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Response to NICE Clarification on Update of TA155

To Dr Meindert Boysen, Programme Director Technology Appraisals

Date 24 December 2011

Concerning **Impact of the Simple Discount Scheme on TA155: ranibizumab in the treatment of wet age-related macular degeneration (wAMD)**

Dear Dr Boysen,

Novartis welcomes the opportunity to provide a detailed response to the query raised in regards to the impact of the Simple Discount Scheme PAS on TA155. The below figures are all derived from the original model submitted in 2006, so as to be comparing 'like with like'. To adjust for a longer treatment duration, the number of injections in year 1 and year 2 has been increased.

Incorporating the Simple Discount Scheme PAS into the original model has a neglibile impact on the cost-effectiveness analysis. The model is attached for reference.

The impact of the Simple Discount Scheme on the cost-effectiveness considered in TA155

Replacement of the RRS with the Simple Discount PAS within the originally submitted cost-utility analysis yielded slightly decreased ICERs in all four populations.

All tables presented for RRS (Scenario 'A' below) are identical to those presented in Tables 3.4-3.8 of the original 1 August 2006 manufacturer submission. The tables presented for the amended PAS include the ████████████████████████████ and an increased number of annual injections to account for those few patients that will exceed 14 injections in the coming years.

As there is no functionality in the 2006 model to account for treatment duration past 1 or 2 years (depending on the trial population chosen), the number of injections has been increased within year 1 or 2 to simulate an extended treatment duration.

The increased number of injections which are both incorporated into the below 'Scenario B' ICER estimates are as follows: (ANCHOR: In year 1, increase from 8 to 9 injections; MARINA: In year 2, increase from 6 to 8 injections). The original model was based upon 1 year RCT data for ANCHOR and 2 year RCT data for MARINA and thus the difference in applying varying increases in injection frequency.

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The estimated incremental costs and benefits presented above may be substantially underestimated as Novartis has input conservative assumptions around injection frequency. Real life data from the RRS has found an average annual injection frequency of ▮ in year 1 and ▮ in year 2. As presented in Figure 1, the original manufacturer base case assumed 8.0 injections in year 1 and 6.0 injections in year 2 based on similar efficacy received in the randomised clinical trials. The ICERs may be further overestimated as the corresponding benefit of extended treatment duration has not been accounted for within the model.

Figure 1. Reduced injection frequency based on real life RRS data
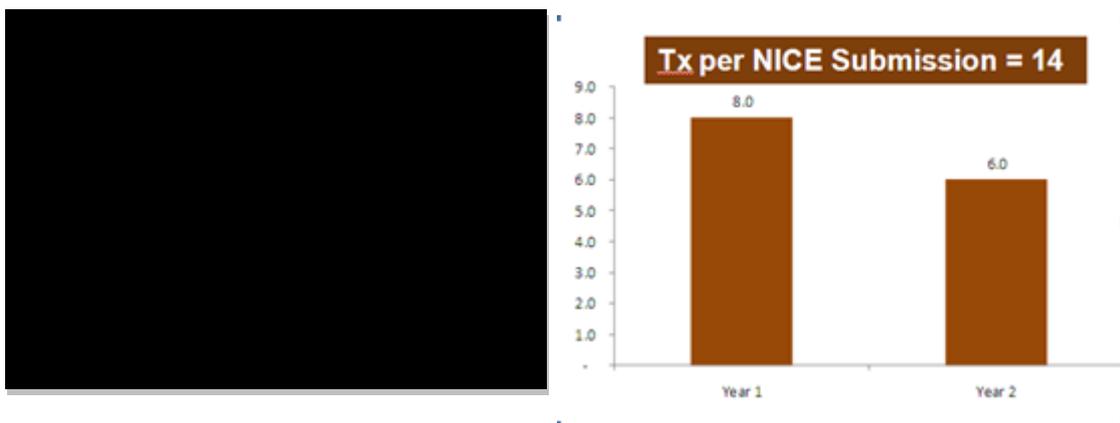
Scenarios:

Scenario A: 2007 RRS
Scenario B: 2011 PAS ▮▮▮▮▮▮▮▮▮ with increased number of annual injections)

These two scenarios have been assessed in the originally presented 4 trial populations:

I. ANCHOR trial, Predominantly classic (PC) choroidal neovascularisation (CNV): (Ranibizumab 0.5mg vs Photodynamic Therapy (PDT))
II. ANCHOR trial, PC CNV: (Indirect comparison of Ranibizumab 0.5mg vs Best Standard Care (BSC))
III. MARINA trial, Occult CNV: (Ranibizumab 0.5mg vs BSC)
IV. MARINA trial, Minimally classic (MC) CNV: (Ranibizumab 0.5mg vs BSC)

I. ANCHOR TRIAL (PC-AMD) Ranibizumab 0.5mg vs PDT

Scenario A: Based on 1 Year ANCHOR data (8 injections in Year 1)

Cost/QALY gained	Costs (£)	QALY	Cost /QALY
Ranibizumab	35,501	4.21	
PDT	34,584	4.01	
Incremental	917	0.20	4,489

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Scenario B: Based on 1 year ANCHOR data (9 injections in Year 1 & ████████████)

Cost/QALY gained	Costs (£)	QALY	Cost /QALY
Ranibizumab	██	██	
PDT	██	██	
Incremental	██	██	3,943

II. ANCHOR TRIAL (PC-AMD) Indirect comparison of Ranibizumab 0.5mg vs BSC (From TAP)

Scenario A: Based on 1 Year ANCHOR/TAP data (8 injections in Year 1)

Cost/QALY gained	Costs (£)	QALY	Cost /QALY
Ranibizumab	35,501	4.21	
BSC	31,432	3.94	
Incremental	4,068	0.28	14,781

Scenario B: Based on 1 year ANCHOR/TAP data (9 injections in Year 1 & ████████ ████)

Cost/QALY gained	Costs (£)	QALY	Cost /QALY
Ranibizumab	██	██	
BSC	██	██	
Incremental	██	██	14,376

III. MARINA (OC-AMD): Ranibizumab 0.5mg vs BSC

Scenario A: Based on 2 Year MARINA data (8 injections in Year 1 & 6 injections in Year 2)

Cost/QALY gained	Costs (£)	QALY	Cost /QALY
Ranibizumab	31,326	4.71	
BSC	22,201	4.36	
Incremental	9,125	0.34	26,454

Scenario B: Based on 2 Year MARINA data (8 injections in Year 1 & 8 injections in Year 2 & ████████████)

Cost/QALY gained	Costs (£)	QALY	Cost /QALY
Ranibizumab	██	██	
BSC	██	██	
Incremental	██	██	26,270

IV. MARINA (MC-OMD): Ranibizumab 0.5mg vs BSC

Scenario A: Based on 2 Year MARINA data (8 injections in Year 1 & 6 injections in Year 2)

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Cost/QALY gained	Costs (£)	QALY	Cost /QALY
Ranibizumab	34,408	4.52	
BSC	25,914	4.19	
Incremental	8,494	0.33	25,796

Scenario B: Based on 2 Year MARINA data (8 injections in Year 1 & 8 injections in Year 2 & ██████████████████

Cost/QALY gained	Costs (£)	QALY	Cost /QALY
Ranibizumab	███	███	
BSC	███	███	
Incremental	███	███	25,573

Regards,

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