

Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults

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NICE clinical guideline 140

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Introduction

Pain is common in advanced and progressive disease. Up to two-thirds of people with cancer experience pain that needs a strong opioid. This proportion is similar or higher in many other advanced and progressive conditions.

Despite the increased availability of strong opioids, published evidence suggests that pain which results from advanced disease, especially cancer, remains under-treated.

Each year 300,000 people are diagnosed with cancer in the UK and it is estimated that there are 900,000 people living with heart failure. Others live with chronic illness such as kidney, liver and respiratory disease, and with neurodegenerative conditions. Many people with these conditions will develop pain for which a strong opioid may be needed.

The 2008 World Cancer Declaration included a target to make effective pain control more accessible. Several key documents highlight the importance of effective pain control, including 'Improving supportive and palliative care for adults with cancer' (NICE cancer service guidance 2004), 'Control of pain in adults with cancer' (Scottish Intercollegiate Guidelines Network guideline 106), 'A strategic direction for palliative care services in Wales' (Welsh Assembly Government 2005) and 'End of life care strategy' (Department of Health 2008).

Strong opioids, especially morphine, are the principal treatments for pain related to advanced and progressive disease, and their use has increased significantly in the primary care setting. However, the pharmacokinetics of the various opioids are very different and there are marked differences in bioavailability, metabolism and response among patients. A suitable opioid must be selected for each patient and, because drug doses cannot be estimated or calculated in advance, the dose must be individually titrated. Effective and safe titration of opioids has a major impact on patient comfort. The World Health Organization has produced a [pain ladder](#) for the relief of cancer pain; strong opioids are represented on the third level of the three-step ladder.

The guideline will address first-line treatment with strong opioids for patients who have been assessed as requiring pain relief at the third level of the WHO pain ladder. It will not cover second-line treatment with strong opioids where a change in strong opioid treatment is required because of inadequate pain control or significant toxicity.

A number of strong opioids are licensed in the UK. However for pain relief in palliative care a relatively small number are commonly used. This guideline has therefore looked at the following drugs: buprenorphine, diamorphine, fentanyl, morphine and oxycodone. Misinterpretations and misunderstanding have surrounded the use of strong opioids for decades, and these are only slowly being resolved. Until recently, prescribing advice has been varied and sometimes conflicting. These factors, along with the wide range of formulations and preparations, have resulted in errors causing underdosing and avoidable pain, or overdosing and distressing adverse effects. Despite repeated warnings from regulatory agencies, these problems have led on occasion to patient deaths, and resulted in doctors facing the General Medical Council or court proceedings. Additional guidance, including advice on reducing dosing errors with opioid medicines, patient safety incidents arising from medication errors involving opioids and safer use of injectable medicines, is available from the [National Patient Safety Agency \(NPSA\)](#).

This guideline will clarify the clinical pathway and help to improve pain management and patient safety. This guideline will not cover care during the last days of life (for example, while on the Liverpool Care Pathway).

Drug recommendations

The guideline assumes that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Who this guideline is for

The target audience is non-specialist healthcare professionals initiating strong opioids for pain in adults with advanced and progressive disease. However, the guideline is likely to be of relevance to palliative care specialists as well.

Patient-centred care

This guideline offers best practice advice on the care of people with advanced and progressive disease, who require strong opioids for pain control. These patients are defined as those in severe pain who may be opioid-naive, or those whose pain has been inadequately controlled on step two of the WHO pain ladder.

Treatment and care should take into account patients' needs and preferences. People with advanced and progressive disease, who require strong opioids for pain control, should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the [Department of Health's advice on consent](#) and the [code of practice that accompanies the Mental Capacity Act](#). In Wales, healthcare professionals should follow [advice on consent from the Welsh Government](#).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

1 Recommendations

Communication

1.1.1 When offering pain treatment with strong opioids to a patient with advanced and progressive disease, ask them about concerns such as:

- addiction
- tolerance
- side effects
- fears that treatment implies the final stages of life.

1.1.2 Provide verbal and written information on strong opioid treatment to patients and carers, including the following:

- when and why strong opioids are used to treat pain
- how effective they are likely to be
- taking strong opioids for background and breakthrough pain, addressing:
 - how, when and how often to take strong opioids
 - how long pain relief should last
- side effects and signs of toxicity
- safe storage
- follow-up and further prescribing
- information on who to contact out of hours, particularly during initiation of treatment.

