



Guideline Summary NGC-9102

Guideline Title

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

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 May. 23 p. (Clinical guideline; no. 140).

Guideline Status

This is the current release of the guideline.

Scope

Disease/Condition(s)

Pain resulting from advanced or progressive disease such as cancer, heart disease, liver disease, lung disease, kidney disease, human immunodeficiency virus (HIV) and terminal neurodegenerative or neuromuscular conditions

Guideline Category

Counseling
Management
Treatment

Clinical Specialty

Anesthesiology
Family Practice
Internal Medicine
Oncology

Intended Users

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Nurses
Patients
Physician Assistants
Physicians
Public Health Departments

Guideline Objective(s)

- To address first-line treatment with strong opioids for patients who have been assessed as requiring pain relief at the third level of the World Health Organization (WHO) pain ladder
- To clarify the clinical pathway and help to improve pain management and patient safety

Target Population

Adults (18 years and older) with advanced and progressive disease, who require strong opioids for pain control

Note: These guidelines are not intended for use in the following patients:

Note: These guidelines are not intended for use in the following patients:

- Children (younger than 18 years)
- Adults without advanced and progressive disease
- Adults who have not yet had a pain assessment to check whether strong opioids are required

Interventions and Practices Considered

1. Providing verbal and written information to patients and carers about opioid treatment
2. Starting strong opioid treatment in titrated doses
3. Seeking specialist advice for patients with severe renal or hepatic impairment and for patients with inadequate response
4. First-line maintenance treatment with oral sustained-release morphine
5. Initiating transdermal patches as first-line treatment in patients not suited for oral opioids
6. Initiating subcutaneous opioids as first-line treatment in patients not suited for oral opioids
7. Oral immediate-release morphine for first-line rescue medication of breakthrough pain in patients on maintenance oral morphine treatment
8. Management of constipation (laxatives, switching opioids)
9. Management of nausea (anti-emetics, switching opioids)
10. Management of drowsiness (doses reduction, switching opioids)

Major Outcomes Considered

- Pain
- Opioid side effects
- Percentage of people who switch to a different opioid
- Adverse events
- Health-related quality of life
- Cost-effectiveness
- Quality-adjusted life years (QALYs)

Methodology

Methods Used to Collect/Select the Evidence

- Hand-searches of Published Literature (Primary Sources)
- Hand-searches of Published Literature (Secondary Sources)
- Searches of Electronic Databases
- Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the Availability of Companion Documents field for the full version of this guidance.

How This Guideline Was Developed

The majority of the clinical questions posed in this guideline are interventional questions. For these questions the eligible studies were restricted to randomised controlled trials or systematic reviews thereof. Such studies were included whether they were published in full or as abstracts only. This decision was made in order to include all high level evidence. However, when such evidence was published in abstract form only, full appraisal and reporting of these studies was hampered by a lack of information and this was always highlighted to the Guideline Development Group (GDG). Moreover, due to a lack of evidence, studies that were not on first-line treatment were also included, and when this was the case, it was also highlighted to the GDG.

Search Strategies

The evidence reviews used to develop the guideline recommendations were underpinned by systematic literature searches, following the methods described in 'The guidelines manual' (2009) (see the Availability of Companion Documents field). The aim of the systematic searches was to comprehensively identify the published evidence to answer the review questions developed by the GDG and Short Clinical Guidelines Technical Team.

The search strategies for the review questions were developed by the Information Services Team with advice from the Clinical Guidelines Technical Team. Structured questions were developed using the PICO (population, intervention, comparison, outcome) model and translated into search strategies using subject heading and free text terms. The strategies were run across a number of databases with no date restrictions imposed on the searches.

The National Health Service (NHS) Economic Evaluation Database (NHS EED) and the Health Economic Evaluations Database (HEED) were searched for economic evaluations. Search filters for economic evaluations and quality of life studies were used on bibliographic databases. There were no date restrictions imposed on the searches.

GDG members were also asked to alert the Clinical Guidelines Technical Team to any additional evidence published

GDG members were also asked to alert the Clinical Guidelines technical team to any additional evidence, published, unpublished or in press, that met the inclusion criteria.

The searches were undertaken between May 2011 and August 2011.

Main Searches

The following sources were searched for the review topics presented in Appendix D of the full version of the original guideline document.

