

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

Technology Appraisal Guidance 68

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

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This guidance is written in the following context:

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.

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1 Guidance

- 1.1 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.
- 1.2 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.
- 1.3 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.
- 1.4 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 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.

2 Clinical need and practice

- 2.1 Age-related macular degeneration (ARMD) is characterised by irreversible damage to the central part of the retina (the macula) resulting in progressive loss of central vision. Peripheral vision is not affected, so individuals retain some useful vision. The condition has two forms, dry (non-exudative or non-neovascular) and wet (exudative or neovascular). The wet form is characterised by the development of new blood vessels beneath the retina, known as choroidal neovascularisation (CNV). CNV can be subdivided into classic and occult forms according to its appearance on investigation by fluorescein angiography. The classic form is associated with more rapid progression than the occult form.
- 2.2 Classic and occult CNV can occur within the same lesion. The following terms are generally used to describe the composition of the lesion.
- **‘Classic with no occult’** – lesions that are composed of classic CNV with no evidence of an occult component.
 - **‘Predominantly classic with occult’** – lesions in which 50% or more of the entire area is classic CNV but some occult CNV is present.
 - **‘Minimally classic’** – lesions in which less than 50% but more than 0% of the area is classic CNV.
 - **‘Occult only’** – lesions in which there is occult CNV with no evidence of classic CNV.
- 2.3 CNV lesions are also classified according to their location relative to the fovea (the area at the centre of the macula that is associated with colour vision and perception of fine detail and where there are no blood vessels to interfere with vision). CNV lesions that extend under the fovea are described as subfoveal.
- 2.4 ARMD usually occurs in people over 50 years of age. On the basis of limited epidemiological data, it is estimated that each year in England and Wales there may be 5000 to 7500 new cases of predominantly classic subfoveal CNV associated with wet ARMD. However, there is a high degree of uncertainty about this estimate.

- 2.5 In people with the wet form of ARMD, the newly formed blood vessels may leak fluid and blood, leading to scar formation and permanent damage to the macula. Individuals lose visual acuity (that is, the ability to detect fine details or small distances) and contrast sensitivity (that is, the ability to see less-well-defined objects, such as faces, clearly). They may also experience distortion of vision, where the edges of objects and straight lines appear wavy. Wet ARMD usually progresses from a localised lesion to an end stage involving the entire macula, with complete or near-complete loss of central vision. It has been estimated that 70% of eyes with CNV will have severe loss of vision within 2 years of diagnosis.
- 2.6 Central vision loss particularly impairs the perception of fine visual detail and colours. Thus, activities such as reading, recognising faces and driving are affected. Significant loss of independence may occur. Rapidly deteriorating vision has an impact on emotional well-being, and individuals are likely to suffer depression and anxiety due to their loss of vision and reduction in independence. However, there is a great deal of individual variation in the ability to cope with loss of vision.
- 2.7 For most patients with ARMD, management consists of 'best supportive care'. Visual rehabilitation, with teaching of skills and the provision of equipment to facilitate reading and other activities of daily living, may help people make the most of their remaining vision. However, the availability of these services is limited, and not everyone has access to high-quality visual rehabilitation.

3 The technology

- 3.1 The aim of photodynamic therapy (PDT) is to destroy CNV lesions without damaging the overlying retina, thereby slowing or halting the progression of vision loss. The treatment involves the infusion of a light-sensitive agent, followed by light activation of the drug. At present only verteporfin (Visudyne), a benzoporphyrin derivative, is available for this indication, but other agents are in development.
- 3.2 Verteporfin is given by intravenous infusion over 10 minutes, at a dose of 6 mg/m² of body surface area. Fifteen minutes after the start of the infusion, a low-powered laser calibrated to a specific wavelength is applied over a circular area slightly larger than the lesion. The laser is not powerful enough to cause any damage on its own, but the light is

absorbed by the drug, which is 'activated', resulting in the formation of cytotoxic free radicals. These free radicals damage the new blood vessels, which may result in their closure.

