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Guideline

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

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This guideline covers prescribing and managing withdrawal from opioids, benzodiazepines, gabapentinoids, Z-drugs and antidepressants. The guideline assumes that non-pharmacological treatment options have been discussed and offered where appropriate before these medicines are prescribed. The guideline does not cover use of opioids prescribed for acute pain, cancer pain or at the end of life.

Who is it for?

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

What does it include?

- the guideline context
- the recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the recommendations and how they might affect practice.

Information about how the guideline was developed is on the guideline's webpage. This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

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Context

Medicines associated with dependence or withdrawal symptoms include benzodiazepines, Z-drugs (such as zopiclone and zolpidem), opioids, gabapentin and pregabalin. Antidepressants, although historically not classified as dependence-forming medicines, can 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.

Although these medicines can provide lasting symptom management for a proportion of people taking them, they do not work for everyone. In addition, they have adverse effects that can outweigh their benefits. Despite this, they may continue to be prescribed for various reasons, including concerns about the risk of unpleasant withdrawal symptoms.

Dependence is characterised by tolerance (the need for increasing doses to maintain the same effect) and withdrawal symptoms if the dose is reduced or the medicine is stopped abruptly. Addiction also features tolerance and withdrawal but has the additional characteristics of cravings, lack of control, overuse and continued use despite harm. There is considerable debate in relation to these definitions, and in practice, the terms are often used interchangeably. This guideline uses the term dependence. Many people who are using medicines at safe doses may also have some features of dependence, but this does not always mean treatment should be stopped. The guideline recommendations, therefore, focus on problems associated with dependence.

There is wide variation in the prescribing of medicines associated with dependence or withdrawal symptoms. This variation closely relates to indices of social deprivation. There is also variation in the provision of services supporting people with a dependence on prescription medicines as part of medicines optimisation. People with a dependence on prescribed medicines may be reluctant to attend addiction

services or seek help from their healthcare professionals because of a perceived association with illegal drug use or alcohol dependence.

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.

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 medicines associated with dependence or withdrawal symptoms

1.1.1 At all stages of prescribing and withdrawal management, aim to foster collaborative, trusting and supportive relationships with people taking 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 or other person close to them.

For a short explanation of why the committee made these recommendations, see the rationale and impact section on supporting people taking medicines associated with dependence or withdrawal symptoms.

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 medicines associated with dependence or withdrawal symptoms

1.2.1 Before starting or continuing treatment with an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant, ensure that all relevant management options, including non-pharmacological treatment 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, and discuss these with them. Factors include:

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

1.2.3 Take steps to reduce the risk of developing problems associated with dependence, and explain these to the person. Steps include starting the medicine at a low dose and avoiding modified-release opioids, either on their own or together with a standard-release (immediate-release) opioid.

1.2.4 At the first appointment, give the person information and advice to help them balance the potential benefit of the medicine and other treatment options in treating their current symptoms with the risk of long-term consequences. Use the NICE guideline on shared decision making to support people when making decisions.

1.2.5 Recognise and acknowledge that decisions about medicines can be difficult for a person who is in distress.

1.2.6 Consider delaying prescribing until after the first appointment to allow time for the person to think about their options, and for you to consult with other members of the healthcare team if needed.

1.2.7 If a shared decision about starting or continuing a medicine cannot be reached and the medicine is not in the person's best interests, 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. You should:

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

For a short explanation of why the committee made these recommendations, see the rationale and impact section on making decisions about prescribing and taking medicines.

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 medicines associated with dependence and withdrawal symptoms

Information and support for people starting a medicine

1.3.1 Before starting treatment with an opioid, benzodiazepine, gabapentinoid, Z-drug or antidepressant, give the person verbal and written information

about the medicine in their preferred format. Ensure that the information is evidence based and understandable by the person. Explain to the person:

- the potential side effects, whether they are likely to be temporary or permanent, whether they might improve or worsen over time
- the additional implications of taking the medicine if the person is pregnant or planning pregnancy, if appropriate
- what the options might be if the medicine does not work
- how difficult it might be to stop the medicine later
- if the medicine is an opioid, benzodiazepine, gabapentinoid or Z-drug:
  - the risk of developing dependence
  - the symptoms and signs of dependence
  - the risk of developing tolerance
- if the medicine is an antidepressant or gabapentinoid:
  - that the effect of the medicine may occur slowly and they might experience side effects before noticing any benefit
  - that any side effects are likely to ease over time.