- Cochrane Database of Systematic Reviews – CDSR (Wiley)
- Cochrane Central Register of Controlled Trials – CENTRAL (Wiley)
- Database of Abstracts of Reviews of Effects – DARE (CRD)
- Health Technology Assessment Database – HTA (CRD)
- CINAHL (EBSCO)
- EMBASE (Ovid)
- MEDLINE (Ovid)
- MEDLINE In-Process (Ovid)
- PsycINFO
- Web of Science (Science Citation Index, Social Science Citation Index, ISI Conference Proceedings)

Economic Search

The following sources were searched to identify economic evaluations and quality of life data featuring the patient population of Topic 1 (first-line treatment with strong opioids).

- Medline
- EMBASE
- NHSEED
- HTA
- HEED

See Appendix D of the full version of the original guideline document for systematic reviews and mapping searches, review questions and review protocols (including inclusion/exclusion criteria), and excluded studies for clinical and economic searches.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the Availability of Companion Documents field for the full version of this guidance.

The Collaborating Centre worked with a group of healthcare professionals (including consultants, general practitioners, and nurses), patients and carers, and technical staff, who reviewed the evidence. See individual Evidence Review sections of the full version of the original guideline document for evidence tables and discussions of evidence quality (assessed by the GRADE [Grading of Recommendations Assessment, Development, and Evaluation] profiles), meta-analyses, and subgroup analyses for each review question.

A review of the economic evidence was conducted. See individual Evidence Review sections of the full version of the original guideline document for analysis of economic evidence for each review question. Also see Appendix F of the full version of the guideline for the full health economic report.

Methods Used to Formulate the Recommendations

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the Availability of Companion Documents field for the full version of this guidance.

Forming and Running the Short Clinical Guideline Development Group (GDG)

Each short clinical guideline is developed by a unique GDG consisting of 10–12 members, supported by the Short Clinical Guidelines Team. Each GDG has a Chair, healthcare professional members and a minimum of two patient and carer members. Co-opted expert advisers are recruited, as appropriate. A Clinical Adviser, who has specific content expertise and additional responsibilities, may also be appointed depending on the topic. Recruitment of the GDG Chair and members is carried out in accordance with NICE's policy.

The GDG makes its decisions using the best available evidence presented to it at GDG meetings by the Short Clinical Guidelines Team. The use of formal consensus methods within the GDG will be considered on a case-by-case basis.

Developing Review Questions

A short clinical guideline has a narrow scope and covers only part of a care pathway. It addresses a maximum of three subject areas covering clinical management. This will result in a small number of key clinical issues. These are broken down into a defined number of review questions — usually one or two per clinical management area. The exact number will be dictated by the size of the short clinical guideline remit and the amount of development time available.

Creating Guideline Recommendations

Explicit methods of linking the evidence to recommendations are used for short clinical guidelines if the topic is suitable. This involves using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Research recommendations are formulated for short clinical guidelines. Their number is dependent on the size of the short clinical guideline remit and the amount of development time available.

Writing the Guideline

There are usually three versions of short clinical guidelines:

- The full guideline – all the recommendations, details of how they were developed and summaries of the evidence they are based on
- The quick reference guide - a summary of recommendations for healthcare professionals
- 'Understanding NICE guidance' – a summary for patients and carers

The full guideline is written by the Short Clinical Guidelines Team, following the principles in chapters 9 and 10 of 'The guidelines manual' (see the Availability of Companion Documents field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The analysis aimed to estimate the cost-effectiveness of strong opioids in patients with advanced and progressive disease for whom previous treatments have failed. The systematic review identified that there were few relevant studies conducted in this area. Furthermore, those studies that were identified had serious limitations and were considered only partially applicable to the guideline. Thus, a new economic evaluation was conducted.

The clinical evidence review showed that oral sustained-release oxycodone and oral sustained-release morphine were equal in effectiveness terms (nine out of nine studies showed no statistically significant differences in pain relief and four out of five studies showed no statistically significant differences in side effects). Thus, economic modelling was not required for this comparison and a decision on cost-effectiveness could be made purely on the basis of the cost of treatment. Thus, since oral sustained-release morphine is cheaper than oral sustained-release oxycodone, oral sustained-release morphine is the more cost-effective treatment option (i.e. provides the same benefit but at a lower cost).