1.1.3 Offer patients access to frequent review of pain control and side effects.

Starting strong opioids – titrating the dose

- 1.1.4 When starting treatment with strong opioids, offer patients with advanced and progressive disease regular oral sustained-release or oral immediate-release morphine (depending on patient preference), with rescue doses of oral immediate-release morphine for breakthrough pain.
- 1.1.5 For patients with no renal or hepatic comorbidities, offer a typical total daily starting dose schedule of 20–30 mg of oral morphine (for example, 10–15 mg oral sustained-release morphine twice daily), plus 5 mg oral immediate-release morphine for rescue doses during the titration phase.
- 1.1.6 Adjust the dose until a good balance exists between acceptable pain control and side effects. If this balance is not reached after a few dose adjustments, seek specialist advice. Offer patients frequent review, particularly in the titration phase.
- 1.1.7 Seek specialist advice before prescribing strong opioids for patients with moderate to severe renal or hepatic impairment.

First-line maintenance treatment

- 1.1.8 Offer oral sustained-release morphine as first-line maintenance treatment to patients with advanced and progressive disease who require strong opioids.
- 1.1.9 Do not routinely offer transdermal patch formulations as first-line maintenance treatment to patients in whom oral opioids are suitable.
- 1.1.10 If pain remains inadequately controlled despite optimising first-line maintenance treatment, review analgesic strategy and consider seeking specialist advice.

First-line treatment if oral opioids are not suitable – transdermal patches

- 1.1.11 Consider initiating transdermal patches with the lowest acquisition cost for patients in whom oral opioids are not suitable and analgesic requirements are stable, supported by specialist advice where needed.
- 1.1.12 Use caution when calculating opioid equivalence for transdermal patches:
- A transdermal fentanyl 12 microgram patch equates to approximately 45 mg oral morphine daily.
 - A transdermal buprenorphine 20 microgram patch equates to approximately 30 mg oral morphine daily.

First-line treatment if oral opioids are not suitable – subcutaneous delivery

- 1.1.13 Consider initiating subcutaneous opioids with the lowest acquisition cost for patients in whom oral opioids are not suitable and analgesic requirements are unstable, supported by specialist advice where needed.

First-line treatment for breakthrough pain in patients who can take oral opioids

- 1.1.14 Offer oral immediate-release morphine for the first-line rescue medication of breakthrough pain in patients on maintenance oral morphine treatment.
- 1.1.15 Do not offer fast-acting fentanyl as first-line rescue medication.
- 1.1.16 If pain remains inadequately controlled despite optimising treatment, consider seeking specialist advice.

Management of constipation

- 1.1.17 Inform patients that constipation affects nearly all patients receiving strong opioid treatment.
- 1.1.18 Prescribe laxative treatment (to be taken regularly at an effective dose) for all patients initiating strong opioids.
- 1.1.19 Inform patients that treatment for constipation takes time to work and adherence is important.
- 1.1.20 Optimise laxative treatment for managing constipation before considering switching strong opioids.

Management of nausea

- 1.1.21 Advise patients that nausea may occur when starting strong opioid treatment or at dose increase, but that it is likely to be transient.
- 1.1.22 If nausea persists, prescribe and optimise anti-emetic treatment before considering switching strong opioids.

Management of drowsiness

- 1.1.23 Advise patients that mild drowsiness or impaired concentration may occur when starting strong opioid treatment or at dose increase, but that it is often transient. Warn patients that impaired concentration may affect their ability to drive and undertake other manual tasks.
- 1.1.24 In patients with either persistent or moderate-to-severe central nervous system side effects:
- consider dose reduction if pain is controlled **or**
 - consider switching opioids if pain is not controlled.

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- 1.1.25 If side effects remain uncontrolled despite optimising treatment, consider seeking specialist advice.

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

How this guideline was developed

NICE commissioned the National Collaborating Centre for Cancer to develop this guideline. The Centre established a Guideline Development Group (see [appendix A](#)), which reviewed the evidence and developed the recommendations.

There is more information about [how NICE clinical guidelines are developed](#) on the NICE website. A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' is [available](#).

3 Implementation

NICE has developed [tools to help organisations implement this guidance](#).

