

**NICE Health Technology Appraisal
Ranibizumab and Pegaptanib for the Treatment of Age-related Macular
Degeneration**

Response to Appraisal Consultation Document

SP Harding, Consultant Ophthalmologist/Honorary Professor,
[REDACTED]

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Thankyou for asking my opinion on the Appraisal Consultation Document for the two technologies being considered by NICE for the treatment of AMD. I have read the guidance documents and have the following comments. This statement should be read as a supplement to the personal statement to the Appraisal Committee submitted on 15th April 2007 which included a declaration of interest.

Recommendation 1.1

The ACD recommends the approval of ranibizumab for better seeing eyes with predominantly classic CNV secondary to AMD. In my opinion this recommendation is not appropriate for the following reasons:

Better seeing eyes

The Appraisal Committee is correct in stating that there is a lack of data on the cost effectiveness of treating the first involved eye. This does not mean that it is reasonable to restrict treatments to the second eye involved (the better seeing eye) for the following reasons:

1. the lack of data applies to most commonly applied ophthalmic treatments and to all treatments for AMD.
2. any given eye may not be treatable due to the natural history (eg. RPE rip, subfoveal haemorrhage) meaning that there can never be certainty that the better seeing eye will be eligible for treatment. The effect of this will be a number of patients will lose sight in both eyes when the first eye could have been treatable.
3. both eyes are always treated in clinical practice. Clinicians know that patients are very concerned about the loss of the second eye when the first has been lost.
4. in patients with bilateral disease there will be great difficulty in deciding which eye to treat.

The restriction was applied to photodynamic therapy in an early ACD in 2001. It was dropped in subsequent ACDs, the FAD and for the final guidance to the NHS. The reasons for this apply equally to pegaptanib and ranibizumab.

Restriction to predominantly classic CNV (also applies to recommendation 1.2)

Restricting ranibizumab to predominantly classic CNV secondary to AMD is unexpected and does not fit with the opinion of clinicians in the UK. It is based on a cost-effectiveness sub-analysis with a number of uncertain assumptions:

1. 24 injections of ranibizumab over 2 years
This is very unlikely to be followed in clinical practice
2. Cost of technology
There is wide uncertainty around the costs of providing intravitreal services in the UK mainly depending on the use of outpatient or day case costs. The cost assumptions in

the modelling performed for the appraisal try to fit a new service into existing NHS tariffs not designed to accurately cost a new service. In my submission of April 2007 I presented the indicative costs from the Liverpool service based on experience with delivery of an AMD clinical service. These fall part way between an outpatient cost which is too low and day case costs which are too high.

3. Subgroup analysis

The use of a subgroup analysis does not appear to be appropriate. The clinical trials did look at subgroups as this allowed comparison with TAP and VIP. However there was no consistent evidence of a different effect across different subgroups. The ICERs for treating all lesion subtypes should be considered.

4. Costs of blindness.

5. These appear to have been underestimated, presumably because there has been an underestimate of the uptake of these services.

Restriction to lack of permanent structural damage to the central fovea

This cannot be assessed accurately and should be withdrawn.

Restriction to recent presumed disease progression

The panel have misinterpreted the use of this criterion in the treatment of neovascular AMD. It is based on the eligibility criteria from the VIP trial and in clinical practice is only applicable to occult no classic lesions. It is therefore not relevant to 1.1 as it currently stands.

Recommendation 1.3

Pegaptanib Therapy

This should in my opinion be available for selected cases where the use of ranibizumab is inappropriate. For example patients may develop hypersensitivity to ranibizumab, be unable to attend every 4 weeks or have no response to ranibizumab.

Registry

I believe that it will be important for these technologies to be adequately monitored to measure compliance with its use within the NHS, its safety and its effectiveness in clinical practice. This approach was adopted for the introduction of PDT for AMD and has helped to set a high standard of clinical care within a managed introduction to the NHS as well as providing important information about safety and effectiveness. Many lessons have been learnt about how best to manage such a monitoring exercise. The most effective method would be to set up a registry linked to the newly established UK network for reading centres with the aim of capturing a minimum data set comprising:

baseline: demographic details, independently assessed diagnosis, treatment delivered

follow-up: distance vision, adverse events, treatment delivered

Recommendations to NICE

1. Remove restriction to better seeing eye
2. Review cost-effectiveness analysis with
 - recalculation of costs of blindness
 - recalculation of costs of service delivery
 - inclusion of all lesion subtypes in one estimate of ICER
3. Recommend introduction of a data collection and monitoring registry