- 3.3 In ARMD, verteporfin PDT is licensed for patients with predominantly classic (see Section 2.2) subfoveal CNV. The marketing authorisation has recently been extended to include patients with CNV that is entirely composed of the occult form. However, the clinical and cost effectiveness of PDT in this indication has not been considered in this appraisal.
- 3.4 The use of PDT in conditions other than ARMD is outside the scope of this appraisal.
- 3.5 A 15-mg vial of verteporfin (sufficient for one PDT treatment) costs £850 (excluding VAT *British National Formulary* 45, March 2003). Patients are re-evaluated every 3 months using fluorescein angiography. If CNV leakage is present, they are offered retreatment.

4 Evidence and interpretation

The Appraisal Committee (see Appendix A) considered evidence from a number of sources, including the Assessment Report, submissions by consultees, and views put forward at the meeting by clinical experts and representatives of patient/carer organisations (see Appendix B).

See Section 2.2 for definition of the terms 'predominantly classic', 'minimally classic' and 'classic with no occult' CNV.

4.1 Clinical effectiveness

- 4.1.1 Two randomised, double-blind, placebo-controlled trials of verteporfin PDT were identified: treatment of age-related macular degeneration with PDT, the 'TAP' study; and verteporfin in PDT, the 'VIP' study. Although the TAP study involved two simultaneous trials using identical protocols, the results have been presented together, and for the purposes of this appraisal it has been treated as one study.
- 4.1.2 The TAP study included patients with ARMD and subfoveal CNV with some evidence of classic CNV, and best-corrected visual acuity between 6/12 and 6/60. Visual acuity of 6/12 means that someone can see at 6 metres the same line of

letters that a person with 'normal' (6/6) vision could see at 12 metres. This is relatively mild visual impairment. Similarly, someone with visual acuity of 6/60 can see at 6 metres what someone with normal vision could see at 60 metres. This corresponds to severely impaired vision. The VIP study was in two parts. One part included patients with CNV related to pathological myopia and was therefore outside the scope of this appraisal. The other part included patients with ARMD, although most had the occult form of CNV (only 6% had predominantly classic CNV).

- 4.1.3 Both studies found less deterioration in visual acuity in the PDT-treated group than in the placebo-treated group. In the TAP trial at 24 months, 47% (95% confidence interval [CI], 42% to 52%) of eyes treated with verteporfin PDT had lost 15 or more letters of visual acuity compared with 62% (95% CI, 56% to 69%) of placebo-treated eyes. For the VIP study in ARMD, the corresponding figures were 54% (95% CI, 47% to 60%) and 67% (95% CI, 58% to 75%). The loss of 15 letters of visual acuity corresponds to being able to read three fewer lines on a standard eye-test chart.
- 4.1.4 A subgroup analysis of the TAP data found that the treatment effect was larger in the 40% of patients (242 of 609) with predominantly classic CNV than in those with minimally classic CNV. In the 'predominantly classic' subgroup at 2 years, 41% (95% CI, 33% to 49%) of eyes treated with verteporfin PDT had lost 15 or more letters of visual acuity compared with 69% (95% CI, 59% to 79%) of placebo-treated eyes. This is the basis of the licensed indication. In patients with minimally classic CNV, verteporfin PDT appeared to have no benefit relative to placebo.
- 4.1.5 The treatment effect was larger in the group of patients whose lesions had no evidence of an occult component (that is, classic with no occult CNV). In these patients at 2 years, 30% (95% CI, 21% to 39%) of eyes treated with verteporfin PDT had lost 15 or more letters of visual acuity compared with 71% (95% CI, 59% to 84%) of placebo-treated eyes. This subgroup included 93 patients in the verteporfin group and 49 in the placebo group (25% of the trial population). The effect in the 'classic with no occult' subgroup was statistically significant relative to the effect in patients with any occult CNV ($p < 0.001$).
- 4.1.6 A further finding from the TAP trial was that PDT with verteporfin reduced the loss of contrast sensitivity – the extent to which this reduction contributes to the effect of verteporfin PDT on quality of life has not been quantified. In

addition, improvement in distortion of vision has been reported anecdotally, but this aspect of the condition was not assessed in the clinical trials.