The clinical review for oral sustained-release morphine versus transdermal buprenorphine did not identify any studies that were of a high enough quality to be used as the basis for an economic model.

The clinical review for oral sustained-release morphine versus transdermal fentanyl did identify significant differences in effectiveness between the studies. Thus, economic modelling was conducted for this comparison. The base case results of the model suggest that, at a cost-effectiveness threshold of £20,000 per quality-adjusted life-year (QALY), transdermal fentanyl is not cost-effective against oral sustained-release morphine at all time points.

The one-way sensitivity analysis that was conducted showed that the model was sensitive to changes in the average maintenance dose, the utility decrement associated with constipation and the probability of discontinuation following a constipation event. However, the incremental cost-effectiveness ratio (ICER) result in all analyses remained above £30,000 and so oral sustained-release morphine remained the more cost-effective treatment in all the analyses considered.

Threshold analysis was conducted on the switching cost required to attain cost-effectiveness at a threshold of £20,000 per QALY. The results showed that switching costs of £3,086 and £1,873 would be required when considering the base case scenario and the scenario with an increased utility decrement (0.20), respectively. These were considerably higher than even the highest switching costs expected by the Guideline Development Group members.

The probabilistic sensitivity analyses (PSA) showed considerable variation around the mean result. However, at a threshold of £20,000 per QALY there was only a 14% probability that transdermal fentanyl would be cost-effective against oral sustained-release morphine.

Refer to Appendix E of the full version of the original guideline document for further details.

refer to Appendix F of the full version of the original guideline document for further details.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline was validated through two consultations.

1. The first draft of the guideline (the full guideline and National Institute for Health and Clinical Excellence [NICE] guideline) were consulted with stakeholders and comments were considered by the Guideline Development Group (GDG)
2. The final consultation draft of the full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the Availability of Companion Documents field for the full version of this guidance.

Communication

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

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

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

Starting Strong Opioids – Titrating the Dose

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.

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.

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.

Seek specialist advice before prescribing strong opioids for patients with moderate to severe renal or hepatic impairment.

First-line Maintenance Treatment

Offer oral sustained-release morphine as first-line maintenance treatment to patients with advanced and progressive disease who require strong opioids.

Do not routinely offer transdermal patch formulations as first-line maintenance treatment to patients in whom oral opioids are suitable.

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

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.

and analgesic requirements are stable, supported by specialist advice where needed.

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

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

Offer oral immediate-release morphine for the first-line rescue medication of breakthrough pain in patients on maintenance oral morphine treatment.

Do not offer fast-acting fentanyl as first-line rescue medication.

If pain remains inadequately controlled despite optimising treatment, consider seeking specialist advice.

Management of Constipation

Inform patients that constipation affects nearly all patients receiving strong opioid treatment.

Prescribe laxative treatment (to be taken regularly at an effective dose) for all patients initiating strong opioids.

Inform patients that treatment for constipation takes time to work and adherence is important.

Optimise laxative treatment for managing constipation before considering switching strong opioids.

Management of Nausea

Advise patients that nausea may occur when starting strong opioid treatment or at dose increase, but that it is likely to be transient.

If nausea persists, prescribe and optimise anti-emetic treatment before considering switching strong opioids.

Management of Drowsiness

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.

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

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

Clinical Algorithm(s)

The full version of the original guideline document includes a care pathway for management of patients with advanced and progressive disease requiring strong opioids (step 3 of World Health Organization [WHO] pain ladder).

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

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Safe and effective prescribing of strong opioids for pain in palliative care of adults with advanced and progressive disease requiring strong opioids (step 3 of World Health Organization [WHO] pain ladder)

Potential Harms

Side effects of opioids include constipation, nausea, and drowsiness.

See section 3 in the full version of the original guideline document (see the Availability of Companion Documents field) for additional details on potential harms associated with recommendations.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Clinical Excellence (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.
- This guideline assumes that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Clinical Excellence (NICE) has developed tools to help organisations implement this guidance (see <http://guidance.nice.org.uk/CG140> ⁵).

