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

Commentary on Appraisal Consultation Document (ACD) from The Royal College of Ophthalmologists.

Thank you for inviting comments from the College on the ACD which are given under the following headings.

1. Has all the relevant evidence been taken into account?

We recognise that NICE has considered the published evidence but we do not believe that this Appraisal Consultation Document has considered all the new evidence accruing which suggests that the number of injections will be less than in the pivotal studies.

2. Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? Are the preliminary views on the resource impact and implications for the NHS appropriate?

We have concerns that the economic modelling is incorrect in the following points, and that as a result the ICER of ranibizumab and pegaptanib are greater than reported. In particular we believe that ranibizumab would be shown to be a cost effective treatment in patients with occult and minimally classic lesions, if the economic modelling takes account of our concerns. Similarly, pegaptanib may be shown to be cost-effective, at least for some lesion types, if these concerns are taken into account.

It is important to appreciate that eyes with minimally classic and occult CNV lesions also lose vision although the rate of vision loss may be slower than the predominantly classic in the short term. Furthermore, a significant proportion (at least 50%) of such lesions will convert to predominantly classic lesions within a year of follow up.

2.1 The ACD assumes that injections will be given as day case episodes, rather than outpatient procedures. We think this is incorrect because the nature of this procedure is unique, being neither a day case or outpatient procedure, but a procedure that most units are planning to deliver in an outpatient setting, in a dedicated clean room. We recognise that the length of time the treatment takes is longer than an ordinary outpatient appointment (4-6 hours), and that the indicative costing of this procedure is unique, neither fitting into an outpatient or day case procedure tariff.

Therefore existing tariffs cannot be applied. (see The Royal College of Ophthalmologists document 'Commissioning Contemporary AMD Services: a guide for commissioners and clinicians' in Appendix 1 attached – table of indicative costs)

2.1 A consensus amongst 160 medical retina specialists attending the Medical Retina Group meeting on 01/07/07, a representative professional society for ophthalmologists dealing with AMD and other medical retina conditions, shows that whilst currently about 50% of respondents are giving these injections as day cases in operating theatres, 90% of respondents expect to offer this service as an outpatient treatment once it became a NHS funded service.

Appendix 2 – Medical Retina Group Consensus July 2007
Appendix 3 – Welsh Medical Retina Group Consensus

2.2 The ACD has based the cost effectiveness calculations for ranibizumab on a regimen of 24 monthly injections over two years. As the College pointed out in its previous comments the regimen advised by the drug manufacturer's licence (8 injections in first year, 6 in second) is likely to be the preferred regime followed by ophthalmologists in the UK. This is confirmed by the Medical Retina Group consensus (see appendix) which showed that less than 1% of medical retina specialists would expect to give monthly injections of ranibizumab.

The College feels that the comments made in this regard in the ACD in paragraph 4.3.10 are misleading as the PIER Study (6 injections in the first year and a planned 4 in the second) had a different dosing regime to the licensing submission of ranibizumab.

2.3 The ACD has not taken account of the evidence from the PrONTO Trial, that monitoring with ocular coherence tomography (OCT), a non-invasive technique, is a means of reducing the number of injections of ranibizumab whilst not affecting the clinical response.

2.4 We believe that pegaptanib should be recommended for NHS use for those cases in which treatment has proved clinically problematic. Examples of this would be patients unable to attend for four weekly injections, allergy or adverse reaction to ranibizumab and cases where ranibizumab is contraindicated due to the patient's general health.

2.5 The effects of visual impairment from disease on the patient, family and society are significant. However such effects seem to have been ignored in determining the effectiveness and cost effectiveness of anti-VEGF therapy.

3. Are the recommendations of the Appraisal Committee sound?

It is our view that both first and second eyes should be treated with anti-VEGF therapy and that it is illogical to restrict treatment to the better eye.

We think there is clinical risk in this policy for the following reasons:

It assumes that all patients will always be able to present to an ophthalmologist for treatment to the second eye in time for it to be effective – which is untrue.

It assumes that the fellow eye will always have a treatable condition – either from AMD or from a condition unrelated to AMD – which is not always the case.

In addition, in the scenario of a patient presenting with an occult or minimally classic lesion in their better (second) eye and a predominant classic lesion in the worst (first) eye, such a patient would be denied all intravitreal anti-VEGF treatment, under the current ACD, despite the proven effectiveness of such treatment.

4. Review of Guidance.

The College is concerned that the proposed review date for the guidance of April 2010 is too late, in such a fast moving medical field, and would recommend April 2009.

5 Summary.

The Royal College of Ophthalmologists recommends that:

Ranibizumab intra-vitreous therapy should be made available to patients with neovascular age-related macular degeneration:

- where any part of the lesion is subfoveal (within 200 µm of the foveal centre)
- without restriction to first or second eye
- irrespective of relative proportions of lesion components
- with a visual acuity of logMAR1.2 or better (6/96 or 4/60)

Treatment should be discontinued where there is lack of a clinical response, for example where vision falls persistently below logMAR 1.2.

Therapy should be delivered in centres with expertise in the diagnosis and management of macular disease, access to standardised vision assessment and lesion imaging, dedicated facilities for intra-vitreous injection and adequate capacity for follow up as indicated in The Royal College of Ophthalmologists Commissioning document.

Pegaptanib intra-vitreous therapy should be made available, under the same criteria, where ranibizumab therapy proves to be clinically problematic.

It is essential that adverse events associated with anti-VEGF should be collected and evaluated by the College.

6. Appendices attached:

1. The Royal College of Ophthalmologists Commissioning Contemporary AMD Services: A guide for commissioners and clinicians. July 2007
2. Consensus of Medical Retina Group Meeting, July 1st 2007
3. Consensus of the Welsh Retinal Group Meeting, June 29th 2007
4. Working Party of The Royal College of Ophthalmologists