems associated with dependence sometimes develop. Be sensitive to the use of terminology that may apportion blame to the person or be perceived adversely.

1.5.4 Acknowledge and discuss with the person any differences between their views and your own about the risks and benefits of the medicine.

1.5.5 Be prepared for queries about prescribing decisions made previously. Explain that our understanding of the balance of risks and benefits of a medicine can change over time. If sufficient clinical detail is available, discuss the possibility that past prescribing was done in the person's best interests using the knowledge available at the time.

1.5.6 Do not stop a medicine abruptly (complete cessation with immediate effect)

unless there are exceptional medical circumstances, such as the occurrence of serious side effects (for example, upper gastrointestinal bleeding from an antidepressant, respiratory depression from an opioid or severe ataxia from a gabapentinoid). In these circumstances, consider:

- scheduling more frequent reviews
- short-term use of medicines to treat the physical symptoms of withdrawal (for example, abdominal cramps and diarrhoea during withdrawal of an opioid).

1.5.7 When planning withdrawal from an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant, take into account:

- the urgency of the withdrawal, for example gradual withdrawal of a medicine that is no longer effective or necessary, or more rapid withdrawal of a medicine that is causing significant harm (the speed of rapid withdrawal depends on the type of medicine and the person's circumstances, see recommendation 1.5.6)
- whether the initial goal should be complete withdrawal or, for people who find complete withdrawal too difficult, whether dose reduction with ongoing review is a more realistic initial aim
- which medicine to reduce first, if the person will be withdrawing from more than 1 medicine
- factors that might increase the person's risk of problems during withdrawal, including:
  - long duration of medicine use
  - high dose of medicine
  - history of withdrawal symptoms
  - history of problems associated with dependence
  - taking an antidepressant with a short half-life
- any concurrent medicines and how these might affect the person's response

to withdrawal

- factors that might influence the timing of the start of the dose reduction, such as the person's circumstances and available support.

Information and support for people withdrawing from a medicine

1.5.8 Before starting withdrawal:

- give the person information about the process of withdrawal that is tailored to their situation and the medicine they are taking
- explain how the withdrawal will be carried out
- consider providing details of sources of peer support, national and local support groups for people who are withdrawing from a medicine.

1.5.9 Discuss withdrawal symptoms with the person and tell them about the support that is available. When discussing withdrawal symptoms, explain that:

- withdrawal can be difficult, and may take several months or more
- support will be available throughout the withdrawal process
- withdrawal symptoms do not affect everyone, and it is not possible to predict who will be affected
- withdrawal symptoms vary widely in type and severity, can affect both physical and mental health, may occur at any time during withdrawal or be delayed in onset and can change over time or persist over a prolonged period
- there are options for managing withdrawal symptoms (see the section on identifying and managing withdrawal symptoms and the section on interventions to support withdrawal)
- some people may experience withdrawal symptoms that can be difficult to distinguish from a re-emergence of their original symptoms or a new disorder, and it is important to discuss these with a healthcare professional if they occur (see recommendation 1.5.17).

Dose reduction

1.5.10 When agreeing a dose reduction schedule with the person:

- explain the risk of abrupt discontinuation and that the rate of safe withdrawal varies between people and can vary over time for the same person
- balance the risk of adverse events from continued exposure to the medicine with minimising the risk of withdrawal symptoms by slow dose reduction and withdrawal
- ensure that the planned rate of reduction is acceptable to the person
- explain that although withdrawal symptoms are to be expected, the reduction schedule can be modified to allow intolerable withdrawal symptoms to improve before making the next reduction
- consider giving the person additional control over the process of dose reduction (for example, by issuing their usual daily dose in a form that allows them to reduce the amount in small decrements at a pace of their choosing, rather than issuing successive prescriptions for reduced daily doses)
- agree regular intervals for reviewing and adjusting the reduction schedule as needed
- ensure the person knows who to contact if problems occur.

