



Pegaptanib and ranibizumab for treatment of age-related macular degeneration (AMD) – Appraisal Consultation Document (ACD)

RNIB and Macular Disease Society

Patient group response

July 2007

Introduction

1. In this document the RNIB and Macular Disease Society respond jointly to the appraisal consultation document (ACD) for Pegaptanib and Lucentis.
2. We find the recommendations in the ACD unacceptable and believe that there should be a thorough reworking of the evidence and assumptions.
3. Our detailed comments are set out in the document. In summary the key points are these:
 - 3.1. The second eye policy for wet AMD patients is an indefensible rationing decision. Outcry about a similar policy that NICE tried to introduce for PDT led to its reversal. There are no sound medical reasons to deny treatment to patients who present with their first eye.
 - 3.2. The decision to exclude pegaptanib was apparently not based on a review of baseline visual acuity. We believe that this should be included in the models used and we agree with the Royal College of Ophthalmologists that clinicians should have the freedom to choose the best available treatment for each individual patient.
 - 3.3. We believe that treatment should be made available for all lesion types. The decision to restrict treatment to 20% of eligible patients by allowing it for only predominantly classic patients has been based on some incorrect cost assumptions leading to unreasonable rationing. Notably the assumption that treatment will be on a day case basis is wrong and does not reflect current practice. While out-patient tariffs are insufficient to cover the full costs of treatment, an appropriate tariff would lie somewhere between the day case scenario and the cost of an out-patient procedure. Using the day case scenario therefore leads to unjustifiably inflated costs.

- 3.4. The ACD does not take adequate account of the costs of blindness and underestimates the take-up of services for blind and partially sighted people. In this document we have expanded our information on these costs which weigh strongly against letting people go blind unnecessarily.

Expansion of our comments

Second eye policy

4. Paragraph 4.3.16 of the ACD is short and leads to the devastating conclusion for patients that AMD, wet or dry, in their first eye should be ignored. They will only be treated when their second eye is affected. It includes this sentence as substantial justification for the policy : 'It understood that the reduction in quality of life of moving from binocular vision to monocular vision was much smaller than the reduction in quality of life from moving from monocular vision to very poor vision'. While we accept that the impact of monocular vision on a person's quality of life is not as severe as the impact of binocular sight loss there are strong arguments against NICE's recommendation to restrict treatment to second eyes.
5. The cursory treatment in the report of this hugely important aspect of who and who not to treat fails to address the factors involved. Unusually for NICE the paragraph is superficial and unscientific. The conclusion implies that treatment of the second eye will invariably be successful and therefore it does not matter that the first eye has been ignored. This is an unjustifiable and dangerous assumption. Patients are subjected to a gamble with their sight. If they lose they become blind in both eyes with all the ensuing social, psychological and medical dependencies which arise for them and their families.
6. First of all, both ranibizumab and pegaptanib are clinically effective in first and second eyes¹. At present, approximately one

¹ Chang, T.: Ranibizumab (Lucentis) Self-reported vision-specific quality of life. 2006 Subspeciality Day. Retina

third of patients present with first eye. Denying treatment to patients who have developed wet AMD in their first eye is not reasonable. Patients with cataracts or glaucoma are treated in their first eye.

7. While there are only few studies of the impact of monocular vision loss on a person's quality of life one study suggests that it may lead to even higher psychological distress than binocular vision loss. This in turn will have an adverse effect on the person's functional ability and quality of life.²
8. The assumption that a “presenting eye” policy is mainly based on ethical grounds is therefore erroneous. It is very much based on the need to safeguard a patient’s quality of life.
9. Furthermore, we would like the Committee to consider a very frequent scenario that illustrates the increased risk of blindness in patients with wet AMD: Patient A has dry AMD in the better seeing eye and has developed wet AMD in the other eye. She is told that no treatment will be provided because the first eye still has good visual acuity. If the patient is then left to lose her sight in the eye that has developed wet AMD and does not develop wet AMD in the other eye she will inevitably go blind since dry AMD is not treatable. The same can happen if she develops wet AMD in the second eye but does not respond to treatment, or if she develops another condition (glaucoma or diabetic retinopathy) or has an accident.
10. It is therefore clear that a decision to restrict treatment for wet AMD to patients who have developed the condition in their second eye cannot be justified on medical or functional grounds.

