



Complete Summary

GUIDELINE TITLE

Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Jun. 23 p. (Technology appraisal guidance; no. 145).

GUIDELINE STATUS

This is the current release of the guideline.

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SCOPE

DISEASE/CONDITION(S)

Locally advanced squamous cell cancer of the head and neck

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Oncology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost-effectiveness of cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck

TARGET POPULATION

Patients with locally advanced squamous cell cancer of the head and neck

INTERVENTIONS AND PRACTICES CONSIDERED

Cetuximab in combination with radiotherapy

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
 - Duration of locoregional control
 - Overall survival
 - Progression-free survival
 - Overall response rate
 - Adverse effects
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT 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Searches of Unpublished Data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): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Centre for

Health Economics, University of York and National Health Service (NHS) Northern and Yorkshire Regional Drug and Therapeutics Centre (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Search Strategy

A systematic literature search was undertaken by the ERG to verify the completeness of the methodology used by the manufacturer to retrieve relevant clinical studies presented in the submission. Although the ERG identified no trials additional to those identified by the manufacturer, the ERG felt that the details of the search strategy provided in the manufacturer's submission were inadequate (a detailed critique is presented in Appendix 1 of the ERG report [see the "Availability of Companion Documents" field]), and carried out a literature search in accordance with the recommendations of NICE. The following databases were searched: Medline, Embase, Medline (R) In-Process, and Cochrane Database of Systematic Reviews.

The following databases were searched for current/ongoing research: Cancer research UK, National Cancer Research Network, Current Controlled Trials register (searched across multiple registers, including, ISRCTN, MRC NHS, and the National Institutes of Health registers), proceedings of the American Society for Clinical Oncology, National Research Register, National Cancer Institute and Scirus, using the free text term 'Head & Neck.'

The inclusion and exclusion criteria and the search strategy used by the ERG are included in Appendix 2 of the ERG report (see the "Availability of Companion Documents" field).

Cost-Effectiveness

Existing Cost-Effectiveness Evidence

As part of the manufacturer's submission a systematic search was undertaken with the aim of identifying all studies evaluating the cost-effectiveness of cetuximab for head and neck squamous cell carcinoma (SCCHN). The date range and sources searched to identify the primary studies were appropriate for this purpose. The results of the search identified no studies which met the inclusion criteria.

The searches undertaken by the manufacturer were replicated by the ERG in order to validate the evidence base considered. The ERG found that the search was reproducible, and the results were consistent with the original search. However, some of the search terms used by the manufacturer would not have retrieved records as intended. Using the same strategy but amending the search terms resulted in more records being identified. However, none of these was deemed by the ERG to match the inclusion criteria. Therefore, the ERG concurs with the manufacturer that there are no existing published cost-effectiveness studies evaluating the use of cetuximab for SCCHN.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

One randomized controlled trial was included.

Cost-Effectiveness

A manufacturer's model was submitted.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Centre for Health Economics, University of York and National Health Service (NHS) Northern and Yorkshire Regional Drug and Therapeutics Centre (see the "Availability of Companion Documents" field).

Clinical Effectiveness

The manufacturer included only one randomised controlled trial (the trial by Bonner et al, *Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck*. N Engl J Med, 2006. 354 (6):p. 567-78.) The trial data are summarized in Table 4.1 of the ERG report (see the "Availability of Companion Documents" field). The trial was subjected to a detailed critical appraisal (presented in Appendix 3 of the ERG report [see the "Availability of Companion Documents" field]), which was then compared with the data presented in the submission.

Cost-Effectiveness

Overview of Manufacturer's Economic Evaluation

The manufacturer's submission is based on a *de-novo* economic evaluation to estimate the cost-effectiveness of treatment with 1) radiotherapy and 2) cetuximab plus radiotherapy. The model uses individual patient data from the Bonner *et al* trial to estimate costs and health effects during the trial period for each patient. Where the data are censored the model extrapolates costs and health effects.

Sensitivity Analyses

The manufacturer's submission includes one-way sensitivity analysis and stochastic sensitivity analysis based on a bootstrapping approach.

Model Validation

The submission claims the cure model used to impute censored progression-free and overall survival has been validated by providing details of a Weibull model fitted to the data which shows the cure model results are conservative towards the cetuximab plus radiotherapy arm, and an exponential model to show that it is consistent with the cure approach.

Critique of the Manufacturer's Economic Evaluation

The ERG has considered the methods applied in the manufacturer's economic evaluation in the context of the critical appraisal questions listed in Table 5.4 of the ERG report (see the "Availability of Companion Documents" field). A critical review of the methods used in the manufacturer's economic evaluation has been undertaken.

Refer to Sections 5.3 - 5.5 of the ERG report (see the "Availability of Companion Documents" field) for details on manufacturer's economic evaluation and its critique by ERG.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under

review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The manufacturer's submission presented a *de novo* economic analysis that compared cetuximab plus radiotherapy with radiotherapy alone. The model used individual patient data from the randomised controlled trial (RCT) to estimate costs and health effects during the trial period for each patient. When trial observations were censored, the model extrapolated costs and health effects.