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

Management plan

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

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

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

1.3.4 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 dosage could be decreased
- check whether the dosage needs to be increased and, if so, how to do this safely.

Prescribing strategies

1.3.5 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 the dose can be adjusted to test effectiveness, safety and acceptability and to determine the lowest effective dose in a reasonable time.

1.3.6 If the person's individual circumstances or the setting (for example, secure settings) mean 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 there.

See also the NICE guideline on physical health of people in prison.

1.3.7 The duration of each individual prescription:

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

Working with other healthcare professionals

1.3.8 Local healthcare teams should ensure that prescribing practice is standardised both within and between teams.

1.3.9 When prescribing at the suggestion of 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 the original prescriber
- follow the recommendations in the section on supporting people taking medicines associated with dependence or withdrawal symptoms 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 would be more beneficial for them.

1.3.10 Healthcare professionals in secondary care who recommend a medicine to be started in primary care should:

- explain to the person that the primary care prescriber will be responsible for the prescription and may need to review the recommendation before prescribing it
- ensure that the primary care prescriber has access to the management plan in the person's medical record.

1.3.11 Healthcare professionals in secondary care who prescribe a medicine they wish to be reviewed and further prescribed in primary care should:

- explain to the person that any further prescriptions of the medicine are the responsibility of the primary care prescriber, who will review the need to continue the medicine
- ensure that the primary care prescriber has access to the management plan in the person's medical record.

1.3.12 If a primary care prescriber has concerns about prescribing a medicine recommended by a healthcare professional in secondary care, the primary care prescriber and the specialist should discuss and agree how the prescribing will be managed. They should involve the person in these discussions and ensure they are made aware if prescribing needs to be delayed while discussions continue.

1.3.13 If possible, ensure that 1 person has overall responsibility for the prescribing. If the 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 as needed, is in place to support this. Pharmacists working in primary care may play a key role in supporting prescribing (see recommendation 1.4.4).

For a short explanation of why the committee made these recommendations, see the rationale and impact section on starting medicines.

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 medicines associated with dependence or withdrawal symptoms

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 dosage
- factors that might indicate a need for frequent reviews, such as:

- whether the person is taking the medicine for the first time
- potential for adverse effects and problems associated with dependence
- use of a medicine outside its licensed indications
- potential for misuse of the medicine.

If the person is taking an antidepressant, also 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, especially if the dose is being reduced. 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 condition or psychosocial 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.

Content of reviews

1.4.5 During the review, discuss the benefits and risks of continuing or stopping the medicine with the person. Base the decision to continue or stop on this discussion, for example:

- 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 benefits the person is gaining from continuing the medicine
- their preferences.

1.4.6 Agree and update the management plan with the person after each review, and give them a copy (see recommendation 1.3.3). Check that they know who to contact if they have problems or concerns.

> For a short explanation of why the committee made these recommendations, see the rationale and impact section on reviewing medicines.
>
> Full details of the evidence and the committee's discussion are in evidence review F: monitoring.

1.5 Withdrawing medicines associated with dependence and withdrawal symptoms

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 with dependency 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. Explain that dependence is an expected effect of these medicines. Be sensitive to the use of terminology that may apportion blame to the person or be perceived adversely.

1.5.4 Acknowledge and discuss any differences between the person's 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 appropriate, 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
- the use of medicines short term to treat the physical symptoms of withdrawal (for example, abdominal cramps and diarrhoea).

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)
- 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 medicines 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
  - taking an antidepressant with:
    - ◊ a short half-life **or**
    - ◊ anticholinergic properties
- 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 and helplines 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 both type and severity, can be physical or psychological, vary in intensity and change over time
- 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 confused with a re-emergence of their original symptoms or a new disorder, and it is important to discuss these with you if they occur (see recommendation 1.5.13).