1.5.11 If the person is withdrawing from an opioid, benzodiazepine, Z-drug or antidepressant, suggest a slow, stepwise rate of reduction proportionate to the existing dose, so that decrements become smaller as the dose is lowered, unless clinical risk is such that rapid withdrawal is needed (see recommendation 1.5.6).

1.5.12 If the person is withdrawing from a gabapentinoid, reduce the dose by a fixed amount at each decrement, unless clinical risk is such that rapid withdrawal is needed (see recommendation 1.5.6).

1.5.13 If the person is withdrawing from a benzodiazepine with a short half-life, consider switching to a benzodiazepine with a longer half-life.

1.5.14 If using a published withdrawal schedule, apply it flexibly to accommodate the

person's preferences, changes to their circumstances and the response to dose reductions.

1.5.15 During withdrawal, offer continued management of the underlying condition for which the medicine was prescribed, if needed.

1.5.16 Ensure the plan for dose reduction or withdrawal is clearly recorded in the overall management plan.

Identifying and managing withdrawal symptoms

1.5.17 Be aware that it can be difficult to distinguish between the re-emergence of underlying conditions and the emergence of withdrawal symptoms. The following may indicate withdrawal symptoms rather than symptoms of an underlying condition:

- rapid or early onset of symptoms after a dose reduction or cessation of the medicine
- symptoms of the underlying illness that the person reports as qualitatively different or more intense than before
- new symptoms that the person has not experienced before.

1.5.18 Follow recommendation 1.2.8 for people who find it difficult to communicate their symptoms, for example people with a learning disability or cognitive impairment.

1.5.19 Use clinical judgement to determine the need for further investigation to rule out new pathology.

1.5.20 If distressing symptoms occur or worsen after a dose reduction:

- determine whether they are withdrawal symptoms or a re-emergence of symptoms that were relieved by the medicine
- if the symptoms are new, think about delaying the next dose reduction, trying a smaller dose reduction or reverting to the previous dose.

Interventions to support withdrawal

1.5.21 Do not treat withdrawal symptoms with another medicine that is associated with dependence or withdrawal symptoms.

1.5.22 Do not offer sodium valproate or buspirone to aid withdrawal from a benzodiazepine.

1.5.23 Consider group cognitive behavioural therapy (CBT) when withdrawing from a benzodiazepine. Discuss the timing of referral for CBT with the person.

Strategies if withdrawal cannot be agreed or is unsuccessful

1.5.24 Follow recommendation 1.2.7 if a shared decision to withdraw cannot be reached and continuing the current prescription is not in the person's best interests. Be aware that medicines associated with dependence and withdrawal symptoms should not be stopped abruptly in most cases (see recommendation 1.5.6) and need to be reduced in line with the section on withdrawing medicines.

1.5.25 If continued use of the medicine may be particularly harmful for the person or others (for example, in a secure setting) and a dose reduction, or a more rapid reduction than the person wishes, is the safest option, consider:

- scheduling more frequent reviews
- short-term use of medicines to treat the physical symptoms of withdrawal (for example, abdominal cramps and diarrhoea during withdrawal of an opioid).

1.5.26 If dose reduction has been unsuccessful (for example because of intolerable withdrawal symptoms or a change in the person's physical, mental or social circumstances) and the current prescription needs to be continued:

- aim to stop any further escalation in dose
- make a plan to attempt dose reduction again at a later date
- clearly record the advice given to the person about the potential harms of

continuing the medicine, and the reasons for continuing without a reduction, in the management plan.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on withdrawing a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in:

- evidence review A: patient information and support
- evidence review C: safe withdrawal
- evidence review D: withdrawal symptoms.

Recommendations for research

The guideline committee has made the following recommendations for research.

Key recommendations for research

1 Multicomponent withdrawal interventions

What are the key components of an effective multicomponent intervention to support dose reduction during withdrawal of opioids?

For a short explanation of why the committee made the recommendation for research, see the rationale section on withdrawing a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review C: safe withdrawal.

