

Medicines optimisation in chronic pain

Key therapeutic topic

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www.nice.org.uk/guidance/ktt21

Key points

- Controlling chronic pain can present significant challenges.
- It is unusual for any analgesic, including strong analgesics like opioids, to completely eliminate chronic pain. The focus of treatment should be on reducing a person's pain with a view to improving their quality of life.
- Using the World Health Organization (WHO) analgesic ladder in people with chronic pain, without taking into account the complexity of the person's individual needs, preferences for treatments, health priorities and lifestyle, may contribute to inappropriate prescribing.
- The use of opioid and non-opioid analgesics, especially gabapentin and pregabalin, can be associated with serious harms and can lead to dependence; these medicines may also be misused or diverted to illegal use.
- Pregabalin and gabapentin were reclassified as class C controlled substances in April 2019, and placed under Schedule 3 of the 2001 Misuse of Drugs Regulations but without the safe custody requirements.
- **Options for local implementation:**
 - Ensure people with chronic pain receive optimal pain treatment with careful consideration of the benefits and risks of treatment options.
 - Be familiar with the range of non-pharmacological interventions that are effective for reducing symptoms and disability in people with chronic pain and the local availability of

- – these services.
 - Assess risk and address harms of medicines where safety issues are a concern, such as opioids, gabapentin and pregabalin.
 - Review and, if appropriate, optimise prescribing of opioids, gabapentin or pregabalin to ensure that it is in line with national guidance.

Evidence context

This key therapeutic topic is concerned with chronic pain. The safe and effective prescribing of strong opioids in adults with advanced and progressive disease is addressed by the NICE guideline on [palliative care for adults: strong opioids for pain relief](#) and is outside the scope of this key therapeutic topic. Care during the last 2 to 3 days of life is covered by the NICE guideline on [care of dying adults in the last days of life](#), and is also outside the scope of this key therapeutic topic.

The NICE guideline on [controlled drugs](#) provides recommendations for using and managing controlled drugs safely. This includes recommendations for prescribers to review prescriptions for controlled drugs, prescribe an appropriate quantity and take into consideration the total opioid load that is being prescribed.

NICE is developing a guideline on [chronic pain: assessment and management](#) (estimated publication August 2020).

NICE is also developing a guideline on [safe prescribing and withdrawal management of prescribed drugs associated with dependence and withdrawal](#) (estimated publication November 2021).

Managing chronic pain

The scope for the NICE guideline in development on [chronic pain](#) states that chronic pain is often difficult to treat and can be associated with many different types of tissue injuries and disease processes. Pain can have a significant impact on individuals and their families and carers, affecting mood, sleep, mobility, role within the family, ability to work as well as other aspects of life. Almost half of people with chronic pain have a diagnosis of depression and two-thirds of people are unable to work outside the home. Attempts to treat chronic pain are costly to the healthcare system. In 2016, £537 million was spent on prescribing analgesics, with at least an additional 50% cost incurred from the prescription of other drug classes such as antidepressants and antiepileptic drugs. The economic impact of pain is high because of absenteeism, poor productivity and people with pain leaving the work force. The annual indirect (productivity) cost of back pain in the UK was

estimated to be between £5 billion and £10.7 billion.

There are a number of guidelines and resources that aim to improve communication between healthcare professionals and patients around managing chronic pain, improving the safety and effectiveness of treatment for pain, and reducing the risks associated with medicines such as opioids, pregabalin and gabapentin. According to the British Medical Association briefing paper [chronic pain: supporting safer prescribing of analgesics](#), the management of chronic pain can present significant challenges for healthcare professionals. It is important that people receive appropriate treatment for their pain with careful consideration of the benefits and risks of their treatment options – see the medicines optimisation: key therapeutic topic on [shared decision making](#). The NICE guideline on [medicines optimisation](#) provides recommendations for the care of all people who are using medicines and also those who are receiving suboptimal benefit from medicines.

