Complete Summary

GUIDELINE TITLE

Guidance on the use of photodynamic therapy for age-related macular degeneration.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Guidance on the use of photodynamic therapy for age-related macular degeneration. London (UK): National Institute for Clinical Excellence (NICE); 2003 Sep. 26 p. (Technology appraisal; no. 68).

GUIDELINE STATUS

This is the current release of the guideline.

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SCOPE

DISEASE/CONDITION(S)

Age-related macular degeneration (ARMD)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Family Practice
Geriatrics
Internal Medicine
Ophthalmology
Optometry

INTENDED USERS

Advanced Practice Nurses
Health Plans
Managed Care Organizations
Optometrists
Physician Assistants
Physicians
Public Health Departments
Utilization Management

GUIDELINE OBJECTIVE(S)

To establish the clinical and cost-effectiveness of photodynamic therapy (PDT) for the neovascular form of wet age-related macular degeneration (ARMD)

TARGET POPULATION

Adult patients (18 or over) with the neovascular form of wet age-related macular degeneration (ARMD)

INTERVENTIONS AND PRACTICES CONSIDERED

Photodynamic therapy

Note: At present only verteporfin (Visudyne), a benzoporphyrin derivative, is available for this indication, but other agents are in development

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Visual acuity
    - Contrast sensitivity
    - Quality of life
    - Side effects of treatment
- 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Searches of Unpublished Data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 appraisal was prepared by the West Midlands Health Technology Assessment Group, Department of Public Health and Epidemiology, The University of Birmingham (see the "Companion Documents" field).

Clinical Effectiveness Review

Data Sources

As the authors of the Assessment Report had completed a systematic review on the same subject within the previous year, no formal scoping search was undertaken. This systematic review was used as the basis for the protocol for this technology assessment, which was undertaken in accordance with the pre-defined protocol. The following sources were searched:

- Bibliographic databases: Cochrane Library 2001 Issue 3; MEDLINE (Ovid) 1993-Aug 2001; EMBASE (Ovid) 1993-Aug 2001; Science Citation Index (Web of Science) 1993-Sept 2001; National Research Register and MRC current controlled trials register - September 2001
- National and international health technology assessment (HTA) sites -- (International Association for Health Technology Assessment [INAHTA], National Horizon Scanning Centre [NHSC], Canadian Co-ordinating Office for Health Technology Assessment [CCOHTA], Danish Institute for Health Technology Assessment [DIHTA], Norwegian Centre for Health Technology Assessment [SMM], July 2001)
- Conference abstracts, (Association for Research in Vision and Ophthalmology [ARVO] 1999, 2000, 2001, European Society of Ophthalmology [SOE] 2001)
- Internet sites (Novartis, Visudyne. [Novartis Ophthalmics, Switzerland])
- Citations of all relevant articles found and the data outline sent to us by Novartis separately from the industry submission.

Inclusion and Exclusion Criteria

One reviewer, using explicit predetermined criteria, made the inclusion and exclusion decisions. These were checked by a second reviewer. Inclusion and exclusion decisions were made independently of the inspection of trial results.

Trials and studies were only included if they met the following criteria:

- Study design: Randomised controlled trials
- Population: Adults with wet age-related macular degeneration (ARMD)
- Intervention: Photodynamic therapy (PDT) using any photosensitive drug

- Comparator: Either no treatment (best supportive care) for subfoveal lesions or laser photocoagulation for juxtafoveal or extrafoveal lesions
- Outcomes: Any of visual acuity, contrast sensitivity, quality of life, side effects of treatment
- Reporting: Only trials where recruitment had closed and which reported follow up results for all or nearly all recruited patients were included

The exclusion criteria were:

1. Randomised controlled trials (RCT) that had not finished recruiting
2. RCTs that had published only baseline characteristics or follow up results for a small proportion of the trial participants
3. Studies carried out on animals

Although items 1, 2 and 3 above were excluded from the analysis of clinical effectiveness, their presence was noted as essential background to the review. Note that although new treatments (anecortave acetate and transpupillary thermotherapy [TTT]) are potential comparators to PDT, it was considered that their development is at too early a stage to merit listing in the inclusion criteria.

