Comments on the ACD Received from the Public through the NICE Website

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	NHS Hampshire is in agreement with the recommendations in the NICE Appraisal Consultation Document (ACD) and Commissioning Support Appraisals Service (CSAS) response, not to recommend Vemurafenib for this indication on the basis that there does not appear to be any published evidence that has considered whether this treatment at its current high cost (approx. Â£2,100 per week) is cost-effective. Vemurafenib is an expensive drug and its long term benefits and safety profile are difficult to quantify.
Section 2 (The technology)	Response to Vemurafenib is rapid but the median duration of response is only 5-6 months as most patients develop resistance to Vemurafenib, manifested by progressive disease, and rapid relapse • There are concerns around the safety of Vemurafenib, as experience on the adverse event profile is still accumulating. •In the BRIM3 study 18% patients develop dermatologic complications including squamous cell carcinomas needing treatment. The impact of extra activity and costs generated from regular dermatological referral, monitoring, evaluation and management, need to be considered
Section 3 (The manufacturer's submission)	Patients must have BRAF V600E mutation-positive tumour status confirmed by a validated test. The efficacy and safety of Vemurafenib in patients with tumours expressing BRAF V600 non-E mutations have not been convincingly established, although response in BRAF-V600K mutant melanoma has been reported. Vemurafenib should not be used in patients with wild type BRAF malignant melanoma. In the phase II and phase III clinical trials, eligible patients were identified using a real-time polymerase chain reaction assay (the cobas 4800 BRAF V600 Mutation Test). Â Although the manufacturer of Vemurafenib is currently making BRAF V600 mutation testing free of charge by funding 3 BRAF reference testing centres in the UK, this may change and the potential cost and activity generated from the Roche cobas 4800 BRAF V600 mutation testing on the NHS would need to be considered.
Section 4 (Consideration of the evidence)	It is not clear where Vemurafenib sits in the clinical pathway of care for people with locally advanced or metastatic BRAF V600E mutation-positive malignant melanoma, given that there are a range of new therapies (Iplimumab, Dabrafenib) currently being investigated. The following elements have not been considered: o Role of Vemurafenib in the adjuvant setting o Impact of combination therapy with Iplimumab and dosage o Their optimal sequencing. Further research is still needed to establish appropriate therapeutic options in clinical practice.
Section 5 (Implementation)	There is a rapid rise in malignant melanoma. Hampshire has a malignant melanoma incidence rate which is higher than the national average. The rates were 19.8 per 100,000 population (2006-2008) 19.6 per 100,000 population (2005-2007) and 18.3 per 100,000 population (2004-2006), significantly worse than the England average (13.6 per 100,000 population, (2006-2008)]. Most (approximately 90%) melanomas are diagnosed early as primary tumours and cured by surgery. Â Around 10% of patients have metastatic disease at diagnosis or relapse with metastatic spread after treatment for apparently localised disease. It is suggested by the manufacturer that of these, approximately 50% of melanoma patients have tumours which harbour BRAF V600 mutations and 85% would eligible for treatment. Although local intelligence on the prevalence of metastatic disease in Hampshire is not available, given the higher incidence, one would expect proportionately higher numbers of patients eligible for treatment with Vemurafenib if recommended. This would also include extra activity and costs generated from regular dermatological referral to address cutaneous adverse events.
Section 6 (Proposed recommendations for further research)	

Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	