- 4.1.7 Some patients treated with verteporfin 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.
- 4.1.8 Overall, verteporfin was found to improve the chance of avoiding appreciable loss of vision (loss of 15 or more letters of visual acuity) over a period of 2 years.

4.2 Cost effectiveness

- 4.2.1 The Appraisal Committee considered three estimates of the cost effectiveness of verteporfin 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 NHS and personal social services. The published study was from North America, and the costs included in that assessment reflect the organisation of healthcare in the USA. This limited its applicability to the evaluation of cost effectiveness in the NHS.
- 4.2.2 All three economic evaluations were based on data from the TAP study. The Assessment Group used the whole trial data to estimate effectiveness, whereas the manufacturer's submission and the published evaluation based estimates on data from the subgroup of patients with predominantly classic subfoveal CNV.

- 4.2.3 The Assessment Group's economic evaluation estimated that it would cost between £151,000 and £182,000 to gain one additional QALY over 2 years (the duration of the TAP study). The Assessment Group did not extrapolate the estimate of cost effectiveness beyond 2 years. However, decline in visual acuity was assumed to be linear with time in both treated and placebo groups. This does not take into account the fact that the change in visual acuity was greatest in the early part of the TAP study and that the difference between treated and placebo groups was established during the first year of treatment. A recalculation, correcting for this assumption of linearity, produced a cost-effectiveness estimate of approximately half that in the original submission, in the region of £80,000 per additional QALY at 2 years.
- 4.2.4 The manufacturer's submission estimated the cost effectiveness to be approximately £70,500 per additional QALY at 2 years for people with predominantly classic CNV. The model also estimated cost effectiveness beyond 2 years. This required some assumptions about long-term outcomes to be incorporated because the clinical trials were only 2 years in duration, although the model was supported by follow-up data from a third year for some of the patients in the TAP study. The model was based on effectiveness data in the subgroup with predominantly classic CNV, and assumed that: a proportion of patients would not respond and would receive no more than two treatments; all patients would receive no further treatment after 42 months; and visual acuity would remain relatively stable after treatment. Using the assumptions regarding long-term outcome and continuation of treatment in this model resulted in continually improving cost effectiveness over time. For example, the manufacturer's model suggested that by 5 years the cost per additional QALY could have fallen to about £33,000, and by 7 years to about £25,000.
- 4.2.5 The published estimate of cost effectiveness was between £61,000 and £122,000 (US \$86,700–173,900, converted to pounds sterling at 2000 rates) per additional QALY at 2 years. The estimate was dependent on visual acuity at the start of therapy. The lower cost per additional QALY was obtained if the patient was assumed to have reasonably good vision in the better-seeing eye at the start of treatment (best-corrected visual acuity 6/12), while the higher estimate was obtained if the patient was assumed to have relatively poor vision in the better-seeing eye at the start of treatment (best-corrected visual acuity 6/60). This analysis also estimated cost effectiveness beyond 2 years. The model assumed that the effectiveness of the treatment would

decline with time by 10% per year. At 11 years (the estimated average life expectancy of patients in the TAP trial), the cost per additional QALY had fallen to £30,600 (\$43,500) for a patient with good initial visual acuity, and to £61,300 (\$87,200) for a patient with poor initial visual acuity.