2 Psychological interventions to support withdrawal

What are the most effective psychological interventions to support withdrawal and help people cope with withdrawal symptoms?

For a short explanation of why the committee made the recommendation for research, see the rationale section on withdrawing a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review C: safe withdrawal.

3 Service models for withdrawal interventions

What service models are most effective in supporting withdrawal from medicines associated with dependence and withdrawal symptoms?

For a short explanation of why the committee made the recommendation for research, see the rationale section on withdrawing a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review C: safe withdrawal.

4 Individual circumstances and the risk of dependence

Do individual circumstances such as social distress, low income or limited access to alternative sources of support lead to an increased risk of problems associated with dependence on prescribed medicines?

For a short explanation of why the committee made the recommendation for research, see the rationale section on making decisions about prescribing and taking a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review E: risk factors.

5 Information for family members or carers

What information and support are needed by family members or carers of people having treatment with an opioid, benzodiazepine, Z-drug, antidepressant or gabapentinoid?

For a short explanation of why the committee made the recommendation for research, see the rationale section on starting a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review A: patient information and support.

Other recommendations for research

6 System-level factors and the risk of dependence

Do system-level factors, such as training received by prescribers alter the risk of developing problems associated with dependence on prescribed medicines?

For a short explanation of why the committee made the recommendation for research, see the rationale section on making decisions about prescribing and taking a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review E: risk factors.

7 Converting to a medicine with a different half-life to aid withdrawal

What is the clinical and cost effectiveness of converting to medicines with a longer half-life to aid withdrawal from benzodiazepines or antidepressants?

For a short explanation of why the committee made the recommendation for research, see the rationale section on withdrawing a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review C: safe withdrawal.

8 Cognitive behavioural therapy (CBT) to support withdrawal from benzodiazepines

What is the most effective model of CBT, including timing of CBT, to support withdrawal from benzodiazepines?

For a short explanation of why the committee made the recommendation for research, see the rationale section on withdrawing a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review C: safe withdrawal.

9 Acupuncture to support withdrawal from opioids

What is the clinical and cost effectiveness of acupuncture (including electroacupuncture) as an adjunct to aid withdrawal from opioids?

For a short explanation of why the committee made the recommendation for research, see the rationale section on withdrawing a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review C: safe withdrawal.

10 Withdrawal interventions for gabapentinoids

What are the most clinically and cost-effective strategies or interventions to aid withdrawal of gabapentinoids?

For a short explanation of why the committee made the recommendation for research, see the rationale section on withdrawing a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review C: safe withdrawal.

11 Aids to support withdrawal

What is the effectiveness of equipment, technologies, practical aids and medicine formulations in supporting people to manage dose reductions, compared with usual practice?

For a short explanation of why the committee made the recommendation for research, see the rationale section on withdrawing a dependence-forming medicine or antidepressant.

Full details of the evidence and the committee's discussion are in evidence review C: safe withdrawal.

Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice.

Supporting people taking a dependence-forming medicine or antidepressant

Recommendations 1.1.1 and 1.1.2

Why the committee made the recommendations

Qualitative evidence was available from studies on opioids, benzodiazepines and antidepressants. Most of the participants were people prescribed these medicines, although some studies included prescribers (GPs, nurses and pharmacists).

The evidence highlighted that some people experience dissatisfaction with treatment and a poor relationship with healthcare professionals. The committee agreed that continuity of care, a tailored approach for each person, and the formation of good relationships are particularly important in this population. The recommendations in the NICE guideline on patient experience in adult NHS services will help to achieve this.

Evidence and the committee's experience showed that the presence of a family member, carer, advocate or other person at appointments can be helpful, especially for people who are older, or who are distressed or find it difficult to take in and remember information.

How the recommendations might affect practice

The recommendations reflect best practice but are not implemented consistently and might involve changes in practice for some providers.