Although analgesics can sometimes work effectively to relieve chronic pain, this is only achieved in a small percentage of people: it is unusual for any analgesic, including strong analgesics like opioids, to completely eliminate chronic pain. So, the focus of treatment should be on reducing a person's pain with a view to improving their quality of life. Evidence also suggests that non-pharmacological treatment may be effective in reducing symptoms and disability in some people with chronic pain and can also augment and complement analgesic use. Healthcare professionals who are responsible for helping people live with chronic pain should be familiar with the range of such non-pharmacological interventions – including physical and psychological therapies – and the local availability of these services ([Chronic pain: supporting safer prescribing of analgesics](#)).

Chronic pain is a complex and variable interplay between biological, psychological and social factors. The World Health Organization's (WHO) [analgesic ladder](#) is often used as a guide to the treatment of chronic pain. However, as stated in [chronic pain: supporting safer prescribing of analgesics](#), the WHO tool was originally developed to assist the treatment of cancer-related pain and it has never been validated in the management of non-cancer-related chronic pain. The analgesic ladder approach suggests that, with increasing reported pain intensity, increasingly strong analgesics should be provided and doses of strong opioids increased until pain is controlled, but good-quality evidence to support the long-term use of opioids in non-cancer pain is lacking. Using the WHO ladder in people with chronic pain, without taking into account the complexity of the person's individual needs, preferences for treatments, health priorities and lifestyle, may contribute to inappropriate prescribing.

The [Opioids Aware](#) resource, a Public Health England (PHE) funded project, contains specific information relating to the clinical use of opioids for pain that aims to support prescribers and

patients in making a fully informed decision to use, or not use, opioids. The resource includes good practice in prescribing, legislation, improving patient safety and minimising harms, clinical assessment and management, opioid dependence, structured approach to opioid prescribing, and information for patients.

Low back pain causes more disability, worldwide, than any other condition. The NICE guideline on [low back pain and sciatica in over 16s: assessment and management](#) recommends that before prescribing analgesia, healthcare professionals should consider using risk stratification (for example, the [STarT back risk assessment tool](#)) at first point of contact, for people presenting with each new episode of low back pain with or without sciatica, to inform shared decision making about stratified management. NICE recommends considering:

- simpler and less intensive support for people with low back pain with or without sciatica who are likely to improve quickly and have a good outcome (for example, providing reassurance, advice to keep active and guidance on self-management)
- more complex and intensive support for people with low back pain with or without sciatica at higher risk of a poor outcome (for example, exercise programmes with or without manual therapy or using a psychological approach).

The guideline recommends non-steroidal anti-inflammatory drug (NSAIDs) for managing low back pain, reserving weak opioids (with or without paracetamol) for managing acute low back pain only when an NSAID is contraindicated, not tolerated or has been ineffective. The guideline recommends that opioids should not routinely be offered for managing acute low back pain and should not be offered for managing chronic low back pain. Antidepressants, anticonvulsants and paracetamol alone are not recommended for low back pain. Pharmacological management of sciatica is covered by the NICE guideline on [pharmacological management of neuropathic pain in adults in non-specialist settings](#).

The NICE guideline on [headaches](#) advises healthcare professionals to be alert to the possibility of medication-overuse headache in people whose headache developed or worsened while they were taking certain commonly used headache treatments for 3 months or more. The guideline makes recommendations on treating medication-overuse headache. These include explaining to people that it is treated by withdrawing overused medication for at least 1 month and to stop abruptly rather than gradually. Headache symptoms are likely to get worse in the short term before they improve and there may be associated withdrawal symptoms.

See NICE's clinical knowledge summaries on [mild to moderate pain](#), [non-specific neck pain](#), [cervical radiculopathy](#), [medication-overuse headache](#) and [shoulder pain](#). The NICE Pathways on [controlled](#)

[drugs](#), [neuropathic pain](#) and [low back pain](#) bring together everything NICE has said on pain in a set of interactive flowcharts. The NICE quality standard on [medicines optimisation](#) describes concise sets of prioritised statements designed to drive measurable quality improvements within these areas.