Dose reduction

1.5.10 When agreeing a dose reduction schedule with the person:

- for opioids, benzodiazepines, Z-drugs and antidepressants, suggest a slow, stepwise rate of reduction proportionate to the existing dose, so that decrements become smaller as the dose is lowered, unless rapid withdrawal is needed
- for gabapentinoids, reduce the dose by a fixed amount at each decrement
- ensure that the rate of reduction is likely to be tolerable for the person
- consider giving the person an element of control over the process of dose reduction (for example, by issuing their usual prescription for a month and encouraging them to reduce the dose by their chosen decrements, rather than issuing successive reduced prescriptions)
- agree regular intervals for reviewing the reduction schedule
- balance the risk of adverse events from continued exposure to the medicines with minimising risk of withdrawal symptoms by slow dose reduction and withdrawal
- if the person is withdrawing from a benzodiazepine, consider switching to a benzodiazepine with a longer half-life.

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

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

Identifying and managing withdrawal symptoms

1.5.13 Be aware that it can be difficult to distinguish between the re-emergence of underlying conditions and the emergence of withdrawal symptoms. The

1 following may indicate withdrawal symptoms rather than symptoms of an
2 underlying condition:

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

8 1.5.14 Use clinical judgement to determine the need for further investigation to
9 rule out new pathology.

10 1.5.15 If distressing symptoms occur or worsen after a dose reduction:

11 • determine whether they are withdrawal symptoms or a re-emergence of
12 symptoms that were relieved by the medicine
13 • if the symptoms are new, think about delaying the next dose reduction
14 or reverting to the previous dose
15 • if symptoms of depression re-emerge during withdrawal from an
16 antidepressant, follow the recommendations on psychological
17 interventions for relapse prevention in the NICE guideline on
18 depression in adults.

19 **Interventions to support withdrawal**

20 1.5.16 Consider group cognitive behavioural therapy (CBT) to support people to
21 manage symptoms when withdrawing from a benzodiazepine. Discuss the
22 timing of referral for CBT with the person.

23 1.5.17 Do not treat withdrawal symptoms with another medicine that is
24 associated with dependence or withdrawal symptoms.

25 1.5.18 Do not offer sodium valproate or buspirone to aid withdrawal from a
26 benzodiazepine.

Strategies if withdrawal cannot be agreed or is unsuccessful

1.5.19 In exceptional circumstances, if a shared decision to withdraw cannot be reached and continuing the current prescription is not in the person's best interests, follow General Medical Council prescribing guidance as in recommendation 1.2.7. Be aware that medicines associated with dependence and withdrawal symptoms cannot be stopped abruptly in most cases (see also recommendation 1.5.6) and need to be reduced in line with the section on withdrawing medicines.

1.5.20 Additional considerations may be needed when continued use of the medicine may be particularly harmful for the person or others (for example, in a secure setting) where a dose reduction, or a more rapid reduction than the person wishes may be the safest practice. In these circumstances, consider:

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

1.5.21 If dose reduction has proved too difficult 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 see the rationale and impact section on withdrawing medicines.

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 interventions.

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 this recommendation see the rationale and impact section on withdrawing medicines.

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 this recommendation see the rationale and impact section on withdrawing medicines.

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 this recommendation see the rationale and impact section on withdrawing medicines.

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

1

2 4 Individual circumstances and the risk of dependence

3 Do individual circumstances such as social distress, low income status or limited
4 access to alternative sources of support lead to an increased risk of dependence on
5 prescribed medicines?

For a short explanation of why the committee made this recommendation, see the rationale and impact section on making decisions about prescribing and taking medicines.

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

6

7 5 Information for family members or carers

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

For a short explanation of why the committee made this recommendation, see the rationale and impact section on starting medicines.