Use of pegaptanib

11. The ACD recognises that there have not been any head-to-head trials of pegaptanib and ranibizumab and that due to the differences in the trial populations, precise direct comparisons are

² Williams et al.: The psychosocial impact of macular degeneration. Arch Ophthalmol 1998;116:514-520

not possible. We would therefore like the Committee to review its decision to recommend against the approval of pegaptanib for use in the treatment of wet AMD. This is particularly relevant for the group of people with good baseline visual acuity (6/12 to 6/24) where results for pegaptanib have shown a significantly increased chance of vision gain compared with patients with a lower visual acuity at baseline. Baseline visual acuity therefore needs to be included in the cost model for pegaptanib. We recognise that this may lead the Appraisal Committee to recommend the use of pegaptanib in patients with good baseline visual acuity only. However, given the different profiles of the two drugs we continue to support the position of the Royal College of Ophthalmologists that calls for both treatments to be made available without restrictions so that clinicians can decide what treatment is best for individual patients.

Rationing of treatment to exclude all lesions except the 20 per cent of patients with predominantly classic CNV

12. Clinical effectiveness.

12.1. All the evidence presented to NICE suggests that ranibizumab is equally effective for all lesion types. The only reason why subtypes were included in the analysis is to determine whether both pegaptanib and ranibizumab are cost-effective in comparison with PDT, which is only effective in patients with predominantly classic CNV. All cost-effectiveness models and scenarios bar one have shown that ranibizumab is cost-effective in all sub-types. Please find below our arguments why the cost-effectiveness data chosen does not reflect current practice either in relation to the costs of treatment or in relation to the costs of blindness.

13. Cost effectiveness

13.1. To establish the true costs of blindness that should be included we would like to present additional evidence that shows that current costs of blindness are higher than assumed by the Assessment Group even if we use the parameters set by

NICE and do not include additional costs such as loss of productivity, disability benefits and informal care.

14. Registration and continuing ophthalmic care

14.1. Due to the nature of the condition with patients progressing over time from registration as partially sighted to registration as blind, registration is not a one-off event. Once patients have been registered partially sighted they have to continue to be seen by their consultants on a regular basis to monitor their deterioration. Because blind registration is linked to additional benefits (Blind person's personal income tax allowance, reduction of 50 per cent on the television licence fee, car parking concessions, free postage for "articles for the blind" and other entitlements) it is important for patients to establish the level of their sight loss. At present 45 per cent of blind and partially sighted people report that they were registered partially sighted first before being registered as blind.³

14.2. In addition, it is important to recognise that people who are registered blind or partially sighted continue to require ophthalmic care. It is wrong to assume that they are no longer seen by medical professionals (optometrists and ophthalmologists) once the medical treatment for their condition has ceased. They continue to require check-ups and under the GOS eye tests for blind and partially sighted people are free. This explains why 57 per cent of a sample of blind and partially sighted people have seen an optician in the past year and 80 per cent had seen an optician in the past three years.⁴

³ Douglas, G., Corcoran, C and Pavey, S. (2006): Network 1000 – Opinions and circumstances of visually impaired people in Great Britain: report based on over 1000 interviews, Visual Impairment Centre for Teaching and Research (VICTAR), School of Education, University of Birmingham

⁴ Pey, T., Nzegwu, F. and Dooley, G. (2006): Functionality and the Needs of Blind and Partially-Sighted Adults in the UK: An Interim Report, Guide Dogs, November 2006

14.3. This is further confirmed by figures that suggest that 50 per cent of registered blind and partially sighted people are currently attending an eye clinic (as measured by an appointment in the last six months, or an arranged appointment in the future). Of these, the majority visit the eye clinic for a "check up" (92 per cent) and/or "to see the ophthalmologist" (77 per cent).⁵

15. **Take-up of services**

15.1. We welcome the fact that the model recognises that the vast majority of people with wet AMD (95 per cent) will get registered as blind or partially sighted. However, in light of this high rate of registration the suggested take-up figures for people receiving low vision aids and low vision rehabilitation need to be revised.