Opioid medicines in chronic pain

Opioid medicines are prescribed to treat moderate to severe pain, but repeated use can lead to dependence and tolerance. Opioid medicines are subject to special legislative controls because there is potential for them to be abused, diverted or cause possible harm. NICE's medicines evidence commentary on [pain management: initial opioid prescriptions and likelihood of long-term opioid use](#) discusses an American observational study that looked at the relationship between early opioid prescribing patterns and likelihood of long-term use. Opioid continuation beyond 1 year was seen more frequently in people who were started on long-acting opioids or tramadol. Likelihood of chronic opioid use increased with larger initial opioid supply, longer treatment durations and where higher starting doses were prescribed.

There has been a marked and progressive rise in prescribing of opioid medicines in the UK over the past decade and the trend to increased prescribing continues. The [Opioids Aware](#) resource provides a helpful summary of the evidence considering the [effectiveness of opioids for long-term pain](#). It concludes that:

- There is little evidence that opioids are helpful for chronic pain.
- A small proportion of people may obtain good pain relief with opioids in the long-term if the dose can be kept low and use is intermittent, but it is difficult to identify these people at the start of treatment.
- The risk of harm increases substantially at doses above an oral morphine equivalent of 120 mg/day, but there is no increased benefit.
- Opioids should be discontinued if the person is still in pain despite using opioids, even if no other treatment is available.
- A detailed assessment of the emotional influences on the person's pain experience is essential for people with chronic pain who also have refractory and disabling symptoms, particularly if they are on high opioid doses.

The [Opioids Aware](#) resource also contains key points on the clinical use of opioids for chronic pain. It highlights that people with chronic pain who do not achieve useful pain relief from opioids within

2 to 4 weeks are unlikely to gain benefit in the long term. NICE's medicines evidence commentary on [chronic pain: patient outcomes with dose reduction or discontinuation of long-term opioid therapy](#) discusses a systematic review, which found that there was some evidence that several types of intervention may be effective at reducing or discontinuing long-term opioid therapy and that pain, function and quality of life may actually improve with opioid dose reduction. People taking opioids should be counselled about the possible adverse effects including the effects on driving and other skilled tasks when initiating or increasing an opioid dose.

There have been several safety concerns highlighted at a national level about the use of strong analgesics such as opioids to manage chronic pain. The PHE resource [Health matters: preventing drug misuse deaths](#) outlines how providers and commissioners can prevent deaths from drug misuse. The [Office for National Statistics annual bulletin on Deaths related to drug poisoning in England and Wales: 2017 registrations](#) gives data on the numbers of deaths involving legal and illegal drugs. It reported that:

- Although two-thirds of drug-related deaths were related to drug misuse, three-quarters of all drug-related deaths involved accidental poisoning.
- Deaths involving heroin or morphine doubled from 579 in 2012 to 1,209 in 2016 but declined to 1,164 in 2017, the first decline since 2012.
- Fentanyl deaths have increased by 29%, rising from 34 deaths in 2015 and 58 deaths in 2016 to 75 deaths in 2017.
- Codeine deaths increased from 131 in 2016 to 156 in 2017, an increase of nearly 20%. However, most other opioid-related deaths have decreased, with buprenorphine, methadone and oxycodone recording fewer deaths in 2017 than in 2016. Tramadol deaths have remained stable, with 184 and 185 deaths in 2016 and 2017, respectively. In June 2014, tramadol was controlled under the Misuse of Drugs Act 1971 as a class C substance.

