1.4 Summary of the ERG's critique of clinical effectiveness evidence submitted

The manufacturer carried out a literature search for randomised evidence related to the efficacy of vemurafenib. Three manufacturer sponsored studies were identified, only one of which was a RCT. The earliest study was a dose ranging trial in a variety of cancers, the second was a single-armed trial in previously treated patients with malignant melanoma that were BRAF V600 mutation positive. The manufacturer stated that it was 'not possible to robustly demonstrate that vemurafenib is a cost-effective use of NHS resources' they appropriately limited their submission to the treatment of patients who had not previously received a systemic treatment.

Table 1 Scenario analyses results

Description	ICER per QALY gained
Base case	£94,267
Overall survival	
October cut of BRIM 3[9] data	£128,060
Base case with 34 month treatment effect	£77,343
Utility estimates	
Base case with higher Hodi mapped PD utility value used to reflect the potential for patients in 'tail' of survival curve to have lower tumour burden and therefore improved HRQoL	£82,017
Hodi[33] EORTC-QLQ-C30 mapped values	£83,643
Hodi[33] SF-36 mapped values	£103,345

ICER=incremental cost effectiveness ratio; QALY=quality adjusted life years

Probabilistic sensitivity analyses

The manufacturer undertook probabilistic sensitivity analysis (PSA) to derive the mean ICER of vemurafenib vs dacarbazine. The manufacturer notes that OS, the parameter subject to the most uncertainty, was not varied probabilistically as they were not able to determine which potential extrapolations should be given a higher likelihood of occurring. The manufacturer highlights that this omission means that the PSA significantly understates the uncertainty associated with the incremental QALY gain provided by vemurafenib.