Decision Support Unit Project Specification Form	
Project Number	
Appraisal title	Dapagliflozin for the treatment of type 2 diabetes
Synopsis of the technical issue	In the appraisal consultation document (ACD) the Committee was minded not to recommend dapagliflozin in combination therapy for treating type 2 diabetes and requested further clarification and analyses from the manufacturers (as outlined in section 1.2-1.4 of the ACD). In its response to the ACD, the manufacturer provided a revised economic model and analyses which attempted to address the issues raised by the Committee. At the second committee meeting (March 5th) the Committee discussed the manufacturers' response to the ACD, but concluded that its concerns about the economic model had not been fully resolved. In particular it was unclear about how changes in weight were modelled over time for the different treatments. Because of time constraints in the post-consultation period, the ERG had not been able to explore this issue fully or to conduct any further sensitivity analyses. The Committee concluded that it was unable to decide on the most plausible ICERs or to make a recommendation on dapagliflozin in combination therapy (as add-on to metformin or insulin) for treating type 2 diabetes until these issues have been resolved. The DSU is requested to review the manufacturers' additional analyses in response to the ACD request to assess how changes in weight are modelled over time for different treatments within the manufacturer's revised economic model. The DSU is also requested to conduct a range of further analyses using the revised economic model in order to help the Committee decide on the most plausible ICERs for dapagliflozin in combination therapy as an add-on to insulin and as an add-on to metformin.

Question(s) to be answered by DSU	How has weight evolution been modelled for the different treatments in the scenarios presented by the manufacturer using its revised economic model? The DSU is requested to describe how these changes are modelled in the manufacturer's revised analyses and to explore their impact on the ICERs using the assumptions described below. To conduct further analyses for the dual therapy and add-on to insulin therapy indications, using the manufacturers revised economic model (submitted following the ACD) as their starting point. The following assumptions should be applied in the base case scenario to reflect the requests made in section 1.3 of the ACD: • An annual average cost of £69.09 for pioglitazone based on the latest February 2013 NHS drug tariff. • An annual cost of £483 (taken from the UKPDS 65 study) for people not experiencing diabetic complications (adjusting the cost for those with complications accordingly to avoid double counting). • Utility decrements for hypoglycaemia (-0.012 for severe -0.004 for symptomatic) and BMI changes (±0.0061 per unit of BMI). • Efficacy estimates from the revised 24 week NMA, which incorporates the manufacturer's changes to the WinBUGs programme code to bring it in-line with the recommendations in TSD2. Where there is a lack of 24 week NMA estimates from a particular comparator (e.g weight / HbA1c data for MET+ SUA), data from the 52 week NMA will be indirectly applied. This will be validated by comparing the ICERs when using data from the pairwise comparison (e.g Study 4) at 24 weeks against the ICERs using the 52 week NMA data. Continued…

	• Treatment related weight loss is regained during year 3 (keeping the 2 year maintenance of treatment related weight loss) to the level expected in a patient with weight gain since baseline of 0.1kg per year. This assumption is applied to both Dapagliflozin and any comparator with weight loss. • Zero prevalence of diabetes complications at baseline (as per the manufacturer's original submission). • HbA1c switching threshold of 7.5% for first and second switch in both indications. The following assumptions will be explored in univariate scenario analysis using the base case scenario, described above, as the starting point: • Efficacy estimates from the revised 52 week NMA which incorporates the manufacturer's changes to the WinBUGs programme code to bring it in-line with the recommendations in TSD2. • The impact of using the manufacturer's original approach to modelling hypoglycaemia which uses the hypoglycaemic fear score. • Changes to the weight evolution which equalise weights between treatment arms at last therapy switch (NB: only pairwise comparisons and not an incremental analysis can be produced from for this scenario). For all of the analyses described above, present an incremental analysis of all relevant comparators in terms of total and incremental costs, QALYs and ICERs (except where the scenario explicitly prevents this as indicated above). For all of the analyses described above, provide an estimate of the proportion of the QALY gains or losses that were attributable to the impact of changes in weight on health-related quality of life (utility). Results for the basecase and scenario analyses described above will be provided using the version of the model which uses mean parameter values. The DSU will endeavour to extract PSA results for the base case scenario described, although it is noted that this may not be feasible within the timeframe available. PSA results for the scenario analysis exploring weight convergence at last therapy will also be extracted, if feasible within the timeframe.

How will the DSU address these questions	The DSU will review the manufacturer's response to the ACD including the revised economic model and conduct additional analyses as appropriate.
DSU deliverables/outcomes (eg report, statement, etc)	Report