Costs and Cost Effectiveness Review

A systematic review of the literature on costs, health economic impact and generic quality of life outcomes of PDT for AMD was carried out. Costs studies include studies reporting primary research on the costs and utilisation of care and cost studies that discuss economic aspects of care and contain useful primary or secondary cost or utilisation data.

The review of economic studies followed the method of Mugford and has subsequently been established in other reviews.

Search

A specific search strategy for information on costs, cost effectiveness and quality of life involved searches of:

- Bibliographic databases: MEDLINE (Ovid) 1993-Aug 2001; NHS Economic Evaluation Database (NHS EED) and the NHS Database of Reviews of Effectiveness (DARE)
- Internet sites of national economics units

Relevant information found during the clinical effectiveness searches was also used. Any economic analysis submitted as part of the Industry submission to NICE could also potentially be included.

The search was broadened to find information to inform the economic model. Searches focused on finding relevant economic information on laser photocoagulation and other possible treatments for AMD, the natural course of wet AMD without treatment and of the consequences of blindness.

Inclusion and Exclusion Criteria, Data Extraction and Quality Assessment

One reviewer, using explicit predetermined criteria, made the inclusion and exclusion decisions for the cost effectiveness review and this was checked by a second researcher. Studies were only included if they met the following criteria:

- Study design: Any study type
- Population: Adults with any AMD
- Intervention: PDT using any photosensitive drug
- Outcomes: Costs, cost consequences, cost utility, cost effectiveness or any generic quality of life

One researcher extracted data from the included studies and a second researcher again checked this.

There were 3 stages used for the review of cost and economic studies. In Stage 1 each study was categorised by one of the investigators on the basis of its title and abstract where available, according to five classification criteria. Studies that were categorised into the relevant classification for this review proceeded to Stage 2. In Stage 2 all potentially relevant studies were read in full and further classified. All papers confirmed as being relevant to this review proceeded to Stage 3. In Stage 3 all relevant articles were assessed according to predetermined quality criteria. The quality of the economic evaluations was assessed according to predetermined criteria. The quality of the cost studies was assessed using predetermined criteria.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

The clinical effectiveness searches identified 417 references. Six randomised controlled trials (RCTs) of photodynamic therapy (PDT) in wet age-related macular degeneration (AMD) were ultimately found of which four are ongoing and two completed. These six were considered as included for the purposes of demonstrating coverage of areas relevant to current and future assessment of the effectiveness of PDT in wet AMD. Only the two completed were considered as included for the purposes of analysing the current evidence on effectiveness of PDT for wet AMD.

Cost Effectiveness

In brief the search identified 64 (plus 7 duplicates) articles that were potentially relevant to this review. Five papers were identified by other means such as personal communications. Only two economic evaluations reached Stage 3 of the review. Both passed the quality assessment and are included. Four cost studies were identified initially but only 3 reached Stage 3 of the review and none of them passed the quality assessment stage. Details of these three studies are given in Appendix 9 of the Assessment Report (see "Companion Documents" field.

Thus two studies were included, to which was added the economic analysis section of the industry submission to the National Institute for Health and Clinical Excellence (NICE).

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 assessment report. The assessment report for this appraisal was prepared by the West Midlands Health Technology Assessment Group, Department of Public Health and Epidemiology, The University of Birmingham (see the "Companion Documents" field).

Data Extraction and Quality Assessment Strategies

Two researchers independently extracted the effectiveness and quality assessment data from all included studies, using predefined criteria. Any discrepancies were recorded and resolved by discussion. The quality of the included studies was assessed using the Jadad scale.

Synthesis of Results

The main method of synthesis was qualitative, supplemented by further quantitative analysis and synthesis where appropriate using Review Manager software version 4.1.

