

Comments on ACD

3.11 The sentence “The probabilities of annual relapse rate and disability progression for fingolimod treatment were calculated from the absolute incidences of these outcomes in the FREEDOMS trial.” is incorrect. Only relative effectiveness measures were derived from the FREEDOMS trial.

3.12 The following statement is incorrect and unclear “an adjustment was made to reflect the time since diagnosis and to account for relapses”. This should state “an adjustment was made to account for relapses”.

3.20 The statement “therefore reasoned that a comparison **with** best supportive care would have been more appropriate.”, for accuracy, should be changed to “therefore reasoned that a comparison **including** best supportive care would have been more appropriate.”. The ERG advocates for an incremental analysis where all relevant comparators are included, and not a sole comparison against best supportive care.

3.21 For clarity, reference back to section 3.16.

3.24 The statement “In addition, Avonex was extendedly dominated by fingolimod and best supportive care (that is, Avonex was more expensive and less effective than either fingolimod or best supportive care)” is incorrect. It should read “In addition, Avonex was extendedly dominated by fingolimod (the ICER of Avonex is higher than that of fingolimod in an incremental analysis, meaning that a unit of health benefit is attained at a higher cost than with fingolimod)”. The notion of extended dominance has been misinterpreted throughout this document – this needs to be corrected.

For accuracy the statement “The ERG considered that this analysis provided further evidence that best supportive care rather than Avonex should have been considered as the primary comparator to fingolimod for population 1b.” should be re-worded to “The incremental analyses show that, in both populations, Avonex is either dominated or extendedly dominated by fingolimod. The ERG considered that the cost effectiveness of fingolimod should be expressed in the context of this incremental analysis.”

3.25 The statement “the ERG had previously explored a number of alternative scenarios for incorporating trial utility data into the model, which were shown to increase the ICERs” is incorrect. The ERG explored a number of scenarios showing that the ICER changes, sometimes increasing sometimes decreasing; the manufacturer selected one scenario that showed the greatest decrease in the ICER without providing justification for this choice.

3.27 The statement “However, for population 1b, Rebif-44 was dominated by best supportive care and extendedly dominated by fingolimod (that is, Rebif-44 was more expensive and less effective than either best supportive care or fingolimod)” is inaccurate. It should be changed to “However, for population 1b, Rebif-44 was extendedly dominated by fingolimod (that is, Rebif-44 was less expensive and less effective than fingolimod, but presents a higher incremental ICER than fingolimod)”

3.28 The statement “To explore this, the ERG re-ran the original model and excluded all **adjustments to** direct treatment effects on relapse rates.” Should be changed to “To explore this, the ERG re-ran the original model and excluded all direct treatment effects on relapse rates.”

3.31 The statement “The ERG cautioned that despite the discounted drug acquisition cost, the remaining uncertainty in the model still remained.” Should be changed to “The ERG cautioned that despite the discounted drug acquisition cost, the remaining uncertainties around the model **and inputs used to inform the model** were still unresolved and unaccounted for.”