Palliative care for adults: strong opioids for pain relief

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

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

**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 This recommendation has been replaced by recommendation 1.5.6 in NICE's guideline on controlled drugs: safe use and management.
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


1.1.15 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.

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.
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 Information for the public

NICE has produced information for the public explaining this guideline.

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

August 2016: Recommendation 1.1.12 was deleted and a link added to NICE's guideline on controlled drugs: safe use and management, which has newer advice on the topic. Two out of date research recommendations were also deleted.

Minor changes since publication

March 2016: Reference to the Liverpool Care Pathway deleted from the introduction.
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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