Return to recommendations

Making decisions about prescribing and taking a

dependence-forming medicine or antidepressant

Recommendations 1.2.1 to 1.2.11

Why the committee made the recommendations

Evidence from qualitative studies of people taking opioids showed that they want the opportunity to discuss all management options before starting the medicine. The evidence also highlighted people's need for support when making decisions about taking prescribed medicines. The committee agreed that reaching a shared decision about a medicine is beneficial for both the prescriber and the person taking the medicine, and that the NICE guideline on shared decision making should be used to support people when making decisions.

Based on the evidence and their experience, the committee agreed that specific factors can increase a person's risk of developing problems associated with dependence. Prognostic evidence from studies of opioids and benzodiazepines demonstrated an increased risk in people diagnosed with mental health problems including depression, anxiety, post-traumatic stress disorder, bipolar disorder, alcohol-use disorder or drug-misuse disorder. The committee agreed, based on their experience, that this also applies to Z-drugs and gabapentinoids, but not to antidepressants, which are not dependence-forming medicines. They noted that a comorbid mental health diagnosis can have a profound impact on people and increase their desire for medicines, and that people with a history of drug misuse may need higher drug doses to obtain the desired effect. There was evidence indicating that, for people prescribed opioids, concurrent use of benzodiazepines increases the risk of problems associated with dependence, as does the presence of painful conditions without a clear, defined diagnosis.

The committee agreed that it is important for healthcare professionals to be mindful of these factors when making prescribing decisions, but the needs of each person should be taken into account when balancing benefits and harms, and these factors alone should not be seen as barriers to prescribing.

The committee noted other factors that were not captured by the evidence but might influence the development of problems associated with dependence, including social distress, access to alternative sources of support and system-level factors such as training or supervision of prescribers. They made a recommendation for research on individual circumstances and the risk of problems associated with dependence, and a

recommendation for research on system-level factors and the risk of problems associated with dependence.

The committee noted that, in their experience, people can often present in distress and may be focused on immediate relief of their symptoms. They also noted the pressure to prescribe that is sometimes felt by healthcare professionals and agreed that in some circumstances, it is advantageous to delay prescribing until after the first discussion about prescribing. They agreed that a short delay would not disadvantage the person and would be beneficial in allowing both the person and the healthcare professional time to reflect on the options.

The committee acknowledged that on occasion, a healthcare professional may not think that prescribing or continuing a medicine is in the person's best interests, but the person disagrees, and a shared decision cannot be reached. In this circumstance, it is the responsibility of the healthcare professional not to prescribe the medicine and to follow General Medical Council guidance.

The committee noted that there are some people with communication difficulties, for example those with a learning disability or cognitive impairment, who may have difficulties describing their symptoms, which can lead to medicines being prescribed inappropriately, or not at all. The committee agreed that, in their experience, additional consideration and support is needed to ensure prescribing decisions are made in the person's best interests, and that the person is able to share in those decisions.

How the recommendations might affect practice

The recommendations are expected to reduce the number of people who develop dependence on medicines by raising awareness of the risk factors and ensuring shared decisions are made based on fully informed discussions of the risks and benefits. This will benefit the healthcare system and improve the health of people taking these medicines.

Return to recommendations

Starting a dependence-forming medicine or antidepressant

Recommendations 1.3.1 to 1.3.14

Why the committee made the recommendations

Information and support for people starting a medicine

Evidence from study participants showed that they were often not given sufficient information about their medicine before starting treatment, particularly the risks of dependence and withdrawal symptoms. Participants also reported a lack of information about side effects, how well the medicine is expected to work, how long it will take to work and the likely duration of treatment. This evidence reflected the committee's experience. The recommendations aim to ensure that all of this information is provided before people begin treatment.

The committee also agreed that it is important to make people aware of how to safely store their medicines and included a cross reference to the NICE guideline on controlled drugs, which covers storage of medicines.

The evidence also showed discrepancies between the information people reported being given and the information their healthcare professionals reported giving them, highlighting the importance of providing both verbal and written information in the person's preferred format that they can take home for later reference.

There was no evidence on the views of family members or carers, so the committee made a recommendation for research on information for family members or carers.

