RNIB/MDS comments on the ACD for the appraisal of dexamethasone intravitreal implant for the treatment of macular oedema secondary to retinal vein occlusion

1. As a general comment we would like to express our appreciation for the fact that the ACD makes it clear where patient expert input has been considered by the Appraisal Committee and what conclusions it has drawn from this input. This makes it easier for us as patient organisations to justify the considerable time and resources spent on participating in the health technology appraisal process.

2. Our response to this particular ACD focuses on three issues:

   a. Use of bevacizumab as comparator
   b. The Appraisal Committee's draft recommendation
   c. The option of departing from the threshold

Use of bevacizumab as comparator

3. The ACD is requesting from the manufacturer an analysis of the clinical and cost effectiveness of dexamethasone intravitreal implant compared with bevacizumab including a cost-effectiveness analysis with varying vial sharing assumptions for treatment with bevacizumab

4. We believe that this decision is not based on a reasonable interpretation of the evidence.

5. We cannot recall the clinical specialists stating that bevacizumab is currently "widely used in the NHS" for this condition (see point 4.5). More importantly, no evidence has been provided for its **routine** use. The STA methods guide states that “relevant comparators are identified, with consideration given specifically to **routine** and **best practice** in the NHS (including existing NICE

guidance) and to the natural history of the condition without suitable treatment. There will often be more than one relevant comparator technology because **routine** practice may vary across the NHS and because best alternative care may differ from routine NHS practice. For example this may occur when new technologies are used inconsistently across the NHS. Relevant comparator technologies may also include those that do not have a marketing authorisation (or CE mark for medical devices) for the indication defined in the scope but that are used **routinely** for the indication in the NHS. Comparator technologies may include branded and non-proprietary (generic) drugs. Sometimes both technology and comparator form part of a treatment sequence, in which case the appraisal may need to compare alternative treatment sequences. The scoping process aims to specify the comparator technologies as precisely as the technology under appraisal. Evidence providers will need to give due regard to all the above considerations when selecting comparator technologies for analyses in the evidence submissions."

6. We would argue that bevacizumab constitutes neither routine nor best practice (as defined by the Royal College of Ophthalmologists) and that the Committee should provide evidence to the contrary before requesting the use of bevacizumab as a comparator in this appraisal. While there is evidence for routine use of bevacizumab in wet age-related macular degeneration we do not believe that there is sufficient evidence for its routine use in retinal vein occlusion.

7. We would like to make it clear at this stage that we will consider appealing against the final NICE decision in this appraisal to ensure that the definition of comparators is clarified. The ACD talks about widespread use (point 4.7) and the fact that a comparator should be 'current or best practice in the NHS' (point 4.25) when in fact the test is whether it is in **routine use and best practice**.

8. Furthermore, we are concerned that the committee has not fully considered the available evidence for the effectiveness and safety of bevacizumab. The ACD stated that the ERG and the Royal College of Ophthalmologists "had identified prospective and retrospective studies and case series for bevacizumab in the treatment of macular oedema secondary to RVO (point 4.25). By contrast point 3.22 states

that both “RCT and non-RCT evidence was available and could have been used in an indirect comparison”. It is clearly important to ensure that the Committee has a clear understanding of the level of evidence available for the use of bevacizumab in RVO. From the above it appears that the reference to RCT evidence may be in relation to the use of bevacizumab in wet AMD rather than RVO. It would help to have this clarified since the evidence for the effectiveness and safety of bevacizumab in RVO is of a significantly lower level.

9. Since no large RCTs have been conducted on the use of bevacizumab in RVO we would argue that a full cost-effectiveness analysis is methodologically unsound.

10. This combined with insufficient evidence of the routine use of bevacizumab for the treatment of macular oedema secondary to RVO in the NHS should lead the Committee to abandon bevacizumab as a comparator.

11. This would seem the right decision to us, particularly given the failure to include ranibizumab as a comparator which is also not in routine use in the NHS but has a significantly better evidence-base for its effectiveness.

12. Finally, we would like to alert the Committee to the impact a cost-effectiveness analysis including bevacizumab is likely to have on patient access to treatment. Even though estimates of the costs of providing bevacizumab for the treatment of any eye condition vary widely and fail to include the costs of pharmacovigilence to ensure patient safety, we acknowledge that dexamethasone intravitreal implant is unlikely to be shown to be cost-effective if compared to bevacizumab. While the result of this cannot be a NICE recommendation to use bevacizumab in the NHS there appears to be an assumption that not recommending dexamethasone intravitreal implant for use in the NHS will lead to the cheaper, unlicensed alternative being made available routinely.

13. We believe that this is misguided. Instead patients are likely to be denied access to any treatment as PCTs are under pressure to cut costs and the result will be avoidable blindness, particularly in people with CRVO who have no other treatment alternatives.

The Appraisal Committee's draft recommendation

14. We understand that the methods guide for technology appraisals requires the Appraisal Committee to issue draft recommendations in relation to the technology under consideration.

15. However, we feel that it is not sufficiently clear why the Appraisal Committee has stated that it is minded **not** to recommend dexamethasone implant for the treatment of RVO given that it appears to have accepted key assumptions in the manufacturer's model (e.g. the '90:10 worse v better seeing eye' split, the need to treat first eyes, the relevance of 10 letter gains). All of these contribute to the large number of ICERs below the £30,000 threshold. In fact at present there is only one of the alternative scenarios (point 3.20) that yielded an ICER of more than £30,000. It would be helpful to have a clear explanation of the Committee's reasoning, i.e. that it made assumptions about the outcome of the additional analyses and the comparison with bevacizumab requested from the manufacturer or that the lack of data about the safety of earlier and more frequent retreatment are sufficient to decide against approval.

Departing from the threshold

17. We would like to remind the Committee of the Citizens Council's report departing from the threshold includes references to the treatment of first or second eyes: "There was little doubt that most of us on the Council felt that the macular degeneration decision was most definitely an instance in which pure cost- effectiveness should have been put to one side. "Inhumane" and "shameful" were just two of the words that members used to describe it."[1] We are pleased to see that the Committee came to the conclusion that "it was appropriate to treat the first eye affected" (point 4.15) and would like to see this reflected in the consideration of cost-effectiveness in case

[1] Report on NICE Citizens council meeting "Departing from the threshold", 27-29 November 2008. Available online at: http://www.nice.org.uk/media/231/CB/NICECitizensCouncilDepartingThresholdFinal.pdf

the additional cost-effectiveness analysis requested from the manufacturer results in more ICERs above the £30,000 threshold.

For any clarification on the above points please contact [redacted], RNIB, e-mail:[redacted]; tel: [redacted]

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