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Patient Resources

Resources

Slide Presentation

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 May. 23 p. (Clinical guideline; no. 140).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 May

Guideline Developer(s)

National Collaborating Centre for Cancer - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Clinical Excellence (NICE)

Guideline Committee

Guideline Development Group

Composition of Group That Authored the Guideline

Guideline Development Group Members: Dr Damien Lonason (*Chair*). Consultant Liaison Psychiatrist and Honorary Senior

Lecturer, University of Manchester; Dr Catherine Stannard, Consultant in Pain Medicine, Frenchay Hospital, Bristol; Professor Mike Bennett, St Gemma's Professor of Palliative Medicine, University of Leeds; Catherine Piggin, Lead Clinical Nurse Specialist, Prospect Hospice, Swindon; Dr Lindsay Smith, General Practitioner, Somerset; Dr Joy Ross, Consultant in Palliative Medicine, Royal Marsden & Royal Brompton NHS Foundation Trusts, London; Dr Mark Taubert, Consultant in Palliative Medicine, Marie Curie Centre Penarth & Velindre NHS Trust, Cardiff; Mrs Margaret Gibbs, Senior Specialist Pharmacist, St Christopher's Hospice, London; Miss Anna-Marie Stevens, Macmillan Nurse Consultant Cancer Palliative Care, Royal Marsden NHS Trust, London; Natalie Laine, Patient and carer member; Vivien Pipe, Patient and carer member

Financial Disclosures/Conflicts of Interest

Declarations of Interests

Dr Damien Longson (*Chair*): No interests declared.

Dr Catherine Stannard: No interests declared.

Professor Mike Bennett: Received fee for masterclass on neuropathic pain assessment. Funded by Pfizer. Classified as personal pecuniary non-specific.

Mrs Catherine Piggin: No interests declared.

Dr Lindsay Smith: No interests declared.

Dr Joy Ross: No interests declared.

Dr Mark Taubert: No interests declared.

Mrs Margaret Gibbs: No interests declared.

Miss Anna-Marie Stevens: No interests declared.

Mrs Natalie Laine: No interests declared.

Ms Vivien Pipe: No interests declared.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

Availability of Companion Documents

The following are available:

- Opioids in palliative care. Safe and effective prescribing of strong opioids for pain in palliative care of adults. Full guideline. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 May. 85 p. (Clinical guideline; no. 140). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Opioids in palliative care. Safe and effective prescribing of strong opioids for pain in palliative care of adults. Appendices. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 May. Various p. (Clinical guideline; no. 140). Electronic copies: Available in PDF from the [NICE Web site](#).
- NICE pathways. Opioids in palliative care overview. Electronic copies: Available from the [NICE Web site](#).
- Opioids in palliative care. Costing report. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 May. 14 p. (Clinical guideline; no. 140). Electronic copies: Available in PDF from the [NICE Web site](#).
- Opioids in palliative care. Costing template. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 May. (Clinical guideline; no. 140). Electronic copies: Available from the [NICE Web site](#).
- Opioids in palliative care: information for patients clinical audit tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 May. (Clinical guideline; no. 140). Electronic copies: Available from the [NICE Web site](#).
- Opioids in palliative care: initiating drug treatment clinical audit tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 May. (Clinical guideline; no. 140). Electronic copies: Available from the [NICE Web site](#).
- Opioids in palliative care: initiating drug treatment electronic audit tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 May. (Clinical guideline; no. 140). Electronic copies: Available from the [NICE Web site](#).
- Opioids in palliative care. Baseline assessment tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012. (Clinical guideline; no. 140). Electronic copies: Available from the [NICE Web site](#).
- Opioids in palliative care. Clinical case scenarios for primary and secondary care. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Jun. 58 p. (Clinical guideline; no. 140). Electronic copies: Available in PDF from the [NICE Web site](#).
- Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults. Slide set. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Jun. 114 p. (Clinical guideline; no. 140). Electronic copies: Available from the [NICE Web site](#).
- Opioids in palliative care. Podcast. Available from the [NICE Web site](#).

The guidelines manual 2009. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009. 15p

- The guidelines manual 2009. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Jan. Electronic copies: Available in PDF from the [NICE Web site](#).

Patient Resources

The following is available:

- Managing pain with strong opioids in people with advanced, progressive disease. Understanding NICE guidance. Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 May. 12 p. Electronic copies: Available from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This summary was completed by ECRI Institute on June 27, 2012.

The National Institute for Health and Clinical Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their clinical guidelines with the intention of disseminating and facilitating the implementation of that guidance. NICE has not yet verified this content to confirm that it accurately reflects that original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE clinical guidelines are prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk.

Copyright Statement

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion-criteria.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.