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Mr.Chris Feinmann

Project Manager Single Technology Appraisals ,

National Institute for Health and Clinical Excellence (NICE) Peter House
Oxford Street
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23rd October 2007

Dear Mr. Feinmann,

Appraisal of ranibizumab and pegaptanib for the treatment of age-related macular Degeneration

We have already responcted in conjunction with the Macular Disease Society and the Royal National Institute of Blind People, setting out the reasons for a new ACD. However, we also wish to respond separately to the current ACD, and the subsequent addenda in so far as we are able. These comments are in addition to our previous submissions.

While we welcome the fact that NICE has considered some of our representations and undertaken further analyses after the first ACD there are a number of remaining
concerns.

Our detailed observations are as follows:

i) Three separate documents (analyses) have been provided as addenda without integration or coordination. It is extremely difficult for consultees to comment
on the innumerable data tables without an accompanying conclusion or
summary which would have helped us in identifying the key points that the Appraisal Committee are going to consider. In addition it would have been
useful to have had a summary document indicating what each of the
documents was contributing to the discussion and dialogue.

ii) There is no indication as to what ICER is being used as the cut off point. While we recognise that an ICER of between 25 and 30 K is taken by NICE as a
cut off we would wish to see a clear statement on what cut off figure will be applied in this particular appraisal.

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iii) The documents provided do not appear to have a clear idea or ability to distinguish differences between an outpatient procedure and day case;
ambiguity in this regard would influence how costs are calculated for service delivery. We would suggest that patient assessment should include a best corrected acuity and retinal imaging tests (optical coherence tomography and fluorescein angiography) as needed and that appropriate procedure codes
are generated. There is currently no specific coding for intravitreal injections delivered in a clean room in an outpatient setting. This is an outpatient procedure which is, however, more demanding of resources than an ordinary outpatient visit or minor procedure but less than a day case unit attendance.
There may need to be a new coding for intravitreal drug delivery. These
points are explained in our AMD Commissioning Guidance document
previously submitted. Usage of the appropriate costings will affect the overall
cost determination of anti-VEGF service delivery.

iv) There are too many scenarios in the addenda which make the analyses overly complex for consultees, without some guidance from the authors of these
reports.

v) There is little hard data on which one can model outcomes in first versus second eyes. This is because there is very little published evidence on changes in
clinical measures of vision in study eyes and fellow eyes. Furthermore none
of the interventional clinical trials break down the data by whether the fellow
eye is the better eye or the worse eye. A recent meta-analysis showed the difficulties in interpreting published outcomes (Wong T, Chakravarthy U,
Klein R et al. The Natural History and Prognosis of Neovascular Age-Related Macular Degeneration A Systematic Review of the Literature and Meta-
analysis. Ophthalmology 2007 August 3. Epub ahead of print). Ideally a
patient level meta-analysis is needed to extract data that would help with the modelling. Without such an approach the analyses on first and second eyes using different scenarios remains at best speculative and subject to error.

vi) The psychological impact of vision loss in either the first or second eye is underestimated or inconsistently evaluated. Williams et al (Arch Ophthalmol
1998; 116: 514-520) assessed the psychological impact of macular
degeneration in older persons who were legally blind in one or both eyes,
and found that psychological distress in both groups was significantly worse
than in un-affected older people. Another study by Brown et al
(Ophthalmology 2001; 108: 643-648) compared quality of life associated with monocular and binocular vision using a time trade off method and concluded
that patient preference, based on quality of life, was better inpatients with
eye disorders who had good bilateral visual acuity, than in those with only
good unilateral visual acuity.

vii) It is our belief that the discussions about whether to treat the first or second eye with wet AMD are absurd as discussed in our earlier response.

It is our considered view that a second ACD addressing all these concerns would be appropriate as previously indicated in our earlier joint submission. However, we hope that such a request will not lead to further undue delay of guidance on the use of anti-VEGFs in the treatment of wet AMD to the detriment of patients.

Yours sincerely

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