15.2. The reason for this is that the take-up figures are taken from a study that looks at all people with sight loss, including those with visual acuity better than the current registration threshold of 6/60. Whilst many of these people will benefit from low vision aids and rehabilitation, Social Services do not pay for their services. By contrast every patient certified by an ophthalmologist as blind or partially sighted will be registered with Social Services and 80 per cent will receive an assessment visit by a rehabilitation officer.⁶ Following this, a low vision assessment and appropriate rehabilitation training for daily living skills (including mobility training) is arranged, and carried out, with the provision of non-optical aids such as daylight bulbs, liquid level indicators, UV shields, signature guides, guide/symbol cane, etc. and training in their use.

15.3. The take-up of low vision aids and rehabilitation is therefore likely to be much higher than 33 per cent and 11 per cent respectively, and much more closely correlated with uptake of

⁵ Unpublished data from Phase II of Network 1000. Personal communication from Graeme Douglas, author of Network 1000. June 2007

⁶ See footnote 3

registration. Please see further information below to substantiate this assertion.

16. Low vision aids

16.1. A survey of 500 service users carried out in England and Wales in 2005⁷ showed that a large majority of respondents used canes (66 per cent), hand-held magnifiers (77 per cent) and 63 per cent used other optical aids. In 70 per cent of cases canes were funded by the local authority whereas hand-held magnifiers were funded in 69 per cent and optical aids in 73 per cent of cases. This is confirmed further by another survey⁸, which states that 74 per cent of blind and partially sighted people have been offered a magnifier following their assessment.

16.2. In addition, the more recent network 1000 study reported that 71 per cent of the registered blind and partially sighted population have used magnifiers for reading and the likelihood of using a low vision aid (LVA) increased with age (73 per cent in those aged over 75).⁹

16.3. Equipment funded by local authorities varies considerably. Home adaptations do not seem to have been included in the cost analysis. The equipment most commonly funded here are bump-ons/tactimarks (used by 46 per cent of respondents and funded by 63 per cent of local authorities) and liquid level indicators (used by 57 per cent of respondents and funded by 70 per cent of local authorities). Also, 73 per cent of blind and partially sighted people used better lighting. This is usually included in a needs assessment because of its importance in falls prevention.

⁷ Improving Lives Community Care Campaign, 2005: Equipped for living – improving equipment services for blind and partially sighted people

⁸ Vale, D. (2004): Unseen – neglect, isolation and household poverty amongst older people with sight loss

⁹ See footnote 2

16.4. Not only is the take-up of services higher than estimated, it is also important to recognize that low vision aids are not one-off costs. Given the deterioration of the condition over time, people with AMD require repeat assessments to establish whether they need a different magnifier or other low vision aid. Social Services have a statutory obligation to reassess service users on an annual basis. Where no deterioration has taken place this may be limited to a phone call but under best practice service users are called every six months and receive a full re-assessment once a year.

17. **Low vision rehabilitation**

17.1. As pointed out above, an assessment by a rehabilitation officer will always include an assessment for a patient's mobility needs. This is confirmed by a survey of services providers carried out by the AMD Alliance UK in 2005¹⁰ which indicates that 94 per cent of Social Services, 65 per cent of specialist teachers and 47 per cent of Local Societies for Blind People provide mobility training. Also, 54 per cent of people surveyed in the "Unseen" report and 66 per cent of those surveyed in the "Equipped for Living" report had been offered a white cane. Latest figures suggest that as many as 79 per cent of those aged between 60 and 80 use white canes. The survey of low vision services providers shows that 86 per cent of services providers always or usually provided training in the use of daily living aids. Most of them also provide more than one training appointment.¹¹

17.2. We recognise that it is difficult to present a complete picture. The Guide Dog report shows that 39 per cent of those offered services following an assessment were offered mobility training, 23 per cent were offered orientation training, 27 per cent daily living skills training, 60 per cent training in the use of their low vision aids, 30 per cent received communication training, 22 per cent counselling and 22 per cent a guide dog assessment.

