

10 July 2007

Dear Mr Feinmann,

Re: Health Technology Appraisal: Ranibizumab and Pegaptanib for the treatment of age-related macular degeneration

Thank you for the opportunity to comment on the Appraisal Consultation Document (ACD) and evaluation report for the above appraisal. As requested I will direct my comments under the following general headings:

- i) whether you consider that all of the relevant evidence has been taken into account

I do not think the committee has sufficiently considered the economic cost of blindness if treatment is restricted to only those patients with predominantly classic choroidal neovascularization e.g. in a paper just published (1) the cost of blindness due to wet AMD is estimated at £7.4 million pounds p.a. for a health care authority of 500,000 people. Therefore the cost of blindness I believe is higher than has been calculated.

- ii) whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate;

The current proposal will deny the majority of patients with Wet AMD the only clinically effective treatment available to them. Treatment for minimally classic and occult no classic lesions would make the £30,000 QALY threshold if assumptions regarding costs of the procedure were based on outpatient costs rather than day case rates. The Royal College of Ophthalmology has produced a commissioning document on the costs of administering this treatment (attached). I would urge the committee to input these costs into their model to see if the £30,000 QALY is then met for all lesion types.

Regardless of cost-effectiveness, Lucentis is extremely clinically effective for all forms of wet AMD and I believe the impact of allowing patients to go blind has been underestimated. Of note, other regulatory bodies in Scotland and Australia have not limited treatment by membrane sub-type and so NICE is at variance with other authorities which have also considered this technology. This I think reflects Nice choosing the worse case scenarios in the various economic models and hence with a more measured set of assumptions these technologies would make the QALY barrier.

If the current proposal stands then clinicians will have to repeatedly perform fluorescein angiograms to determine whether membranes have become predominantly classic (as they can do) and thus permitting treatment. There will be a considerable increase in management costs by having to repeatedly perform this invasive procedure (fluorescein angiography) on all patients with wet AMD to identify whether they are predominantly classic or not. This additional cost would be unnecessary if all membrane types could be treated and this additional cost should be weighed against the cost of offering an extremely clinically effective treatment to all patients with wet AMD. This extra cost does not appear to have been factored into the committee's calculations. Around 40 % of minimally classic lesions convert to predominantly classic lesions over time (2) and so there will be a considerable increase in workload in having to follow patients to see if they become eligible for treatment. If we were allowed to treat all patients then most patients could be managed by non-invasive OCT assessments rather than having to have repeated fluorescein angiograms. It is also not clear whether (as per the cohort study for PDT) clinicians would be required to submit all fluorescein angiograms to a reading center for assessment. If this was the case this would also generate further costs which would be unnecessary if we were allowed to treat all membrane types.

I also believe treating only one eye is an extremely flawed approach to treatment for several reasons:

- 1) Patients may only develop predominantly classic choroidal neovascularization in their first eye.

Under current recommendations if a patient develops predominantly classic CNV in their first eye, treatment is not permitted and this eye is allowed to go blind. If this patient subsequently develops a minimally classic or occult choroidal neovascular membrane in their second eye then NICE guidance does not permit treatment for the second eye either and the patient is left severely visually impaired when if treatment in any eye was allowed he could have most likely been maintained with good vision in both eyes. **Current NICE guidance of treating only the better eye will therefore result in many patients being denied clinically effective treatment in either eye and in my opinion is unworkable.** It will also be extremely difficult for clinicians to deny a clinically effective treatment to patients.

- 2) Patients may not respond equally to treatment in both eyes.

Again if a patient is allowed to go blind in their first eye and either is unresponsive to treatment in their second eye or suffers a complication such as endophthalmitis then you cannot roll back the clock and treat the first eye which by this stage is likely to have formed a disciform scar. Therefore there will be another cohort of patients who have been allowed to be blind in both eyes under the current proposals. If either eye treatment was allowed, these patients also could be saved from severe visual impairment. This is a very different situation to single eye cataract surgery where if there is a complication in one eye then surgery can proceed in the second eye. This is not possible for macular degeneration patients if the first eye has been allowed to become permanently scarred and irreparable.

- 3) This decision is at variance with previous NICE guidance on the clinical effectiveness and cost effectiveness of photodynamic therapy for age related macular degeneration (<http://www.nice.org.uk/TA068>).

As was discussed at the committee meeting, similar arguments regarding treating only one eye were initially suggested in the technology appraisal for photodynamic therapy for age related macular degeneration. NICE decided during that appraisal that it was valid to treat both eyes. Therefore the current proposals contradict previous NICE guidance. NICE made a very careful assessment of one versus two eye treatments at that time and I believe the same arguments over the benefits of treating both eyes stand. To allow only one eye treatment for one treatment for wet AMD and two eye treatment for another is irrational. Again it is unworkable to have one set of NICE guidance permitting photodynamic therapy in both eyes and a second set of NICE guidance limiting treatment for the same condition to only one eye.

- 4) There is clear evidence from studies in respected journals that being sighted in two eyes results in significant functional vision gains (3;4) and I believe this benefit has been underestimated by the committee.

I also believe that Macugen should be made available to the NHS as well. This is because of possible safety concerns with Lucentis as highlighted in the Sailor study and ongoing studies which suggest that initial dosage with Lucentis and maintenance dosage with Macugen is as effective in preserving vision as a Lucentis only treatment. At present I believe that most clinicians would choose to use Lucentis as it is more effective. However a combination algorithm may emerge in the future where Lucentis and Macugen are combined. The evidence for this is not fully available as yet but it would be useful to have the option of using Macugen in the future if preliminary data is confirmed.

- iii) whether you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS.

I believe the current recommendations are fatally flawed and do a great disservice to the thousands of patients who will be allowed to become blind when their sight could be saved. I urge the committee to reconsider this recommendation.

To summarise, I strongly feel that Lucentis should be offered to patients for either eye and all membrane sub-types of wet AMD. Macugen should also be permitted at the clinician's discretion. There will be additional costs related to blindness and additional fluorescein angiograms if this is not permitted and I do not think these additional costs have been considered. It would be tragic if patients in England and Wales are denied this clinically effective treatment while patients in Scotland can avail of it.

Yours sincerely,

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Reference List

- (1) Lotery AJ, Xu X, Zlatava G, Loftus J. Burden of Illness, Visual Impairment, and Health Resource Utilisation of Patients with Neovascular Age-Related Macular Degeneration: Results from the United Kingdom Cohort of a Five-Country Cross-Sectional Study. *Br J Ophthalmol* 2007 May 15.
- (2) Bressler SB, Pieramici DJ, Koester JM, Bressler NM. Natural history of minimally classic subfoveal choroidal neovascular lesions in the treatment of age-related macular degeneration with photodynamic therapy (TAP) investigation: outcomes potentially relevant to management--TAP report No. 6. *Arch Ophthalmol* 2004 March;122(3):325-9.
- (3) Javitt JC, Steinberg EP, Sharkey P, Schein OD, Tielsch JM, Diener M et al. Cataract surgery in one eye or both. A billion dollar per year issue. *Ophthalmology* 1995 November;102(11):1583-92.
- (4) Elliott DB, Patla A, Bullimore MA. Improvements in clinical and functional vision and perceived visual disability after first and second eye cataract surgery. *British Journal of Ophthalmology* 1997 October 1;81(10):889-95.