- 4.2.6 None of the above models considered the cost effectiveness of PDT in the subgroup of patients with classic with no occult CNV. Notwithstanding the general concerns about the validity of basing estimates of effectiveness on subgroup analyses (see Section 4.3.2), given the biological plausibility of a different effect in classic versus occult CNV and the larger treatment effect observed (see Section 4.1.5), an adjustment to the Assessment Group's model was made using the 2-year results from the TAP study. The paper reported subgroup data only for the primary endpoint (loss of 15 or more letters). Therefore, as the model contained seven possible visual acuity outcomes, estimates had to be made for the subgroup of the rates of other possible visual acuity outcomes (loss of 30 or more letters, loss of between 15 and 29 letters, loss of between 5 and 14 letters, no change, gain of between 5 and 14 letters, gain of between 15 and 29 letters, or gain of 30 or more letters). This was done by adjusting the probabilities for each of the above outcomes for the whole trial population on the basis of the relative risk for the primary endpoint data (that is, loss of 15 or more letters) for the subgroup.
- 4.2.7 On the basis of these estimates of effectiveness of PDT in people with classic with no occult CNV, the cost per additional QALY of treating individuals in this subgroup was between £10,000 and £57,000 at 2 years, depending on the assumptions regarding progression of the disease with and without treatment over the trial period. More specifically, the estimate of £10,000 was based on the assumption that change in visual acuity occurred immediately, at the beginning of the trial period, whereas the estimate of £57,000 was based on the assumption that change occurred gradually over the 2-year period. A third scenario, in which visual acuity was assumed to change most rapidly during the first year and remain relatively stable during the second year, produced a cost per additional QALY of £26,000. This third scenario reflected the progress of the patients in the TAP study most closely, and was viewed by the Appraisal Committee as being the most reasonable estimate of cost effectiveness for this subgroup.

- 4.2.8 This estimate of £26,000 per additional QALY at 2 years was scrutinised further by the manufacturer, and further modelling was undertaken on behalf of the manufacturer and submitted to the Committee for consideration. This analysis included the use of more detailed information on the pertinent patient subgroups from the TAP trial, and an extrapolation of the TAP trial results to 5 years using further data from the extension study of the TAP trial. This additional analysis generated a cost per QALY gained at 2 years of £23,000 for people with classic with no occult CNV and £55,000 for all people with predominantly classic CNV. At 5 years, these cost-effectiveness ratios reduced to around £8500 for people with classic with no occult CNV and £34,000 for the whole predominantly classic group. The analysis also demonstrated that for people with predominantly classic CNV with any element of occult CNV (that is, excluding people with classic with no occult CNV), the estimated cost per additional QALY was about £164,000 at 2 years and about £120,000 at 5 years.

4.3 *Consideration of the evidence*

- 4.3.1 The Committee reviewed the evidence available on the clinical and cost effectiveness of PDT for wet ARMD, having considered evidence from people with ARMD, those who represent them, and clinical experts, on the nature of the condition and the value placed by users on the avoidance of loss of vision. It was also mindful of the need to ensure that its advice took account of the effective use of NHS resources.
- 4.3.2 The Committee noted that the licensed indication for PDT, and two of the three cost-effectiveness analyses, were based on data from the subgroup with predominantly classic subfoveal CNV in the TAP trial. The Committee considered that, in general, subgroup analyses should be interpreted with caution even if, as was the case with these subgroups, they have been identified a priori as part of the trial protocol. Such analyses may exaggerate the potential treatment benefit and may provide a much less sound basis for an estimate of effectiveness than the results of a whole trial. The Committee accepted, however, that a difference in response according to specific types of lesion composition was a biologically plausible assumption on which to base the predetermined subgroup analyses. Two of the subgroup analyses performed on the data from the TAP study were based on lesion composition. One compared the effectiveness of PDT in treating predominantly classic CNV with its effectiveness in treating minimally classic CNV (the basis of

the licensed indication; see Section 4.1.4). The other compared the effectiveness of PDT in treating classic with no occult CNV with its effectiveness in treating classic lesions with any proportion of occult CNV. The Committee found the latter analysis more convincing than the former, in terms of biological plausibility and because of the higher degree of statistical significance for this subgroup analysis (see Section 4.1.5). On the basis of this information, the Committee concluded that PDT appears to have a larger treatment effect in patients with classic with no occult CNV.