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

11

Other recommendations for research

System-level factors and the risk of dependence

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

> For a short explanation of why the committee made this recommendation, see the rationale and impact section on making decisions about prescribing and taking medicines.
>
> Full details of the evidence and the committee's discussion are in evidence review E: risk factors.

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 this recommendation see the rationale and impact section on withdrawing medicines.
>
> Full details of the evidence and the committee's discussion are in evidence review C: safe withdrawal.

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 this recommendation see the rationale and impact section on withdrawing medicines.

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

1

2 **Acupuncture to support withdrawal from opioids**

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

For a short explanation of why the committee made this recommendation see the rationale and impact section on withdrawing medicines.

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

5

6 **Withdrawal interventions for gabapentinoids**

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

For a short explanation of why the committee made this recommendation see the rationale and impact section on withdrawing medicines.

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

9

10 **Aids to support withdrawal**

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

For a short explanation of why the committee made this recommendation see the rationale and impact section on withdrawing medicines.

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

1

2 # Rationale and impact

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

5 ## Supporting people taking medicines associated with dependence
6 ## or withdrawal symptoms

7 Recommendations 1.1.1 and 1.1.2

8 ### Why the committee made the recommendations

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

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

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

22 ### How the recommendations might affect practice

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

25 Return to recommendations

Making decisions about prescribing and taking medicines

Recommendations 1.2.1 to 1.2.7

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.

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 appointment. 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.

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 disorders 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 was important for healthcare professionals to take these factors into account when making prescribing decisions, but the needs of each individual should be taken into account when balancing benefits and harms and these factors should not be seen as barriers to prescribing.

In the committee's experience, starting with a low dose of opioid reduces the risk of problems associated with dependence, and this was supported by evidence 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 (such as slow-release morphine or oxycodone) and transdermal preparations (such as fentanyl or buprenorphine patches).

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 research recommendation on individual circumstances and the risk of dependence, and a research recommendation on system-level factors and the risk of dependence.

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 medicines

Recommendations 1.3.1 to 1.3.13

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 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 information in a written form that the person 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 by the committee. The committee's experience and evidence from studies on opioids indicate 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, that 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.

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, secondary and tertiary services. 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

1 this is consistent with NHS England's guidance on responsibility for prescribing
2 between primary and secondary/tertiary care.

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

7 How the recommendations might affect practice

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

17 Return to recommendations

18 Reviewing medicines

19 Recommendations 1.4.1 to 1.4.6

20 Why the committee made the recommendations

21 Frequency of reviews

22 There was no evidence on the frequency of reviews, so the committee based the
23 recommendations on their experience. They agreed that prescribing is an ongoing
24 process that should be monitored with regular reviews tailored to the person, the
25 medicine they are taking and the presence of any risk factors. These could be held
26 by phone, video or face-to-face. They also agreed that the frequency of reviews
27 could be increased during dose adjustments, particularly dose reductions, to ensure
28 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 less adverse events and clinical harm caused by prescribed medicines.

Return to recommendations

Withdrawing medicines

Recommendations 1.5.1 to 1.5.21

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 avoiding 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 committee experience, it was 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 and helplines 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. Based on their experience, they agreed that tolerability is the most important factor to take into account when deciding the speed of dose reduction. 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 was common practice and could 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, and 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.

Interventions to support withdrawal

There was little evidence on psychological interventions to support withdrawal or relieve withdrawal symptoms. Heath economic analysis showed that group cognitive behavioural therapy (CBT) alongside dose reduction can improve 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 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 discussed that there may be particular difficulties where continued use of the medicine is especially hazardous, for example, in a secure setting, and they 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, but this should be balanced by savings accrued from a reduction in unplanned hospitalisations due to adverse drug events and less medicines prescribed and reviews. Providing CBT to people during withdrawal from benzodiazepines would initially need additional

1 resources, but in the long term will generate savings and improve quality of life as
2 found in the health economics analysis.

3 Return to recommendations

4 Finding more information and committee details

5 To find NICE guidance on related topics, including guidance in development, see the
6 NICE webpage on medicines management.

7 For details of the guideline committee, see the committee member list.

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