

Palliative care for adults: strong opioids for pain relief

Clinical guideline

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www.nice.org.uk/guidance/cg140

Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

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

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

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

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Overview

This guideline covers safe and effective prescribing of strong opioids for pain relief in adults with advanced and progressive disease. It aims to clarify the clinical pathway for prescribing and help to improve pain management and patient safety. Care during the last 2 to 3 days of life is covered by [NICE's guideline on care of dying adults in the last days of life](#).

Who is it for?

- Healthcare professionals
- People who are taking or being offered strong opioids and their families and carers

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 [NICE's cancer service guideline on improving supportive and palliative care for adults with cancer](#), the [Scottish Intercollegiate Guidelines Network guideline on control of pain in adults with cancer](#), the Welsh Assembly Government (2005) [A strategic direction for palliative care services in Wales](#) and the [Department of Health and Social Care \(2008\) End of life care strategy](#).

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 \(WHO\)](#) has produced a [pain ladder](#) for the relief of cancer pain; strong opioids are represented on the third level of the 3-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.

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.

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 mg to 30 mg of oral morphine (for example, 10 mg to 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

- 1.1.14 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 (see the [Driver and Vehicle Licensing Agency's Assessing fitness to drive: a guide for medical professionals](#)) 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.

Recommendation for research

The guideline development group has made the following recommendation for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

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.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the [NICE topic page on end of life care](#).

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

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

Update information

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 recommendations for research were also deleted.

Minor changes since publication

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

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