- 4.3.3 The Committee was persuaded that for the classic with no occult subgroup, on the basis of the reported enhanced clinical effectiveness of PDT (see Section 4.1.5), the cost effectiveness of this treatment is likely to be considerably greater than for the whole of the predominantly classic subgroup, and very considerably greater than for the subgroup of people with predominantly classic with some occult CNV (see Sections 4.2.6 to 4.2.8). Therefore, on the basis of current evidence, the Committee concluded that PDT was likely to be cost effective for people with classic with no occult CNV but not for those with predominantly classic with some occult CNV.
- 4.3.4 The Committee also noted the considerable uncertainties surrounding the cost-effectiveness estimates, which might increase or decrease their value. In particular, the Committee noted that the utilities might not fully take into account the beneficial effects of treatment on contrast sensitivity, that the utility estimates were based on visual acuity in the better-seeing eye and that the entire duration of treatment effect is not known. The Committee considered that even accounting for these potential uncertainties and taking the most optimistic view of the utility gain from effects of PDT on contrast sensitivity, its view on the relative cost effectiveness of the subgroups considered in Section 4.3.3 would not be materially affected.
- 4.3.5 The Committee considered the effect of visual acuity at baseline on the overall cost effectiveness of treatment. One of the economic evaluations suggested that the treatment was more cost effective in patients with good best-corrected visual acuity at baseline (6/12) than in patients with poor visual acuity (6/60) (see Section 4.2.5). However, in the absence of evidence to indicate a level of visual acuity below which treatment is no longer worthwhile, the Committee concluded that treatment was indicated in patients with classic with no occult CNV whose best-corrected visual acuity was 6/60 or better. This was the minimum level of visual

acuity required for entry into the TAP study. There is no evidence of the effectiveness of PDT in patients with greater impairment of visual acuity.

- 4.3.6 The Committee heard from experts in the field and carefully discussed with them the considerable uncertainty about the most appropriate treatment regimen for PDT. In view of the high cost of each PDT treatment, a key issue in determining cost effectiveness is the number of treatments received by patients. In the TAP study, patients received further treatment if there was evidence of CNV leakage on fluorescein angiography, regardless of whether their visual acuity had deteriorated further. It is uncertain whether it is necessary to continue treatment once vision has stabilised, even if CNV leakage, as defined by fluorescein angiography, is still present. Neither is it known whether further treatment is indicated if visual acuity declines significantly despite treatment, nor whether a regimen involving more frequent treatment in the early phase might be more effective. The Committee also heard from experts that there was evidence from both published studies and personal clinical observations that considerable interobserver disagreement existed in the correct classification of CNV membrane composition from the results of fluorescein angiography. In particular, the concordance between observers was much better when classifying small classic with no occult lesions than was the case for complex lesions with mixed membrane types. The Committee considered that, in view of the disparity in both clinical and cost effectiveness among the various subgroups of lesion composition, absolute clarity in diagnosis from the angiography was essential to ensure that appropriate groups of patients were treated as indicated in the guidance section. The Committee concluded that a method of confirming the diagnosis of membrane type and composition, such as centralised 'reading centres' for fluorescein angiograms, would help to ensure both accuracy of diagnosis and, through appropriate case selection, the most cost-effective use of PDT.
- 4.3.7 The Committee noted that individuals with predominantly classic with some occult CNV who had already embarked on a course of treatment might experience loss of well-being as a result of unanticipated treatment changes. The Committee therefore considered it appropriate that these patients should continue to receive treatment until their clinical condition indicates that it is appropriate to stop.