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

Cost Effectiveness

The Appraisal Committee considered three estimates of the cost effectiveness of verteporfin photodynamic therapy (PDT): one was performed by the Assessment Group, another was commissioned by the manufacturer and submitted for this appraisal, and a third was found in the published literature. All three evaluations expressed the benefits of treatment in terms of quality adjusted life years (QALYs). The values of the QALYs were derived from a study that related utility (health-related quality of life) to visual acuity in the better-seeing eye. Thus, the assumption that patients were receiving treatment in their better-seeing eye was inherent in all the analyses. The analyses by the Assessment Group and in the manufacturer's submission included costs to the National Health Service (NHS) and personal social services. The published study was from North America, and the costs included in that assessment reflect the organization of healthcare in the United States. This limited its applicability to the evaluation of cost effectiveness in the NHS.

See Section 4.2 of the original guideline document for a detailed discussion of the cost-effectiveness analysis.

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

- Photodynamic therapy (PDT) is recommended for the treatment of wet age-related macular degeneration for individuals who have a confirmed diagnosis of **classic with no occult** subfoveal choroidal neovascularisation (CNV) (that is, whose lesions are composed of classic CNV with no evidence of an occult component) and best-corrected visual acuity 6/60 or better. PDT should be carried out only by retinal specialists with expertise in the use of this technology.
- PDT is not recommended for the treatment of people with **predominantly classic** subfoveal CNV (that is, 50% or more of the entire area of the lesion is classic CNV but some occult CNV is present) associated with wet age-related

macular degeneration, except as part of ongoing or new clinical studies that are designed to generate robust and relevant outcome data, including data on optimum treatment regimens, long-term outcomes, quality of life, and costs.
- The use of PDT in **occult** CNV associated with wet age-related macular degeneration was not considered because the photosensitising agent (verteporfin) was not licensed for this indication when this appraisal began. No recommendation is made with regard to the use of this technology in people with this form of the condition.
- Patients currently receiving treatment with PDT could experience loss of well-being if their treatment is discontinued at a time they did not anticipate. Because of this, all National Health Service (NHS) patients who have begun a course of treatment with PDT at the date of publication of this guidance should have the option of continuing to receive treatment until their clinical condition indicates that it is appropriate to stop.

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 photodynamic therapy for treatment of age-related macular degeneration

POTENTIAL HARMS

Some patients treated with verteporfin photodynamic therapy (PDT) have reported visual disturbances (abnormal vision, decreased vision, visual field defect) after treatment. Some of these disturbances involved severe loss of vision. In most patients who experienced severe loss of vision after verteporfin PDT there was partial or complete recovery of vision to baseline values. Other adverse effects reported in clinical trials of verteporfin PDT included infusion-related pain--primarily presenting as back pain--and photosensitivity reactions in the form of sunburn following exposure to sunlight, usually within 24 hours of treatment.

For full details of side effects and contraindications, see the Summary of Product Characteristics available at http://emc.medicines.org.uk/.

CONTRAINDICATIONS

CONTRAINDICATIONS

Verteporfin is contra-indicated in patients with porphyria, severe liver impairment, or known hypersensitivity to verteporfin or any other component of the infusion, including egg proteins, or who are breastfeeding. It is produced from porcine hemin as a starting material so vegetarians and people of Muslim and Jewish faiths should be notified. It should not be used in people with uncontrolled high blood pressure, unstable cardiovascular disease, active hepatitis or moderate to severe liver disease. Concomitant medications that reduce the effectiveness of liver catabolism may prolong systemic photosensitivity.

For full details of side effects and contraindications, see the Summary of Product Characteristics available at http://emc.medicines.org.uk/.