In July 2008, the National Patient Safety Agency, which is now part of [NHS Improvement](#), issued a rapid response report about [reducing dosing errors with opioid medicines](#). This followed incidents being reported to the National Reporting and Learning System (NRLS) concerning people receiving unsafe doses of opioid medicines, where a dose or formulation was incorrect based on their previous opioid dose. A [review of medicines-related safety incidents involving controlled drugs reported to the NRLS over 7 years](#) found the risk of death with controlled drug incidents was significantly greater than with medication incidents generally. Five controlled drugs (morphine, diamorphine, fentanyl, midazolam and oxycodone) were responsible for 113 (88%) of 128 medication incidents reporting death or severe harm. The [September 2008 edition of Drug Safety Update](#) highlighted evidence of unintentional overdose of fentanyl following inappropriate

prescribing of fentanyl patches, including prescribing in unlicensed indications and in opioid-naive people. In the [October 2018 edition of Drug Safety Update](#), the Medicines and Healthcare products Regulatory Agency (MHRA) issued advice about fentanyl patches on the need to provide clear information to patients and caregivers about how to minimise the risk of accidental exposure, and the importance of appropriate disposal of patches.

The Care Quality Commission and the NHS England Patient Safety Team (patient safety sub-group) have developed [checklists](#) for healthcare professionals, supporting the safer use of several opioids. Checklists are available for the safer use of fentanyl and buprenorphine transdermal patches, oral oxycodone medicines and MS syringe drivers. The patient safety sub-group also produce [patient safety newsletters](#) to share patient-related controlled drugs incidences, learning and signpost to relevant guidance.

Regulations introduced on 1 October 2015 widened the availability of naloxone with the aim of reducing the number of related deaths and harm. The Department of Health, MHRA and PHE have jointly published a [factsheet](#) explaining these regulations and how they can be implemented. An alert on [minimising the risk of distress and death from inappropriate doses of naloxone](#) supports NHS organisations in ensuring that local protocols and training related to use of naloxone reflect best practice. See also the NHS publication [What naloxone doses should be used in adults to reverse urgently the effects of opioids or opiates?](#)

Non-opioid medicines in chronic pain

Other types of analgesics are also used to manage chronic pain, particularly neuropathic pain. For managing neuropathic pain, the NICE guideline on [pharmacological management of neuropathic pain in adults in non-specialist settings](#) recommends offering a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for neuropathic pain (except trigeminal neuralgia). Regular clinical reviews are recommended to assess and monitor the effectiveness of treatment so that treatment with medicines can be optimised.

The use of both gabapentin and pregabalin can lead to dependence and these medicines may be misused or diverted. PHE and NHS England have published [advice for prescribers on the risk of misuse of pregabalin and gabapentin](#). In April 2019, [pregabalin and gabapentin were reclassified as class C controlled substances](#), and placed under Schedule 3 of the 2001 Misuse of Drugs Regulations but without the safe custody requirements. In the [October 2017 edition of Drug Safety Update](#), the MHRA highlighted that gabapentin has been associated with a rare risk of severe respiratory depression even without concomitant opioid medicines. It noted that people with compromised respiratory function, respiratory or neurological disease, renal impairment,

concomitant use of central nervous system depressants, and older people might be at higher risk of experiencing severe respiratory depression.

The NHS publication [What is the evidence to support the use of nefopam for the treatment of persistent/chronic pain](#) is a helpful resource discussing the risks and benefits of nefopam, a centrally acting non-opioid analgesic. This summary concludes that nefopam appears no more potent than NSAIDs; however, it is commonly associated with adverse drug reactions and is toxic in overdose. It states that nefopam may sometimes be preferred because alternatives are contraindicated or ineffective, or used as add-on therapy when pain is inadequately controlled. The summary advises that prescribers should consider whether the potential benefits outweigh the risks of adverse effects in individual patients, with treatment being reviewed regularly.

Practice examples and shared learning

A PHE resource provides specific guidance on [managing persistent pain in secure settings](#) along with a case study on the [development of a chronic non-cancer pain clinic in South Gloucester prisons](#) showing how this guidance can be implemented in practice.

NHS Improvement [resources](#) are available that highlight the difficulties in prescribing opioids to manage chronic pain and offer advice and guidance to all healthcare professionals who are responsible for administering them.

NHS England is supporting the implementation of the [national low back pain pathway](#) that supports implementation of recommendations in the NICE guideline on [low back pain and sciatica in over 16s: assessment and management](#), and aims to:

- rapidly identify and refer potentially serious pathology
- provide expeditious access to interventions such as nerve root blocks or surgical discectomy where indicated
- provide effective and timely care for sufferers with acute low back pain to improve outcomes and reduce disability.