5 Recommendations for further research

- 5.1 Several randomised controlled trials of PDT are ongoing, including two placebo-controlled trials of verteporfin PDT, one in patients with minimally classic CNV using standard or reduced laser settings, and one in patients with occult CNV.
- 5.2 The Committee recommended that further research is needed on the use of PDT for individuals with predominantly classic (see Section 2.2) subfoveal CNV related to ARMD. The primary objectives of this research should be to determine the optimum treatment regimen and long-term benefit of PDT, and to add to the current evidence on quality of life for this group of individuals.
- 5.3 At present it is not known whether population screening for ARMD would be practical or cost effective. Research on screening for ARMD is being commissioned by the UK HTA programme.

6 Implications for the NHS

- 6.1 The current best estimate suggests that in England and Wales as many as 5000–7500 new cases of classic with no occult and predominantly classic CNV associated with wet ARMD occur each year. It is not known how many of these would fulfil the criteria for treatment outlined in Section 1.1. In the TAP study, which mostly recruited people whose lesions had some classic component, 23% of patients had classic with no occult lesions. In the most recent report from the PDT users group national surveillance programme, 300 of 757 registered eyes (40%) had classic with no occult CNV. As a guide, treatment of 1000 patients per year with the current PDT regimen would cost in the region of £4 million in the first year, rising to £8.3 million by the third year, and remaining constant thereafter (at current costs, excluding VAT).
- 6.2 Wet ARMD can progress rapidly. For a PDT service to be as effective as possible, individuals with early wet ARMD and without serious loss of vision will need to be fast-tracked through the referral and waiting list processes in order to receive treatment before further loss of vision occurs.

7 Implementation and audit

- 7.1 Clinicians who provide care for people with wet ARMD should review local practice and policies regarding the use of PDT to take account of the guidance set out in Section 1.
- 7.2 Local guidelines, protocols or care pathways that refer to the care of people with wet ARMD should incorporate the guidance in Section 1.
- 7.3 To measure compliance locally with the guidance, the following criteria can be used. Further details on suggestions for audit are presented in Appendix C.
- 7.3.1 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 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.
- 7.3.2 PDT is carried out only by a retinal specialist with expertise in its use.
- 7.3.3 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 (see Section 1.2).

8 Related guidance

- 8.1 There is no related guidance for this technology.

9 Review of guidance

- 9.1 The review date for a technology appraisal refers to the month and year in which the Guidance Executive will consider any new evidence on the technology, in the form of an updated Assessment Report, and decide whether the technology should be referred to the Appraisal Committee for review.
- 9.2 The guidance on this technology will be reviewed in September 2006.

Andrew Dillon
Chief Executive
September 2003

Appendix A

Appraisal Committee members and NICE project team

A. Appraisal Committee members

NOTE The Appraisal Committee is a standing advisory committee of the Institute. Its members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. The Appraisal Committee meets twice a month other than in December, when there are no meetings. The Committee membership is split into two branches, with the chair, vice-chair and a number of other members attending meetings of both branches. Each branch considers its own list of technologies and ongoing topics are not moved between the branches.

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.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declaration of interests, are posted on the NICE website.

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
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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
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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

B. NICE Project Team

Each appraisal of a technology is assigned to a Health Technology Analyst and a Technology Appraisal Project Manager within the Institute.

Dr Alec Miners
Technical Lead,
NICE project team

Janet Robertson
Technical Lead,
NICE project team

Nina Pinwill
Project Manager,
NICE project team

Appendix B

Sources of evidence considered by the Committee

The following documentation and opinions were made available to the Committee:

- A** The assessment report for this appraisal was prepared by West Midlands Health Technology Assessment Group, Department of Public Health and Epidemiology, The University of Birmingham:

Meads C, Hyde C, Salas C, et al, *Clinical effectiveness and cost utility of photodynamic therapy for wet age-related macular degeneration*, January 2002

- B** The following organisations accepted the invitation to participate in this appraisal. They were invited to make submissions and comment on the draft scope, assessment report and the appraisal consultation document. Consultee organisations were provided with the opportunity to appeal against the FAD:

