ADDENDUM

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP (LRiG)

Vemurafenib for the treatment of locally advanced or metastatic BRAF V600 mutation positive malignant melanoma

This report was commissioned by the NIHR HTA Programme as project number 11/43/01

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Contains confidential data

UNIVERSITY OF LIVERPOOL

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP

A MEMBER OF THE RUSSELL GROUP

On 13 April 2012 Roche asked the Department of Health to consider a patient access scheme (PAS) relating to the purchase of vemuarfenib. The PAS is a simple discount involving a reduction of [redacted] to the current list price of vemurafenib (£1,750 per pack, a week's supply) which is applied at the point of invoice. The discount covers all populations for which vemurafenib has an European Medicines Agency (EMA) marketing authorisation and the scheme will remain in place until the publication of any revised NICE guidance relating to vemurafenib.

Following acceptance of the PAS by the Department of Health the Evidence Review Group (ERG) has put together an addendum to accompany their critique of the clinical and cost-effectiveness evidence submitted by the manufacturer to the National Institute for Health and Clinical Excellence (NICE) as part of the Single Technology Appraisal (STA) process. The evidence submitted by the manufacturer was in support of the use of vemurafenib for the treatment of locally advanced or metastatic BRAF V600 mutation positive malignant melanoma.

This addendum comprises four tables. Table 1 shows results from the base case cost-effectiveness analysis submitted by the manufacturer to NICE as well as revisions to those results that followed from the ERG's corrections and amendments to the manufacturer's economic model. Table 2 shows the impact of the PAS on the results that are displayed in Table 1. Results from an analysis, undertaken by the ERG, which looked at the potential impact on costs of limiting the vemurafenib treatment period are displayed in Table 3 and figures showing the impact of the PAS on these results are displayed in Table 4.

Figures highlighted in [redacted] are commercial in confidence.

Table 1 Revised base-case cost-effectiveness analysis incorporating corrections and amendments identified by the ERG

	Dacarbazine			Vemurafenib			Incremental			ICER
	Cost per patient	Life years per patient	QALYs per patient	Cost per patient	Life years per patient	QALYs per patient	Cost per patient	Life years per patient	QALYs per patient	Cost per QALY gained
Manufacturer's base case analysis	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	**£94,267**
Correct discounting logic	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£93,783
Amend dacarbazine admin. costs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£94,646
Amend post-progression utility value	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£82,664
ERG estimate of dacarbazine costs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£94,289
Amend long-term monitoring costs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£89,745
ERG overall survival model	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£230,175
Revised base case analysis with all ERG changes	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	**£224,704**

The single most important factor in increasing the ICER is the ERG's estimation of OS gain. If this change is not accepted then the revised base-case ICER is £78,620 per QALY gained.

Table 2 Revised base-case cost-effectiveness analysis incorporating corrections and amendments identified by the ERG and impact of the PAS

	Dacarbazine			Vemurafenib			Incremental			ICER
	Cost per patient	Life years per patient	QALYs per patient	Cost per patient	Life years per patient	QALYs per patient	Cost per patient	Life years per patient	QALYs per patient	Cost per QALY gained
Manufacturer's base case analysis	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	**£56,410**
Correct discounting logic	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£56,148
Amend dacarbazine admin. costs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£56,789
Amend post-progression utility value	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£49,467
ERG estimate of dacarbazine costs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£56,431
Amend long-term monitoring costs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£51,888
ERG overall survival model	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£133,138
Revised base case analysis with all ERG changes	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	**£129,962**

If the ERG's estimation of OS gain is not accepted then, with the PAS, the revised base-case ICER is £45,618 per QALY gained.

Table 3 Revised base-case cost-effectiveness analysis relating to days of vemurafenib treatment

	Manufacturer's base case		Results with ERG changes to the economic model	
Maximum vemurafenib treatment period (days)	**Cost of vemurafenib & admin**	**ICER per QALY gained**	**Cost of vemurafenib & admin**	**ICER per QALY gained**
112	[redacted]	£55,205	[redacted]	£126,225
140	[redacted]	£62,045	[redacted]	£143,392
168	[redacted]	£67,500	[redacted]	£157,120
196	[redacted]	£72,432	[redacted]	£169,563
224	[redacted]	£75,982	[redacted]	£178,546
Unlimited (to progression)	[redacted]	**£94,267**	[redacted]	**£224,704**

Table 4 Revised base-case cost-effectiveness analysis relating to days of vemurafenib treatment and incorporating the impact of the PAS

	Manufacturer's base case		Results with ERG changes to the economic model	
Maximum vemurafenib treatment period (days)	**Cost of vemurafenib (PAS) & admin**	**ICER per QALY gained**	**Cost of vemurafenib (PAS) & admin**	**ICER per QALY gained**
112	[redacted]	£33,718	[redacted]	£72,754
140	[redacted]	£37,691	[redacted]	£82,726
168	[redacted]	£40,860	[redacted]	£90,701
196	[redacted]	£43,725	[redacted]	£97,930
224	[redacted]	£45,788	[redacted]	£103,148
Unlimited (to progression)	[redacted]	**£56,410**	[redacted]	**£129,962**