Complete Summary

GUIDELINE TITLE

Tacrolimus and pimecrolimus for atopic eczema.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Tacrolimus and pimecrolimus for atopic eczema. London (UK): National Institute for Clinical Excellence (NICE); 2004 Aug. 45 p. (Technology appraisal; no. 82).

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references drugs for which important revised regulatory information has been released.

On January 20, 2006, U.S. Food and Drug Administration (FDA) announced the approval of updated labeling for two topical eczema drugs, Elidel Cream (pimecrolimus) and Protopic Ointment (tacrolimus). The labeling will be updated with a boxed warning about a possible risk of cancer and a Medication Guide (FDA-approved patient labeling) will be distributed to help ensure that patients using these prescription medicines are aware of this concern. The new labeling also clarifies that these drugs are recommended for use as second-line treatments. This means that other prescription topical medicines should be tried first. Use of these drugs in children under 2 years of age is not recommended. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **
SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Atopic eczema

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Dermatology
Family Practice
Internal Medicine
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To assess the effectiveness and cost-effectiveness of pimecrolimus and tacrolimus for atopic eczema treatment relative to current standard treatments (emollients and topical corticosteroids)

TARGET POPULATION

Adults and children aged 2 years and older with atopic eczema

INTERVENTIONS AND PRACTICES CONSIDERED

1. Tacrolimus
2. Pimecrolimus

MAJOR OUTCOMES CONSIDERED

- Effectiveness (immediate response rates, sustained response rates, avoidance of flares)
- Duration of treatment; changes in therapy
- Adverse effects of interventions
- Quality of life
- 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 assessment report. The assessment report for this technology appraisal was prepared by the Peninsula Technology Assessment Group (PenTAG) (see the "Companion Documents" field).

Search Strategy

Electronic databases were searched for published studies and recently completed and ongoing research. Appendix 3 of the assessment report details the databases searched and the full search strategy (see the "Companion Documents" field). Bibliographies were also searched for further relevant publications. Experts in the field and the manufacturers of pimecrolimus and tacrolimus were asked to provide relevant information. The Trial Coordinator of the Cochrane Skin Group, searched their Skin Registry for randomised controlled trials of pimecrolimus or tacrolimus against any comparator.

Identification of Trials

Identification of relevant trials was made in two stages. Initially, the abstracts returned by the search strategy were examined independently by two researchers. Disagreements were resolved by discussion. Full texts of the identified studies were obtained. Two researchers examined these independently for inclusion or exclusion and disagreements were resolved by discussion.

Inclusion Criteria and Exclusion Criteria

Studies were included in the review if they fulfilled the following criteria:

Interventions:

- Pimecrolimus for the treatment of mild to moderate atopic eczema
- Tacrolimus for the treatment of moderate to severe atopic eczema

Comparator:

Current standard treatment--topical corticosteroids in conjunction with emollients and emollients alone were considered as comparators.

Population:

Adults and children (aged two and over) with mild to moderate (pimecrolimus) or moderate to severe (tacrolimus) atopic eczema (the licensed indications)

Study Design:

Systematic reviews or randomised controlled trials (RCTs)

Exclusion

Populations without atopic eczema, including those with a diagnosis of:

- Eczema secondary to other inherited or acquired disorders of immunodeficiency
- Seborrhoeic eczema
- Allergic or irritant contact eczema
- Nummular (discoid) eczema
- Fungal or parasitic skin infections
- Cutaneous T-cell lymphoma

Study Design:

- Non-randomised studies, case-control studies, case series, or case reports
- Studies on other types of eczema
- Studies in which insufficient details about baseline characteristics or methodology were given to allow quality assessment (e.g., conference abstract)
- Pre-clinical and biological experimentation in vitro, in animal models, or in humans
- Studies not reporting patient based outcomes
- Studies not available in English

Although the protocol suggested that systemic treatments would also be considered as comparators, strong clinical opinion was given that these were not appropriate comparators for pimecrolimus or tacrolimus and so have not therefore been considered as alternatives.