Within the evidence, peer support (for example, through online forums) was identified as a valuable complement to information provided by healthcare professionals. The committee agreed with this finding and recommended that prescribers should consider supplementing information with details of peer support networks.

Management plan

Evidence and the committee's experience demonstrated the value of agreeing a management plan with the person. The plan should include practical information about the medicine, including how to take it safely, and set out when the medicine will be reviewed. The importance of giving a copy of the plan to the person was highlighted both in the evidence and the committee's experience.

The committee's experience and evidence from studies on opioids indicated that long-

term treatment is a risk factor for dependence, and that higher doses taken long term increase this risk further. Therefore, the management plan should be reviewed regularly to ensure that the dosage remains optimal, the benefits of the medicine continue to outweigh the potential harms and the medicine is not continued when it is no longer needed.

Prescribing strategies

Although the evidence was limited, the committee agreed that there was some indication that starting a medicine at a low dose may reduce the risk of problems associated with dependence and the risk of withdrawal symptoms. This was supported by evidence in the risk factor review showing a dose–response association between higher doses of opioids and incident addiction to opioids when taken long term. Evidence and the committee's experience also showed that standard-release opioids are less frequently associated with problems compared with modified-release opioids unless clinical considerations or the person's circumstances dictate otherwise. The committee noted this only applied to opioid formulations and not to the other medicines considered.

The committee agreed, based on their experience, that it is important to take particular care during dose adjustments. Although pharmacological tolerance is a property of medicines described in this guideline, if a person has an initially favourable response that then diminishes, it is rarely helpful to increase the dose to try to restore the clinical benefit. This is because such an approach increases the risk of harmful prescribing, and also because the loss of benefit is rarely due to pharmacological tolerance, but due to other factors.

In the committee's experience, there may be individual circumstances in which adjustments are needed to the prescription to ensure it is safe and practical. If it is not possible for people to hold their own medicines, in secure settings for example, twice-daily administration may be difficult.

To avoid unnecessary long-term use of a medicine, prescribers should ensure that each prescription is in line with the management plan and complies with good practice guidance and relevant legislation.

Working with other healthcare professionals

The committee based these recommendations on their experience. They agreed that standardised prescribing practice can help to ensure continuity of care.

The committee's recommendations emphasise the importance of clear communication between primary and secondary care. They also stress the importance of giving clear explanations to people about arrangements for their care across services.

The committee agreed that it is vital that a new prescriber taking over a person's care acquires sufficient knowledge about the person to determine whether the prescription should be continued, establishes a therapeutic relationship with the person and takes the same care they would if they had been the original prescriber.

Primary and secondary care prescribers should ensure that they discuss and agree medicines to be prescribed or continued in primary care, and ensure that the person is kept involved and informed about these discussions. The committee noted that this is consistent with NHS England's guidance on responsibility for prescribing between primary and secondary/tertiary care (2018).

The committee recognised the difficulties involved in achieving and maintaining continuity of care and communication across settings, and agreed that it is helpful to have 1 prescriber take overall responsibility for a person's prescribing. It was noted that pharmacists may play an important role here.

How the recommendations might affect practice

The recommendations reflect best practice, but there are variations in their implementation, and they may involve a change of practice for some providers. Longer consultations or additional follow up may be needed to allow for full discussion of treatments and treatment options when starting or reviewing a medicine. However, enabling effective conversations about risks and benefits could reduce unnecessary prescribing, which would have large health benefits for the person and economic benefits for the healthcare service, for example, by preventing unplanned hospital admissions from harms caused by the medicines and reducing the need for additional healthcare support for people with dependence.

Return to recommendations

Reviewing a dependence-forming medicine or antidepressant

Recommendations 1.4.1 to 1.4.6

Why the committee made the recommendations

Frequency of reviews

There was no evidence on the frequency of reviews, so the committee based the recommendations on their experience. They agreed that prescribing is an ongoing process that should be monitored with regular reviews. The frequency of these reviews should be tailored to the person, the medicine they are taking and the presence of any risk factors. They could be held by phone, video or face to face. The committee also agreed that the frequency of reviews could be increased during dose adjustments, to ensure safety and early identification of any withdrawal symptoms.