¹⁰ McLaughlan, B. et al (2005): A question of Independence – a call for action to improve sight loss support services across the UK

¹¹ See footnote 7

17.3. However, even though it is difficult to match the figures from different surveys it is clear that the assumption of a 33 per cent take-up of low vision aids and an 11 per cent take-up for low vision rehabilitation in no way reflects current practice.

18. **Community care**

18.1. The Appraisal Group model assumes that only 6 per cent of people with AMD receive community care from a home care worker. The Network 1000 survey indicates that significant numbers of people (52 per cent) employ paid help and that the likelihood of this increases with age.¹² Whilst we realise that many older people pay for home care out of their own income, this is less likely in the case of people with sight loss since 82% of them live in or on the margins of poverty [“Unseen” Report].

19. **Additional costs of blindness through higher use of health resources**

19.1. **Falls.** We welcome the fact that sight-related falls are included in the analysis. However, we are not sure why the only element included is hip replacements. People with wet AMD double their risk of fall-related admissions to hospital and the need for medical treatment.¹³ This goes well beyond hip replacements. The Audit Commission estimated in 2000 that there had been 190,000 A&E attendances in 1999, which resulted from falls by people with a visual impairment. Nearly half of these happened as a direct result of the visual impairment. The cost of these falls was £130 million. There are two aspects that suggest that fall-related cost in people with wet AMD may be even higher:

¹² See footnote 8

¹³ Soubrane G, Cruess A, Lotery A, Pauleikoff D, Monès J, Xu X, Zlateva G, Buggage R, Conlon J, and Goss T: Burden of illness, visual impairment, and health resource utilization of neovascular age-related macular degeneration patients: results from a five-country cross-sectional study. 2006.

- People with wet AMD double their risk of developing clinical depression, thereby further increasing their risk of experiencing falls.
- The 2000 Audit Commission report states that it is likely that the number of deaths following hip fractures is underestimated.

19.2. Overall use of health resources. The annual average cost per patient across Europe is significantly higher for people with wet AMD than for control patients in general medical care. For the UK it is estimated that the average annual per patient cost is £3,823.89 for people with AMD against £517.05 for the control group¹⁴. These figures include direct vision related and non-vision related medical costs as well as direct non-medical related costs such as government-sponsored assisted living facilities or nursing homes, assistance for daily activities, and social benefits received.

19.3. We recognise that NICE can only include in its calculations costs incurred by the NHS and Social Services. Nonetheless we would like to reiterate once more the importance of seeing the wider picture and recognising that the costs of blindness to society go well beyond NHS and Social Services costs. In the majority of cases people who have lost their sight due to AMD are supported by informal carers who may have to give up their own jobs to take on the role of carer. What is more, many people with AMD are also carers. If they are allowed to lose their sight this will have a considerable knock-on effect in terms of costs to society when they become unable to continue in their carer role and the State has to pay for professional care or admissions to nursing homes. This is a common scenario that reinforces the argument that it is cheaper to treat patients with wet AMD than to let them lose their sight.

¹⁴ Lotery, A. J., Xu, X., Zlatava, G. and Loftus, J: Br. J. Ophthalmol. Published online 15 May 2007

20. **Conclusions regarding the cost of blindness.** The evidence presented above shows that the cost model used by the Assessment Group does not reflect the true costs of blindness. And this is based on an assessment of current standard practice, **not** best practice or indeed need. The models used show a poor grasp of the reality of blindness through wet AMD and the health and social care costs associated with it. The ACD recognises that assumptions about the take-up of low vision services have a major impact on the cost-effective analysis. We believe that the model needs to be adjusted to include the costs presented above. As a minimum the Assessment Group should use the scenario that assumes a high take-up of the services.

Final Assessment of the ACD

21. Finally, we recognise that NICE has to take difficult decisions about resource allocation in the NHS. Treatments that are provided on the NHS have to be cost-effective. NICE plays an important role in assessing cost-effectiveness against established criteria. Unfortunately, in this instance, the evidence presented to NICE has been interpreted in a way that overestimates the costs of treatment and under-estimates the enormous clinical benefits of the new treatments as well as the cost of non-treatment.

22. We believe that a revision of the ACD is in the best interest of patients and the health economy.



The Macular Disease Society



RNIB