Data Extraction Strategy

Data were extracted by one researcher and checked by another. Actual numbers were extracted where possible (see Appendices 5 and 6 in the assessment report) and, where necessary, analyses were recalculated on an intent to treat basis using the number of patients randomised as the denominator. Such analyses retain the minimisation of bias provided by randomisation but provide the most conservative estimates of effectiveness.

NUMBER OF SOURCE DOCUMENTS

Nine publications relating to eight randomised controlled trials (RCTs) of pimecrolimus were included. Twelve publications reporting on ten trials of tacrolimus were included.

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

Meta-Analysis of Randomized Controlled Trials
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 assessment report. The assessment report for this technology appraisal was prepared by the Peninsula Technology Assessment Group (PenTAG) (see the "Companion Documents" field).

Methods of Analysis

Study results were tabulated. Where statistical significance was not reported for differences in proportions, these were calculated by the Peninsula Technology Assessment Group (PenTAG) at a 0.05 level using Confidence Interval Analysis software and are presented in the text (see "Companion Documents" field).

Meta-analyses were undertaken using random effects models for trials of similar intervention (for example tacrolimus versus topical corticosteroids) in order to estimate a weighted treatment effect across trials. A random effects model was used throughout in order to avoid the assumption of a single underlying treatment effect. Although this approach is more conservative it is less sensitive to underlying statistical heterogeneity. All meta-analyses were performed in the Cochrane Collaboration's Review Manager 4.2.2 (2003). Effectiveness on dichotomous outcomes was estimated with relative risk ratios (RR) and 95% confidence intervals (CI). Continuous outcomes were presented as standardised mean differences (SMD). Heterogeneity was tested using a $\bullet^2$ test with significant heterogeneity indicated by $p<0.05$. The analysis was stratified by age (adult or child), the nature of the intervention, and by duration of treatment.

The main outcome for trials of pimecrolimus was treatment success, measured as the proportion whose eczema was "clear" or "almost clear" (score 0-1) according to the Investigator's Global Assessment (IGA) compared to those who scored two or more. For tacrolimus a dichotomous outcome was created from reported results

using the Physician's Global Evaluation (PGE) of 90% or better (the categories of "Clear" and "Excellent Improvement", score 0-1) compared to the rest.

Pruritus score was measured on a scale of 0 (none) to 3 (severe) and treatment success was assumed to mean no or mild pruritus (score 0-1).

The incidence of skin infections was analysed for tacrolimus using a combined rate for bacterial and viral infections as the presentation of data did not allow their separation. In pimecrolimus, results are presented separately for bacterial and viral infections. Incidence of skin burning was also analysed as this outcome was presented consistently across the trials.

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 Committee considered economic analyses submitted by the manufacturers of both products and a model developed by the Assessment Group (see the "Companion Documents" field). There was only one relevant published economic analysis and this was conducted from the perspective of the US healthcare system and had methodological problems that limited its value. The Assessment Group analysis consisted of eight separate models, each relating to different cohorts of people with atopic eczema. See Section 4.2 of the original guideline document for a detailed discussion and more information.

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

- Topical tacrolimus and pimecrolimus are not recommended for the treatment of mild atopic eczema or as first-line treatments for atopic eczema of any severity.
- Topical tacrolimus is recommended, within its licensed indications, as an option for the second-line treatment of moderate to severe atopic eczema in adults and children aged 2 years and older that has not been controlled by topical corticosteroids (see below), where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.
- Pimecrolimus is recommended, within its licensed indications, as an option for the second-line treatment of moderate atopic eczema on the face and neck in children aged 2 to 16 years that has not been controlled by topical corticosteroids (see below), where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.
- For the purposes of this guidance, atopic eczema that has not been controlled by topical corticosteroids refers to disease that has not shown a satisfactory clinical response to adequate use of the maximum strength and potency that is appropriate for the patient's age and the area being treated.
- It is recommended that treatment with tacrolimus or pimecrolimus be initiated only by physicians (including general practitioners) with a special interest and experience in dermatology, and only after careful discussion with the patient about the potential risks and benefits of all appropriate second-line treatment options.

