Dear Jeremy
Please find our comments upon the Alemtuzumab model below.
We have not used the tabulated format as our comments are general and we have not re run the model to produce results based upon these comments. However, we feel that re analysis incorporating the changes suggested by these comments would be desirable.

Alemtuzumab for treating relapsing forms of multiple sclerosis [ID539]: Manufacturers Model

Biogen Idec would like to thank the National Institute for Health and Care Excellence (NICE) for the opportunity to review and comment on the Appraisal Consultation Document (ACD) for alemtuzumab for treating relapsing forms of multiple sclerosis. Our comments are in relation to the robustness of the health economic model for alemtuzumab, whereby we support the case for additional analysis to be conducted in order to reduce the uncertainty around the clinical and cost-effectiveness of alemtuzumab, when compared to other available treatments.

MODEL STRUCTURE

The overall structure appears consistent with previous models used in previous NICE appraisals based on EDSS; however, we note that the structure does not allow for the regression of disability between EDSS states. Excluding regression will result in the patient population progressing more rapidly to higher EDSS states and SPMS than it would be expected under real-world conditions. This has an impact on the reliability of the ICER of alemtuzumab versus other available comparators.

MTC RESULTS

The hazard ratios and relative rates of relapses are difficult to interpret and threaten the face-validity of the model; for example, the hazard ratio for Betaferon is 1.21, with BSC 1.0. Particular attention should be paid to the results showing interferon1-b having worse clinical outcomes than BSC.
Further, the MTC treatment effects do not appear to be consistent with the head-to-head studies available, which threatens the predictive validity of the MTC.

MONITORING AND ADMINISTRATION ASSUMPTIONS.

Assumptions on the use of resources for the monitoring and administration of alemtuzumab appear reasonable. However the monitoring has not allowed any MRI costs for alemtuzumab, which would be expected especially in the first year. It is recommended that MRI be considered for inclusion in the model for alemtuzumab including any associated costs such as a neurology visit.

ADVERSE EVENTS

The adverse events rates unduly bias in favour of alemtuzumab. A comprehensive and transparent list of adverse events for alemtuzumab should be provided and included in the MTC analyses by the manufacturer. In particular the adverse event rates for human papillomavirus infection, including cervical dysplasia (2%) and superficial fungal infections (12%) should be considered.

The long term effects of alemtuzumab on immune function and the potential for thyroid malignancy is unknown but could potentially incur additional costs and disutility. Long-terms results for a cohort of patients are available but unpublished. These should be incorporated to validate the predictive aspect of the model.

Yours sincerely, [redacted].