Content of reviews

Evidence and the committee's experience highlighted the importance of weighing up the benefits and risks of continuing or stopping the medicine as part of each review, and of updating the management plan after every review.

How the recommendations might affect practice

Tailored review schedules should reduce unnecessary appointment time and increase the efficiency of treatment monitoring. Although the frequency of reviews may be increased for some people, the cost is expected to be mitigated by the current move to online, phone and video consultations. Moreover, upfront costs of more frequent tailored reviews could be offset by downstream savings such as reducing the number of people needing help from addiction services and reducing the number of medicines being prescribed, with potential health benefits because of fewer adverse events and less clinical harm caused by prescribed medicines.

Return to recommendations

Withdrawing a dependence-forming medicine or antidepressant

Recommendations 1.5.1 to 1.5.26

Why the committee made the recommendations

Making shared decisions about withdrawing medicines

The committee agreed that withdrawal should be considered when a medicine is no longer beneficial, the harms outweigh the benefits, or the person would like to withdraw. A small amount of evidence indicated that including the benefits of withdrawal and information about the process in discussions with the person can increase the likelihood that their withdrawal will be successful.

Qualitative evidence highlighted that people can be reluctant or anxious about discussing dependence and report feelings of fear, worry or anxiety surrounding discontinuation. The committee agreed that, in their experience, this can be addressed by explaining that dependence is an expected effect of the medicine, and some people experience problems associated with dependence. They also agreed it was important to avoid using language that ascribes blame to the person. The committee also thought it important to acknowledge and discuss differences of opinion and to be prepared for queries about the reasons for past prescribing.

Evidence from studies on benzodiazepines and antidepressants showed that a gradual, stepwise dose reduction is more beneficial than abrupt discontinuation. The committee agreed that this evidence can be extrapolated to opioids, Z-drugs and gabapentinoids, and that none of these medicines should be stopped abruptly. However, the committee acknowledged clinical experience of exceptional circumstances in which stopping treatment abruptly might be necessary, for example if a serious side effect has occurred. In their experience, this would usually be done within a hospital setting.

Based on their experience, the committee agreed that individual factors can affect the withdrawal process and should be taken into account when planning withdrawal. The plan for withdrawal should also take into account the urgency of withdrawal.

Information and support for people withdrawing from a medicine

Based on both the qualitative evidence and their experience, the committee agreed that the provision of information and support is vital for people withdrawing from a medicine. Knowing what to expect, and having reassurance that they will have support and help with managing withdrawal symptoms, will increase the likelihood of a successful withdrawal. There was some qualitative evidence, reflected in the committee's experience, that support groups can be beneficial for people during the withdrawal process.

Dose reduction

The evidence comparing different speeds of dose reduction was inconclusive and the committee agreed that most of the studies did not reflect clinical practice. The committee are aware there are different terms used to describe reduction schedules. Based on their experience, they agreed that flexibility in schedules is needed, and tolerability is the most important factor to take into account when deciding the speed of dose reduction, and therefore a descriptive schedule incorporating these factors should be recommended. Although tolerability varies across individuals, most people find a stepwise, decremental dose reduction process tolerable and effective. With opioids, benzodiazepines, Z-drugs and antidepressants, a rate of reduction proportionate to the existing dose is suggested. For gabapentinoids, the dose can be reduced by a fixed amount at each decrement, with the amount of reduction tailored to the person.

In the committee's experience, people who have some control over their own dose reduction schedule often have a more successful withdrawal than those whose schedule is decided for them. The committee also agreed that a flexible reduction schedule that is regularly reviewed and revised when needed is an important contributor to a successful outcome.