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 judgment. 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

- Clinicians who provide care for people with wet age-related macular degeneration (ARMD) should review local practice and policies regarding the use of photodynamic therapy (PDT) to take account of the guidance (see "Major Recommendations" field).
- Local guidelines, protocols or care pathways that refer to the care of people with wet ARMD should incorporate the guidance in Section 1 of the original guideline.
- To measure compliance locally with the guidance, the following criteria can be used. Further details on suggestions for audit are presented in Appendix C of the original guideline.
    - PDT is provided to individuals with wet ARMD in either of the following circumstances.
        - The individual has a confirmed diagnosis of classic with no occult subfoveal choroidal neovascularisation (CNV) and best-corrected visual acuity 6/60 or better.
        - The individual is receiving treatment with PDT at the date of publication of this guidance and opts to continue to receive treatment until his or her clinical condition indicates that it is appropriate to stop.
    - PDT is carried out only by a retinal specialist with expertise in its use.
    - An individual who has predominantly classic CNV associated with wet ARMD and is not already receiving treatment is not provided with PDT, unless the individual is participating in an appropriately designed clinical study.

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

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Guidance on the use of photodynamic therapy for age-related macular degeneration. London (UK): National Institute for Clinical Excellence (NICE); 2003 Sep. 26 p. (Technology appraisal; no. 68).

ADAPTATION

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

DATE RELEASED

2003 Sep

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: Dr Jane Adam, Radiologist, St George's Hospital, London; Dr Sunil Angris, General Practitioner, Waterhouses Medical Practice, Staffordshire; Dr Darren Ashcroft, Senior Clinical Lecturer, School of Pharmacy and Pharmaceutical Sciences, University of Manchester; Professor David Barnett (*Chair*) Professor of Clinical Pharmacology, University of Leicester; Professor Carol Black (up to June 2002) Consultant Physician, Royal Free Hospital & University College London; Professor John Brazier, Health Economist, University of Sheffield; 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 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; Professor Cam Donaldson, PPP Foundation Professor of Health Economics, School of Population and Health Sciences & Business School, Business School -- Economics, University of Newcastle upon Tyne; Professor Jack Dowie, Health Economist, London School of Hygiene; Dr Paul Ewings, Statistician, Taunton & Somerset NHS Trust, Taunton; 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; Ms Ruth Lesirge, Lay Representative, previously Director, Mental Health Foundation, London; Dr George Levvy, Lay Representative, Chief Executive, Motor Neurone Disease Association, Northampton; Dr Gill Morgan, Chief Executive, NHS Confederation, London; Professor Miranda Mugford (up to November 2002) Health Economist, University of East Anglia, Norwich; Ms Siân Richards (up to December 2002) Chief Executive, Cardiff Local Health Board; Professor Philip Routledge, Professor of Clinical Pharmacology, College of Medicine, University of Wales, Cardiff; Dr Rhiannon Rowsell, (up to December 2002) Medical & Regulatory Affairs, Director, AstraZeneca UK Ltd, Luton; Dr Stephen Saltissi, Consultant Cardiologist, Royal Liverpool University Hospital; Mr Miles Scott, Chief Executive, Harrogate Health Care NHS Trust; Professor Andrew Stevens (*Vice-Chair*) Professor of Public Health, University of Birmingham; Professor Ray Tallis (up to January 2003) Consultant Physician, Hope Hospital, Salford; Professor Mary Watkins, Professor of Nursing, University of Plymouth; Dr Norman Waugh, Department of Public Health, University of Aberdeen

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:

- Photodynamic therapy for age-related macular degeneration. Summary. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Sep. 2 p. (Technology appraisal 68). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Clinical effectiveness and cost utility of photodynamic therapy for wet age-related macular degeneration. Assessment report. NHS R&D HTA Programme; 2002 Jan. 109 p. 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. ref: N0304. 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:

- The use of photodynamic therapy for age-related macular degeneration. Understanding NICE guidance -- information for people with age-related macular degeneration, their families and carers, and the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Sep. 14 p. (Technology appraisal 68).

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 Department of Health Publications Order Line 0870 1555 455. ref: N0305. 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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