Clarification Released 2004 Dec 9

In respect to the final point in the above guidance, the Institute confirms that it recommends that pimecrolimus and tacrolimus are initiated only by physicians (including general practitioners) who have achieved specific recognition in the field of eczema care (e.g., have been formally recognized through their Primary Care Trust as having a special interest and experience in dermatology). However, methods of accreditation may vary locally and the guidance does not stipulate that accreditation must necessarily be achieved through the general practitioner with special interest (GPwSI) framework.

CLINICAL ALGORITHM(S)

None provided

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

Appropriate use of tacrolimus and pimecrolimus for the treatment of atopic eczema

POTENTIAL HARMS

- Tacrolimus: Side effects include a burning or tingling sensation, pruritus, erythema, folliculitis, herpes simplex infection, acne, increased sensitivity to hot and cold, and alcohol intolerance. Lymphadenopathy has also been reported.
- Pimecrolimus: Side effects include a burning sensation, pruritus, erythema, skin infections (including folliculitis and rarely impetigo, herpes simplex and zoster and molluscum contagiosum), papilloma (rarely), and local reactions such as pain, paraesthesia, peeling, dryness, oedema, and worsening of eczema.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Tacrolimus: Contraindications include pregnancy, infected lesions, and exposure to long periods of sunlight or artificial sunlight. Those with rare skin diseases such as Netherton's syndrome in which the skin's barrier properties are affected may also be contraindicated due to increased risk of significant percutaneous absorption. Vaccinations cannot be given during treatment and for some time afterwards--28 days for live attenuated vaccines and 14 days for inactivated vaccines.
- Pimecrolimus: Contraindications include pregnancy, infected lesions, viral infections (such as warts, chicken pox, herpes simplex), prolonged exposure to sunlight and artificial sunlight, and Netherton's syndrome. The cream should not be applied to mucous membranes or eyes.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Audit

- All clinicians who care for people with atopic eczema should review their current practice and policies to take account of the guidance set out in Section 1 of the original guideline document (and the "Major Recommendations" field).
- Local guidelines or care pathways for people with atopic eczema should incorporate the guidance.
- To measure compliance locally with the guidance, the following criteria could be used. Further details on suggestions for audit are presented in Appendix C of the original guideline document.
    - Topical tacrolimus and pimecrolimus are not prescribed for the treatment of mild atopic eczema or as first-line treatments for atopic eczema of any severity.
    - Topical tacrolimus is considered, within its licensed indications, as an option for the second-line treatment of moderate or severe atopic eczema in adults and children aged 2 years and older that has not been controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.
    - Pimecrolimus is considered, within its licensed indications, as an option for the second-line treatment of moderate atopic eczema on the face and neck in children aged 2 to 16 years that has not been controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.
    - Treatment with tacrolimus or pimecrolimus is initiated only by a physician with a special interest and experience in dermatology.
    - Treatment with tacrolimus or pimecrolimus is initiated only after careful discussion between the prescribing physician and the patient about the potential risks and benefits of all appropriate second-line treatment options.
- Local clinical audits could also include measurement of compliance with recognised guidelines for the management of atopic eczema and the effectiveness of patient education on the use of treatments for atopic eczema.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Foreign Language Translations
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

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Tacrolimus and pimecrolimus for atopic eczema. London (UK): National Institute for Clinical Excellence (NICE); 2004 Aug. 45 p. (Technology appraisal; no. 82).