The committee noted that there was evidence for converting treatment from lorazepam to diazepam before withdrawal. This is because diazepam has a longer half-life and is therefore considered to allow better management of the pace of reduction, and potentially reduce withdrawal symptoms. Withdrawing from a short-acting benzodiazepine such as lorazepam can be difficult because withdrawal symptoms can occur very quickly. The committee agreed that switching to a benzodiazepine with a longer half-life is common practice and can be considered for people withdrawing from a benzodiazepine. Despite being common practice, there is a lack of evidence to support conversion to a preparation with a longer half-life, so the committee made a recommendation for research on converting to a medicine with a different half-life to aid withdrawal. The committee agreed

this recommendation for research should also apply to antidepressants.

Identifying and managing withdrawal symptoms

The committee recognised that it can be difficult to differentiate withdrawal symptoms from symptoms of a new or existing underlying condition. They agreed that withdrawal symptoms are often characterised by rapid onset after the dose of a medicine is reduced or the medicine is stopped, or there are qualitative differences from previous symptoms of the underlying illness, or there are new symptoms that have not previously occurred.

The committee agreed that if symptoms occur or worsen after a dose reduction, it is important to try to determine whether they are withdrawal symptoms or a re-emergence of symptoms of the original condition. If they are likely to be withdrawal symptoms, the committee agreed that the next dose reduction may need to be delayed, or the person may need to revert to the previous dose.

The evidence did not inform of the frequency or prevalence of symptoms, and the committee agreed that withdrawal symptoms could vary widely between individuals in terms of which symptoms were experienced, but also in terms of their intensity and duration. The committee also agreed that, based on the current evidence, it would not be helpful to include a list of symptoms in the recommendation because this could be misleading and result in symptoms being overlooked if they are not on the list or wrongly implying new symptoms do not need further investigation.

Interventions to support withdrawal

There was little evidence on psychological interventions to support withdrawal or relieve withdrawal symptoms. Health economic analysis showed that group cognitive behavioural therapy (CBT) alongside dose reduction can improve discontinuation rates and quality of life for people during withdrawal from benzodiazepines and reduce costs for the NHS. There was no clear evidence on the most effective model or timing of CBT, so the committee also made a recommendation for research on CBT to support withdrawal from benzodiazepines. Evidence on other psychological interventions, or psychological interventions for other medicines, was too limited to inform recommendations, so the committee made a recommendation for research on psychological interventions to support withdrawal.

The committee agreed, based on their experience, that using another medicine associated

with dependence and withdrawal symptoms to treat withdrawal symptoms does not aid withdrawal and can lead to harms.

The evidence did not support the use of pharmacological interventions to aid withdrawal, but was very limited for most pharmacological interventions. The committee agreed that sodium valproate and buspirone taken during withdrawal from a benzodiazepine are not only ineffective but are associated with harm and should not be used.

There was some evidence that a multicomponent intervention is beneficial during withdrawal from an opioid. However, the relative effectiveness of each component was not clear, so the committee made a recommendation for research on multicomponent withdrawal interventions.

Although acupuncture is commonly used in addiction services to manage dependence on illicit opioids, and there is some evidence supporting its use to aid withdrawal from opioids, evidence on its overall effectiveness is lacking. The committee made a recommendation for research on acupuncture to support withdrawal from opioids.

There was no evidence on the effectiveness of any withdrawal strategies or interventions to aid withdrawal from a gabapentinoid, so the committee made a recommendation for research on withdrawal interventions for gabapentinoids.

The committee were aware of specific equipment, practical aids and technologies used to support withdrawal but there was no evidence on these. They made a recommendation for research on aids to support withdrawal.

The committee discussed whether different service models, such as virtual clinics or specialist pharmacy input, would be effective in helping people withdraw from medicines. No evidence was identified in these areas and the committee made a recommendation for research on service models for withdrawal interventions.

Strategies if withdrawal cannot be agreed or is unsuccessful

The committee recognised that it may not be possible to reach a shared decision with the person about withdrawal and referred to the General Medical Council guidance for advice on how to handle this. They acknowledged particular difficulties if continued use of the medicine is especially hazardous, for example in a secure setting, and recommended steps that can be taken to manage withdrawal in this situation.