4 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

4.1 Communication

What are the most clinically effective and cost-effective methods of addressing patient and carer concerns about strong opioids, including anticipating and managing adverse effects, and engaging patients in prescribing decisions?

Why this is important

We know from qualitative work that patients do not always understand how to take strong opioids or the difference between sustained-release and rescue medication. Patients, their carers and some clinicians fear the adverse effects of these drugs and believe that strong opioids, especially morphine, can be negatively associated with adverse effects and death. To improve adherence and to enable patients and carers to benefit from the proven analgesic effects of strong opioids, research should be undertaken to determine how to address the main concerns of patients, the level of information they require and the best time and methods to deliver this. The benefits of greater involvement in this process by specialist nurses or pharmacists should also be examined in research.

4.2 Side effects

Is prophylactic prescription of anti-emetic treatment or availability of anti-emetic treatment at the patient's home more effective in reducing nausea than the availability of prescription on request for patients starting strong opioids for the treatment of pain in advanced or progressive disease? The outcomes of interest are nausea, time to control of nausea, patient acceptability of treatment, concordance and use of healthcare resources.

Why this is important

Patients may experience transient nausea when starting opioid treatment and opioid-induced nausea often responds to anti-emetic treatment. When nausea occurs, timely review by a healthcare professional to start anti-emetic treatment can be difficult to achieve in the community

setting. Prescription of routine anti-emetic treatment when starting opioids is controversial. It is important to evaluate the positive and negative impact of this strategy; while it may reduce opioid-induced nausea, improve adherence with opioid treatment, and reduce use of healthcare resources, the added burden to the patient and overall cost effectiveness are currently unclear.

4.3 Side effects

Is early switching of opioid, on development of side effects, more effective at reducing central side effects than persisting with current opioid and dose reduction in patients starting strong opioids? The outcomes of interest are time to clinically effective pain control with acceptable side effects.

Why this is important

The common gastrointestinal opioid-induced side effects such as constipation or nausea can often be managed with concomitant medications. A significant proportion of patients starting strong opioids experience central side effects that patients report as distressing and often limit daily activities. Although central side effects may be transient, persistent symptoms can be difficult to treat and cause significant morbidity. The clinical strategy of opioid switching has been shown to reduce central side effects. The impact of early switching, rather than dose reduction or a 'watch and wait' strategy has not been formally evaluated but may improve both time to opioid response and health-related quality of life.

5 Other versions of this guideline

5.1 Full guideline

The full guideline, 'Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults', contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for Cancer.

5.2 NICE pathway

The recommendations from this guideline have been incorporated into a [NICE pathway](#).

5.3 'Understanding NICE guidance'

A summary for patients and carers ('[Understanding NICE guidance](#)') is available.

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N2737).

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about strong opioids in advanced and progressive disease.

6 Related NICE guidance

- [Neuropathic pain: the pharmacological management of neuropathic pain in adults in non-specialist settings](#). NICE clinical guideline 96 (2010).
- [Chest pain of recent onset: assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin](#). NICE clinical guideline 95 (2010).
- [Low back pain: early management of persistent non-specific low back pain](#). NICE clinical guideline 88 (2009).
- [Rheumatoid arthritis: the management of rheumatoid arthritis in adults](#). NICE clinical guideline 79 (2009).
- [Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin](#). NICE technology appraisal 159 (2008).
- [Metastatic spinal cord compression: diagnosis and management of adults at risk of and with metastatic spinal cord compression](#). NICE clinical guideline 75 (2008).
- [Osteoarthritis: the care and management of osteoarthritis in adults](#). NICE clinical guideline 59 (2008).
- [Improving supportive and palliative care for adults with cancer](#). NICE cancer service guidance (2004).

7 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations. Please see our website for information about updating the guideline.

Appendix A: The Guideline Development Group, National Collaborating Centre and NICE project team

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About this guideline

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

The guideline was developed by the National Collaborating Centre for Cancer, which is based at the Velindre NHS Trust. The Collaborating Centre worked with a group of healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, who reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#).

The recommendations from this guideline have been incorporated into a [NICE Pathway](#). We have produced a [summary for patients and carers](#). Tools to help you put the guideline into practice and information about the evidence it is based on are also [available](#).

Your responsibility

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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