I. Manufacturer/sponsors:

- Novartis Pharmaceuticals Ltd

II Professional/specialist and patient/carer groups:

- Age Concern Cymru
- Age Concern England
- British Geriatrics Society
- Department of Health
- The College of Optometrists
- Help the Aged
- The Macular Disease Society
- Royal College of General Practitioners
- Royal College of Nursing Ophthalmic Forum
- Royal College of Ophthalmologists
- Royal National Institute for the Blind
- Sense
- Wales Council for the Blind
- Welsh Assembly Government

III Commentator organisations (without the right of appeal):

- Moorfields Eye Hospital
- NHS Quality Improvement Scotland
- West Hull PCT (formerly East Riding & Hull Health Authority)

C The following individuals were selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups. They participated in the Appraisal Committee discussions and provided evidence to inform the Appraisal Committee's deliberations. They gave their expert personal view on photodynamic therapy by attending the initial Committee discussion and/or providing written evidence to the Committee. They were also invited to comment on the ACD:

- Dr Robert Thompson, Chairman, The Macular Disease Society
- Mr Jonathan Dowler, Consultant Ophthalmologist, Moorfields Eye Hospital
- Professor Alan Bird, Professor of Clinical Ophthalmology, University College London
- Professor Usha Chakravarthy, Professor of Ophthalmology and Vision Science, Queen's University and Royal Victoria Hospitals, Belfast

Appendix C

Detail on criteria for audit of the use of PDT for the treatment of wet ARMD

Possible objectives for an audit

An audit on PDT for the treatment of people with wet ARMD could be carried out to ensure that the technology is used appropriately.

Possible people to be included in an audit

An audit could be carried out on people being seen for treatment of wet ARMD over a suitable time period for audit, for example, 1 year.

Measures that could be used as a basis for audit

The measures that could be used in an audit of PDT for the treatment of wet ARMD are as follows.

Criterion	Standard	Exception	Definition of terms
<p>1. PDT is provided to an individual in the following circumstances:</p> <p>a. The individual has:</p> <p>i) a confirmed diagnosis of classic with no occult subfoveal CNV and</p> <p>ii) best-corrected visual acuity 6/60 or better</p> <p>b. 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</p>	<p>100% of people with wet ARMD who meet the circumstances in 1</p>	<p>A The individual declines PDT</p>	<p>'Classic with no occult subfoveal CNV' means lesions that extend under the fovea with no evidence of an occult component. The diagnosis of classic with no occult subfoveal CNV is made by fluorescein angiography, preferably confirmed at a centralised reading centre where or when such centres are available.</p> <p>Clinicians will need to agree locally on how the information needed is documented for audit purposes.</p>

Criterion	Standard	Exception	Definition of terms
2. PDT is carried out by a retinal specialist with expertise in its use	100% of people receiving PDT	None	Clinicians will need to agree locally on the expertise needed to carry out PDT, for audit purposes.
3. An individual who has predominantly classic CNV associated with wet ARMD is provided with PDT	0% of patients who have predominantly classic CNV associated with wet ARMD	<p>A The individual is participating in a clinical study</p> <p>B 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.</p>	<p>'Predominantly classic' means that 50% or more of the entire area of the lesion is classic CNV but some occult CNV is present.</p> <p>A clinical study is designed to generate robust and relevant outcome data, including data on optimum treatment regimens, long-term outcomes, quality of life and costs.</p> <p>Clinicians will need to agree locally on how the information needed is documented for audit purposes.</p>

Calculation of compliance

Compliance with each measure described in the table is calculated as follows.

$$\frac{\text{Number of people whose care is consistent with the criterion *plus* plus the number of people who meet any exception}}{\text{Number of people to whom the measure applies}} \times 100$$

Clinicians should review the findings of the measurement, identify whether practice can be improved, agree on a plan to achieve any desired improvement, and repeat the measurement of actual practice to confirm that the desired improvement is being achieved.



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