Savings from implementation are estimated to be £900,000 per million population. The [North of England regional back pain programme](#) is a regional approach supporting the national implementation programme. Free online resources are accessible for both patients and healthcare professionals.

PrescQIPP have published a number of resources on pain-related topics and analgesia, including bulletins on [pregabalin and gabapentin prescribing in neuropathic pain](#) and [non-neuropathic pain](#).

[Practical resources on quality prescribing for chronic pain](#) are also available from the [Effective Prescribing and Therapeutics Branch](#) of NHS Scotland. These include an EMIS template for chronic pain review, audits and patient information.

[Live Well with Pain](#) offers a range of knowledge, skills, tools and resources to help clinicians enable patients to become clearer about their needs, manage or cope with their pain well and make better use of the healthcare available to them.

There are several NICE [shared learning case studies](#) relating to chronic pain, showing how NICE guidance and standards have been put into practice by some NHS organisations:

- [Best evidence for a better back \(BE FABB\) – A triage, assessment and education service for patients with low back pain with or without sciatica.](#)
- [The Integrated Pain and Spinal Service \(IPASS\): A unique, integrated and collaborative approach to persistent pain management.](#)
- [Implementing a program to provide improved access to physiotherapy and enhanced management for patients with low back pain and sciatica.](#)
- [The joint pain advisor approach for knee and hip pain.](#)
- [Medicines optimisation for neuropathic pain.](#)
- [Self-management for chronic knee pain: using group physiotherapy to teach exercises and coping strategies.](#)
- [Physiotherapy low back pain drop-in services.](#)
- [Improving educational resources for people with back pain in Sheffield.](#)
- [A language specific and culturally adapted pain management programme.](#)

Prescribing data, metrics or supporting resources

At this point, the following prescribing data, indicators and resources have been identified to support this topic.

The Care Quality Commission [controlled drugs annual report for 2017](#) found that the top 6 schedule 2 and 3 controlled drugs prescribed in primary care (number of items) were tramadol, buprenorphine, morphine sulfate, methadone, oxycodone and fentanyl.

The total use in primary care in England of gabapentin has increased year on year from 1.5 million prescriptions dispensed in 2007 to 7.1 million in 2017 and 7.4 million in 2018 (4% relative increase from 2017 and 393% increase from 2007). Pregabalin use has increased from 0.7 million prescriptions dispensed in 2007 to 6.3 million in 2017 and 7.0 million in 2018 (11% relative increase from 2017 and 900% increase from 2007; [Prescription cost analysis – England 2018](#)).

The [NHS Business Services Authority](#) produces 2 sets of reports for [controlled drug monitoring](#):

- comparator charts available for the last 2 quarters' prescribing data
- analysis reports that can be accessed through the [information services portal](#).

These reports monitor the prescribing of schedule 2 and 3 controlled drugs to enable controlled drug accountable officers to highlight potential causes for concern within the prescribing of controlled drugs through demonstrating variance in prescribing between organisations, and by identifying prescribers or organisations exhibiting unusual prescribing behaviour ([NHS Business Services Authority controlled drug monitoring](#)).

A [series of indicators](#) have been developed to inform safer prescribing practice to help pharmacists, clinicians and patients review prescribed medication and prevent harm. These include indicators about pain.

Update information

September 2019: This topic was retained for the 2019 rapid update of medicines optimisation: key therapeutic topics. Minor editorial changes have been completed. In addition, information on the reclassification of pregabalin and gabapentin has been updated, a link to a NICE guideline in development has been added, a Medicines and Healthcare products Regulatory Agency (MHRA) safety alert has been added, new resources and shared learning examples have been added, and prescribing data have been updated.

About this key therapeutic topic

This document summarises the evidence base on this key therapeutic topic that has been identified to support medicines optimisation. **It is not formal NICE guidance.**

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