National Institute for Health and Clinical Excellence

Centre for Health Technology Evaluation

Pro-forma Response

ERG report

Dexamethasone intravitreal implant for the treatment of macular oedema caused by retinal vein occlusion (RVO)

Please find enclosed the ERG report prepared for this appraisal.

You are asked to check the ERG report from Aberdeen HTA Group to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by **5pm, Monday 13 December 2010** using the below proforma comments table. All factual errors will be highlighted in a report and presented to the Appraisal Committee and will subsequently be published on the NICE website with the Evaluation report.

The attached proforma document should act as a method of detailing any inaccuracies found and how and why they should be corrected.

Issue 1

Description of problem	Description of proposed amendment	Justification for amendment
The ERG report identifies proportions of simulations which resulted in illogical parameter estimates. It then goes on to state: “As far as the ERG can ascertain, the only logical restriction placed upon these parameters is that the HRQoL cannot exceed 1.” P 52. Restrictions were placed on several parameters.	Restrictions are applied to the following parameters (in all versions of the electronic model provided): • Mean BCVA by health state was restricted to prevent visual acuity in a state being worse (or better) than the next poorest (or best) health state • WSE and BSE VFQ-UI linear regression slopes were restricted to prevent increasing visual acuity being associated with reduced HRQoL • The percentage of patients retreated in each cycle were restricted to prevent the proportion of patients retreated in a subsequent cycle exceeding the proportion treated in the previous cycle These parameters are highlighted by a blue cell colour and accompanying text boxes in column T of the ‘Data & References’ sheet.	These restrictions address some of the concerns raised by the ERG with regard to illogical parameter values estimated in probabilistic analysis.

Issue 2

<table>
<tr><th>Description of problem</th><th>Description of proposed amendment</th><th>Justification for amendment</th></tr>
<tr>
<td>
The ERG were unable to recreate the cost estimate used for cataract extraction (p. 57). After revisiting the source data, it is believed that the footnote to Table 113 of the original submission remains accurate and that the cost of cataract extraction was calculated as described within the written submission (note that the citation in the electronic model was incorrect because it did not include day cases).

Table 1 presents the data used in the calculation of this estimate.

Table 1: Calculation of costs of cataract surgery
<table>
<tr><th>Currency Code</th><th>Currency Description</th><th>Activity</th><th>National Average Unit Cost</th><th>sheet</th></tr>
<tr><td>BZ24A</td><td>NSO with LOS 2 days or more</td><td>389</td><td>£2,580</td><td>TEI</td></tr>
<tr><td>BZ24C</td><td>NSO with LOS 1 day or less</td><td>1,007</td><td>£797</td><td>TEI</td></tr>
<tr><td>BZ24A</td><td>NSO with LOS 2 days or more</td><td>6,006</td><td>£2,037</td><td>TNEI_L</td></tr>
<tr><td>BZ24C</td><td>NSO with LOS 1 day or less</td><td>1,090</td><td>£1,134</td><td>TNEI_L</td></tr>
<tr><td>BZ24C</td><td>NSO with LOS 1 day or less</td><td>7,121</td><td>£481</td><td>TDC</td></tr>
<tr><td>BZ24A</td><td>NSO with LOS 2 days or more</td><td>19</td><td>£629</td><td>TNEI_S</td></tr>
<tr><td>BZ24C</td><td>NSO with LOS 1 day or less</td><td>9,886</td><td>£410</td><td>TNEI_S</td></tr>
<tr><td></td><td></td><td></td><td>£892.08</td><td></td></tr>
</table>
Abbreviations: NOS, Non-Surgical Ophthalmology; LOS, length of stay
</td>
<td>The cost of cataract extraction was calculated as described in Table 113 of the written submission.</td>
<td>This amendment is not believed to have a significant impact on the results of the analysis as the alternative cost estimated by the ERG is similar to that in the original written submission.</td>
</tr>
</table>

Issue 3

Description of problem	Description of proposed amendment	Justification for amendment
In section 1.2 the ERG report describes visual acuity based on mean letter count as the primary outcome measure of the GENEVA studies. In fact the primary endpoints of both studies were based on the proportion of patients achieving ≥15 letter change from baseline in the study eye as measured by the ETDRS method.	Section 1.2 should be amended to reflect the primary efficacy endpoint of the GENEVA trial programme.	This is inaccurately cited in the ERG report at present

Issue 4

Description of problem	Description of proposed amendment	Justification for amendment
In section 1.2 the ERG report states that all patients in the GENEVA trial programme could get retreatment after day 180. Patients were only retreated if they met the retreatment criteria specified within the protocol.	Section 1.2 should be amended to reflect that patients were only retreated if they met the retreatment criteria specified in the protocol (BCVA was < 84 letters or the retinal thickness by OCT was > 250 µm in the central 1 mm macular subfield and, in the investigator's opinion, the procedure would not put the patient at significant risk.)	This is inaccurately cited in the ERG report at present

Issue 5

Description of problem	Description of proposed amendment	Justification for amendment
In section 1.3 the ERG report highlights that a serious error persisted in the cost effectiveness model provided. We believe that this has now been corrected and a revised model is supplied alongside this proforma.	Clarification that the issue has since been addressed.	The issue identified has now been resolved within the model framework and the impact on ICERS quantified and described.

Issue 6

Description of problem	Description of proposed amendment	Justification for amendment
In section 1.3 the ERG report states: "Based on conversations with clinical experts, the ERG believes that dexamethasone implantations could be given on an outpatient basis, and that the day case cost used in the industry submission is therefore too high, thereby reducing the cost-effectiveness of dexamethasone treatment". This is incorrect; if costs reduce whilst outcomes remain unchanged then this increases the cost effectiveness of treatment (and decreases the ICER)	This should be re-phrased to read: Based on conversations with clinical experts, the ERG believes that dexamethasone implantations could be given on an outpatient basis, and that the day case cost used in the industry submission is therefore too high, thereby increasing the cost-effectiveness of dexamethasone treatment	This is a factual inaccuracy .

Issue 7

Description of problem	Description of proposed amendment	Justification for amendment
In section 1.4 the ERG report states: "Lack of comparisons with other therapeutic options, and in particular the anti-VEGF drugs, ranibizumab and bevacizumab. Admittedly, there are no head to head trials, but an indirect comparison could have been attempted." However ranibizumab was not included as a comparator in the original scope agreed with NICE. We have since offered to provide an indirect comparison based evaluation of cost effectiveness which was declined.	The potential comparators detailed should be in accordance with the scope issued for this STA	Ranibizumab was not included in the original scope.