ADAPTATION

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

DATE RELEASED

2004 Aug

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence - 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

Dr Darren Ashcroft, Senior Clinical Lecturer, School of Pharmacy and Pharmaceutical Sciences, University of Manchester; Professor David Barnett, Professor of Clinical Pharmacology, University of Leicester; Mr Brian Buckley, Vice Chairman, InContact; Professor John Cairns, Professor of Health Economics, Health Economics Research Unit, University of Aberdeen; Professor Mike Campbell, Statistician, Institute of General Practice & Primary Care, Sheffield; Dr Mark Chakravarty, Head of Government Affairs and NHS Policy, Procter and

Gamble Pharmaceuticals (UK) Ltd, Egham, Surrey; Dr Peter I Clark, Consultant Medical Oncologist, Clatterbridge Centre for Oncology, Wirral, Merseyside; Dr Mike Davies, Consultant Physician, University Department of Medicine & Metabolism, Manchester Royal Infirmary; Mr Richard Devereaux-Phillips, Public Affairs Manager, Medtronic Ltd; Professor Jack Dowie, Health Economist, London School of Hygiene; Professor Gary A Ford (Vice-Chair), Professor of Pharmacology of Old Age/Consultant Physician, Newcastle upon Tyne Hospitals NHS Trust; Dr Fergus Gleeson, Consultant Radiologist, The Churchill Hospital, Oxford; Ms Sally Gooch, Director of Nursing, Mid-Essex Hospital Services NHS Trust, Chelmsford; Professor Trisha Greenhalgh, Professor of Primary Health Care, University College London; Miss Linda Hands, Clinical Reader in Surgery, University of Oxford; Professor Peter Jones, Professor of Statistics and Dean, Faculty of Natural Sciences, Keele University; Professor Robert Kerwin, Professor of Psychiatry and Clinical Pharmacology, Institute of Psychiatry, London; Ms Joy Leavesley, Senior Clinical Governance Manager, Guy's and St Thomas' NHS Trust; Ms Rachel Lewis. Staff Nurse (Nephrology), Hull Royal Infirmary; Dr Ruairidh Milne, Senior Lecturer in Public Health, National Coordinating Centre for Health Technology Assessment, University of Southampton; Dr Neil Milner, General Medical Practitioner, Sheffield; Dr Rubin Minhas, General Practitioner with a Special Interest in Coronary Heart Disease, Primary Care CHD Lead, Medway PCT & Swale PCT; Mr Miles Scott, Chief Executive, Harrogate Health Care NHS Trust; Professor Mark Sculpher, Professor of Health Economics, University of York; Dr Ken Stein, Senior Lecturer, Peninsula Technology Assessment Group (PenTAG), University of Exeter; Professor Andrew Stevens (Chair), Professor of Public Health, University of Birmingham

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) from the National Institute for Health and Clinical Excellence (NICE) Web site.

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

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Tacrolimus and pimecrolimus for atopic eczema. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2004 Aug. 2 p. (Technology appraisal 82). Electronic copies: Available in

Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

- The effectiveness and cost-effectiveness of pimecrolimus and tacrolimus for atopic eczema. Assessment report. Exeter (UK): Peninsula Technology Assessment Group (PenTAG); 2004 Jan 26. 281 p. (Technology appraisal 82). Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Clarification of guidance on the use of tacrolimus and pimecrolimus for atopic eczema. London (UK): National Institute for Health and Clinical Excellence (NICE); 2004 Dec 9. Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

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

Additionally, Audit Criteria can be found in Appendix C of the original guideline document.

PATIENT RESOURCES

The following is available:

- Tacrolimus and pimecrolimus for atopic eczema: understanding NICE guidance - information for people with atopic eczema, their families and carers, and the public. London: National Institute for Health and Clinical Excellence. 2004 Aug. 10 p. Available in English and Welsh in Portable Document Format (PDF) 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 NGC summary was completed by ECRI on October 6, 2005. This summary was updated by ECRI on January 31, 2006, following release of a public health advisory from the U.S. Food and Drug Administration regarding the use of Elidel Cream (pimecrolimus) and Protopic Ointment (tacrolimus).

The National Institute for Health and Clinical Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their Technology Appraisal guidance with the intention of disseminating and facilitating the implementation of that guidance. NICE has not verified this content to confirm that it accurately reflects the original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE technology appraisal guidance is

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.aspx.

NGC, AHRQ, and its contractor ECRI 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, 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.

© 1998-2006 National Guideline Clearinghouse

Date Modified: 9/25/2006