The base-case analysis compared cetuximab plus radiotherapy with radiotherapy alone and resulted in an incremental cost-effectiveness ratio (ICER) of 6400 pounds sterling per quality-adjusted life year (QALY) gained. The manufacturer undertook a univariate sensitivity analysis, which demonstrated that the model was not sensitive to change when assessing the effect of uncertainty in a variety of inputs. Relatively large variability was observed when the timeframe of the analysis changed from a lifetime to the period of the trial follow-up, resulting in an ICER of 20,000 pounds sterling per QALY gained.

The Evidence Review Group (ERG) reviewed the economic model and identified a number of concerns. The most important of these was that the only RCT informing the economic analysis (the Bonner trial [Bonner et al, *Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck*. N Engl J Med, 2006. 354(6): p. 567-78.]) did not match the patient population specified in the manufacturer's decision problem.

In addition, the ERG identified a series of issues and uncertainties about the methods for extrapolation of the trial data, assessment of health-related quality of life (HRQoL), and estimation of resource use and costs. The ERG concluded that the methods used were probably appropriate but was unable to determine, in the majority of cases, the likely influence of using alternative methods on the results of the economic model. However, the ERG concluded that altering the method of extrapolation would be unlikely to cause the ICER to increase to above 20,000 pounds sterling.

The ERG felt that although the economic analyses undertaken by the manufacturer demonstrated that cetuximab in combination with radiotherapy was cost effective compared with radiotherapy alone under a broad range of different assumptions (assuming a threshold of 20,000 pounds sterling per QALY), the cost-effectiveness estimates might not be directly applicable to the population specified in the manufacturer's decision problem.

Following an appeal hearing, the Appeal Panel requested that the manufacturer provide subgroup survival data (derived from the Bonner trial) for each of the separate Karnofsky performance-status score subgroups (Karnofsky performance-status scores of 100%, 90%, 80%, 70% and less than 70%). The manufacturer stated that the number of patients in some of the subgroups was small (numbers ranged from 12 to 91), and this should be taken into consideration when interpreting these data. For patients with Karnofsky performance-status scores of 100% and 90%, the survival hazard ratios (HRs) were in favour of cetuximab plus radiotherapy over radiotherapy alone. For patients with Karnofsky performance-status scores of 80%, 70% and less than 70%, the survival HRs were in favour of radiotherapy alone over cetuximab plus radiotherapy.

The manufacturer was further asked by the Appeal Panel to provide cost-effectiveness estimates for the subgroup analyses described above. The analyses were conducted using the manufacturer's original cost-effectiveness model. The manufacturer's analysis gave ICERs for cetuximab in combination with radiotherapy versus radiotherapy alone of 13,151 pounds sterling and 4,467 pounds sterling per additional QALY gained for patients with Karnofsky performance-status scores of 100% and 90%, respectively. For patients with Karnofsky performance-status scores of 70%, radiotherapy alone dominated

cetuximab in combination with radiotherapy (that is, radiotherapy alone was more effective in terms of QALYs gained and was less expensive). For patients with Karnofsky performance-status scores of 80% and less than 70%, the manufacturer reported ICERs for cetuximab in combination with radiotherapy versus radiotherapy alone of 58,200 pounds sterling and 37,000 pounds sterling per additional QALY gained, respectively.

The Committee considered the ICER presented by the manufacturer in its original submission and the ERG's original comments. The Committee noted that the ICER of 6400 pounds sterling for cetuximab in combination with radiotherapy versus radiotherapy alone was robust to the main sensitivity analyses. The Committee considered the ICERs presented by the manufacturer for each Karnofsky performance-status score subgroup separately. It noted that the ICERs for patients with a score of 90% or greater were favourable and similar to the overall estimate in the base case. The Committee was persuaded that although there was uncertainty about the number of patients within the subgroups who would have met the criteria to receive chemoradiotherapy, cetuximab in combination with radiotherapy is cost effective for patients with a Karnofsky performance-status score of 90% or greater and for whom chemoradiotherapy is not an option. However, for those with a Karnofsky performance-status score of 80% or less, the HR for survival did not favour cetuximab and therefore the ICERs were unfavourable. The Committee therefore was unable to recommend cetuximab for people with low performance status.

Refer to Sections 3 and 4 of the original guideline document for details of the economic analyses provided by the manufacturer, the ERG comments, and the Appraisal Committee considerations.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Cetuximab in combination with radiotherapy is recommended as a treatment option only for patients with locally advanced squamous cell cancer of the head and neck whose Karnofsky performance-status score is 90% or greater and for whom all forms of platinum-based chemoradiotherapy treatment are contraindicated.