The committee recognised that dose reduction may sometimes be too difficult and agreed, based on their experience, that in this circumstance the aim should be to stop any further dose escalation and to make a plan to try again later. They stressed the importance of recording the reasons for continuing the medicine and the advice given to the person in the management plan.

How the recommendations might affect practice

At present, there is limited provision of services within the NHS specifically to support withdrawal from prescribed medicines. There are some local centres that have established good practice in this area, but they are not widely available. It is expected that implementing these recommendations will increase the number of people needing specialist withdrawal services. Additional resources will be needed to increase the provision of these services by expanding existing centres or creating additional ones in areas where these services are not available. This should be balanced by savings accrued from a reduction in unplanned hospitalisations to treat adverse drug events, fewer medicines prescribed and hence fewer medicine reviews. Providing CBT to people during withdrawal from benzodiazepines would initially need additional resources, but in the long term will generate savings and improve quality of life.

Return to recommendations

Context

Medicines associated with dependence include benzodiazepines, Z-drugs (such as zopiclone and zolpidem), opioids, gabapentin and pregabalin. Antidepressants, although historically not classified as dependence-forming medicines, can nevertheless cause withdrawal symptoms when they are stopped. This guideline focuses on medicines that are usually used for conditions that are chronic, complex and difficult to treat, such as anxiety and insomnia, chronic pain including neuropathic pain, depression and generalised anxiety disorder. It also covers medicines that were initially prescribed for acute pain but continue to be prescribed over a longer term.

These medicines can provide lasting symptom management with a favourable balance of benefits and adverse effects for many people. But like all medicines, they do not work for everyone and can have negative consequences that outweigh their benefits. Even when people are not getting clinical benefit, these medicines may sometimes continue to be prescribed for various reasons, including concerns about the risk of unpleasant withdrawal symptoms or fear of worsening of the underlying condition.

Dependence is characterised by both tolerance (the need for increasing doses to maintain the same effect) and withdrawal symptoms. Dependence is a common and well described property of a number of medicines and is not in itself a contraindication to continued or new prescribing. Dependence becomes clinically important if treatment reduction or cessation is needed.

Dependence is different from addiction. Addiction also features tolerance and withdrawal but is accompanied by additional characteristics of cravings, lack of control, overuse and continued use despite harm. Addiction is also associated with problematic behaviours including unsanctioned dose escalations and seeking early prescriptions or prescriptions from multiple prescribers. There is considerable debate about these definitions and in practice the terms are often used interchangeably. This guideline uses the term 'problems associated with dependence' to refer to these behaviours; the term 'addiction' has not been used because of its potential to stigmatise.

This guideline applies to people prescribed a medicine associated with dependence and withdrawal symptoms, and is not limited to people at high risk of developing problems associated with dependence.

There is wide variation in the prescribing of medicines associated with dependence or withdrawal symptoms. People with a dependence on prescribed medicines may be reluctant to seek help from their healthcare professionals because of a perceived stigma of dependence, which they may associate with illicit drug use or alcohol misuse.

Professional and policy bodies have issued guidelines on the clinical use of medicines associated with dependence or withdrawal symptoms. However, there are few guidelines that focus on avoiding dependence and managing withdrawal from prescribed medicines. This guideline aims to meet the need for evidence-based advice in these areas. It supports safe practice in all settings in which medicines associated with dependence or withdrawal are prescribed.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the NICE topic page on medicines management.

For full details of the evidence and the guideline committee's discussions, see the evidence reviews. You can also find information about how the guideline was developed, including details of the committee.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see resources to help you put NICE guidance into practice.

Update information

Minor changes since publication

April 2026: We added links to the Medicines and Healthcare products Regulatory Agency's (MHRA's) safety advice and patients leaflets on dependence-forming medicines at the start of section 1.3.

ISBN: 978-1-4731-4508-5