Patients currently receiving cetuximab in combination with radiotherapy for the treatment of locally advanced squamous cell cancer of the head and neck who do not meet the criteria outlined in the above section should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

When using Karnofsky performance-status score, clinicians should be mindful of the need to secure equality of access to treatment for patients with disabilities. Clinicians should bear in mind that people with disabilities may have difficulties with activities of daily living that are unrelated to their prognosis with respect to cancer of the head and neck. In such cases clinicians should make appropriate judgements of performance status taking into account the person's usual functional capacity and requirement for assistance with activities of daily living.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on a single randomized controlled trial and a *de novo* economic analysis.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck

POTENTIAL HARMS

The most common side effects of cetuximab are mild or moderate infusion-related reactions such as fever, chills, nausea, vomiting, headache, dizziness or dyspnoea that occur soon after the first cetuximab infusion. Skin reactions develop in more than 80% of patients and mainly present as an acne-like rash or, less frequently, as pruritus, dry skin, desquamation, hypertrichosis or nail disorders (for example, paronychia). The majority of skin reactions develop within the first 3 weeks of therapy.

For full details of side effects and contraindications, see the summary of product characteristics (SPC).

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance represents the view of the Institute, 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. The guidance does not, however, 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.
- 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 which would be inconsistent with compliance with those duties.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organizations in meeting core and developmental standards set by the Department of Health in "Standards for better health" issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by the National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- "Healthcare Standards for Wales" was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.
- NICE has developed tools to help organisations implement this guidance (listed below). These are available on the NICE website (www.nice.org.uk//TA145 [see also the "Availability of Companion Documents" field]).
 - Costing report and costing template to estimate the savings and costs associated with implementation
 - Audit support for monitoring local practice

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides

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

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Jun. 23 p. (Technology appraisal guidance; no. 145).

ADAPTATION

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

DATE RELEASED

2008 Jun

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Professor David Barnett, Professor of Clinical Pharmacology, University of Leicester; Dr David W Black, Director of Public Health, Derbyshire County PCT; Mr Brian Buckley, Chairman, Incontact; Dr Carol Campbell, Senior Lecturer, University of Teesside; Professor Mike Campbell, Professor of Medical Statistics, University of Sheffield; Professor David Chadwick, Professor of Neurology, Liverpool University; Dr Peter Clarke, Consultant Medical Oncologist, Clatterbridge Centre for Oncology, Merseyside; Ms Jude Cohen, Manager of Resources & Administration, United Kingdom Council for Psychotherapy (UKCP); Dr Christine Davey, Senior Researcher, North Yorkshire Alliance Research and Development Unit; Dr Mike Davies, Consultant Physician, Manchester Royal Infirmary; Mr Richard Devereaux-Phillips, Public Affairs Manager, Medtronic; Dr Rachel A Elliott, Lord Trent Professor of Medicines and Health, University of Nottingham; Mrs Eleanor Grey, Lay member; Dr Dyfrig Hughes, Senior Research Fellow in Pharmacoeconomics, Centre for the Economics of Health and Policy in Health, University of Wales; Dr Catherine Jackson, Clinical Lecturer in Primary Care Medicine, Alyth Health Centre; Dr Peter Jackson, Clinical Pharmacologist, University of Sheffield; Professor Peter Jones, Pro Vice Chancellor for Research & Enterprise, Professor of Statistics, Keele University; Ms Rachel Lewis, Practice Development Facilitator, Manchester PCT; Damien Longson, Consultant in Liaison Psychiatry, North Manchester General Hospital; Professor Jonathan Michaels, Professor of Vascular Surgery, University of Sheffield; Dr Eugene Milne, Deputy Medical Director, North East Strategic Health Authority; Dr Simon Mitchell, Consultant Neonatal Paediatrician, St Mary's Hospital, Manchester; Dr Richard Alexander Nakielny, Consultant Radiologist, Royal Hallamshire Hospital, Sheffield; Dr Katherine Payne, Health Economics Research Fellow, University of Manchester; Dr Martin J Price, Head of Outcomes Research, Janssen-Cilag; Dr Philip Rutledge, GP and Consultant in Medicines Management, NHS Lothian; Mr Miles Scott, Chief Executive, Bradford Teaching Hospitals NHS Foundation Trust; Professor Mark Sculpher, Professor of Health Economics, University of York; Professor Andrew Stevens, Chair of Appraisal Committee C; Dr Cathryn Thomas, GP and Associate Professor, University of Birmingham; Mr William Turner, Consultant Urologist, Addenbrookes Hospital, Cambridge

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Jun. 2 p. (Technology appraisal 145). Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck. Costing template and report. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Jun. Various p. (Technology appraisal 145). Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck. Audit support. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. 5 p. (Technology appraisal 145). Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Cetuximab plus radiotherapy for the treatment of locally advanced squamous cell cancer of the head and neck. Evidence review group's report. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Feb. 85 p. (Technology appraisal 145). Available in Portable Document Format (PDF) from the [NICE Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1608. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Jun. 4 p. (Technology appraisal 145).

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

Print copies: Available from the NHS Response Line 0870 1555 455. ref: N1609. 11 Strand, London, WC2N 5HR.

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

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