NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Technology appraisals

Patient access scheme submission

Melanoma (unresectable/metastatic $BRAF^{V600}$ mutation-positive) - dabrafenib

30th April 2014

1 Introduction

The 2009 Pharmaceutical Price Regulation Scheme (PPRS) (www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpriceregulationscheme/2009PPRS) is a non-contractual scheme between the Department of Health and the Association of the British Pharmaceutical Industry. The purpose of the 2009 PPRS is to ensure that safe and cost-effective medicines are available on reasonable terms to the NHS in England and Wales. One of the features of the 2009 PPRS is to improve patients' access to medicines at prices that better reflect their value through patient access schemes.

Patient access schemes are arrangements which may be used on an exceptional basis for the acquisition of medicines for the NHS in England and Wales. Patient access schemes propose either a discount or rebate that may be linked to the number, type or response of patients, or a change in the list price of a medicine linked to the collection of new evidence (outcomes). These schemes help to improve the cost effectiveness of a medicine and therefore allow the National Institute for Health and Care Excellence (NICE) to recommend treatments which it would otherwise not have found to be cost effective. More information on the framework for patient access schemes is provided in the 2009 PPRS (www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpriceregulationscheme/2009PPRS.

Patient access schemes are proposed by a pharmaceutical company and agreed with the Department of Health, with input from the Patient Access Schemes Liaison Unit (PASLU) within the Centre for Health Technology Evaluation at NICE.

2 Instructions for manufacturers and sponsors

This document is the patient access scheme submission template for technology appraisals. If manufacturers and sponsors want the National Institute for Health and Care Excellence (NICE) to consider a patient access scheme as part of a technology appraisal, they should use this template. NICE can only consider a patient access scheme after formal referral from the Department of Health.

The template contains the information NICE requires to assess the impact of a patient access scheme on the clinical and cost effectiveness of a technology, in the context of a technology appraisal, and explains the way in which background information (evidence) should be presented. If you are unable to follow this format, you must state your reasons clearly. You should insert 'N/A' against sections that you do not consider relevant, and give a reason for this response.

Please refer to the following documents when completing the template:

- 'Guide to the methods of technology appraisal' (http://publications.nice.org.uk/guide-to-the-methods-of-technology-appraisal-2013-pmg9)
- 'Specification for manufacturer/sponsor submission of evidence' (http://www.nice.org.uk/aboutnice/howwework/devnicetech/singletechnologyappraisalsubmissiontemplates.jsp) and
- Pharmaceutical Price Regulation Scheme 2009 (www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpriceregulationscheme/2009PPRS).

For further details on the technology appraisal process, please see NICE's 'Guide to the single technology appraisal (STA) process' and 'Guide to the multiple technology appraisal (MTA) process' (http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp). The 'Specification for manufacturer/sponsor submission of evidence' provides details on disclosure of information and equality issues.

Make the submission as brief and informative as possible. Only mark information as confidential when absolutely necessary. Sufficient information must be publicly available for stakeholders to comment on the full content of the technology appraisal, including details of the proposed patient access scheme. Send submissions electronically to NICE in Word or a compatible format, not as a PDF file.

Appendices may be used to include additional information that is considered relevant to the submission. Do not include information in the appendices that has been requested in the template. Appendices should be clearly referenced in the main submission.

When making a patient access scheme submission, include:

- an updated version of the checklist of confidential information, if necessary
- an economic model with the patient access scheme incorporated, in accordance with the 'Guide to the methods of technology appraisal' (http://publications.nice.org.uk/guide-to-the-methods-of-technology-appraisal-2013-pmg9).

If you are submitting the patient access scheme at the end of the appraisal process, you should update the economic model to reflect the assumptions that the Appraisal Committee considered to be most plausible. No other changes should be made to the model.

3 Details of the patient access scheme

3.1 Please give the name of the technology and the disease area to which the patient access scheme applies.

Dabrafenib was granted marketing authorisation by the European Medicines Agency (EMA) on 26th August 2013 for treatment in monotherapy for adult patients with unresectable or metastatic melanoma with a $BRAF^{V600}$ mutation.

3.2 Please outline the rationale for developing the patient access scheme.

The rationale behind the patient access scheme is to provide dabrafenib at a cost-effective price to the NHS.

3.3 Please describe the type of patient access scheme, as defined by the PPRS.

The patient access scheme is a straight discount to the dabrafenib list price. The discount will apply at the point of invoicing for the product and the scheme will be implemented from the time of positive NICE guidance, expected in September 2014.

3.4 Please provide specific details of the patient population to which the patient access scheme applies. Does the scheme apply to the whole licensed population or only to a specific subgroup (for example, type of tumour, location of tumour)? If so:

- **How is the subgroup defined?**
- **If certain criteria have been used to select patients, why have these have been chosen?**
- **How are the criteria measured and why have the measures been chosen?**

The scheme applies to the whole population licensed for dabrafenib, namely, patients with unresectable or metastatic $BRAF^{V600}$ mutation positive melanoma.

3.5 Please provide details of when the scheme will apply to the population specified in 3.4. Is the scheme dependent on certain criteria, for example, degree of response, response by a certain time point, number of injections? If so:

- **Why have the criteria been chosen?**
- **How are the criteria measured and why have the measures been chosen.**

Implementation of the scheme is dependent only upon positive NICE guidance for dabrafenib. The straight discount will apply at the point of invoicing from the time of positive NICE guidance. No additional criteria will need to be met.

3.6 What proportion of the patient population (specified in 3.4) is expected to meet the scheme criteria (specified in 3.5)?

The scheme is applicable to 100% of the population treated with dabrafenib in the NHS in England and Wales.

3.7 Please explain in detail the financial aspects of the scheme. How will any rebates be calculated and paid?

The straight discount will be applied automatically at the point of invoicing for purchases of dabrafenib packs made by NHS Providers on behalf of NHS patients. The proposed discount will be reflected on the invoice.

3.8 Please provide details of how the scheme will be administered. Please specify whether any additional information will need to be collected, explaining when this will be done and by whom.

No additional information will need to be collected.

3.9 Please provide a flow diagram that clearly shows how the scheme will operate. Any funding flows must be clearly demonstrated.

N/A, the schemes will not impact on funding flows and will not require additional resource by NHS staff.

3.10 Please provide details of the duration of the scheme.

Subject to positive NICE guidance for dabrafenib, the proposed scheme would be in place until NICE review, subject to the normal NICE review process, and subject to Department of Health agreement.

3.11 Are there any equity or equalities issues relating to the scheme, taking into account current legislation and, if applicable, any concerns identified during the course of the appraisal? If so, how have these been addressed?

There are no equity or equality issues relating to the schemes. This has been confirmed through the PASLU review.

3.12 If available, please list any scheme agreement forms, patient registration forms, pharmacy claim forms/rebate forms, guides for pharmacists and physicians and patient information documents. Please include copies in the appendices.

The discounts will apply automatically and no forms will be required for the implementation of the schemes.

3.13 In the exceptional case that you are submitting an outcome-based scheme, as defined by the PPRS, please also refer to appendix B.

N/A, the schemes are financial schemes (straight discounts at the point of invoice).

Cost effectiveness

3.14 If the population to whom the scheme applies (as described in sections 3.4 and 3.5) has not been presented in the main manufacturer/sponsor submission of evidence for the technology appraisal (for example, the population is different as there has been a change in clinical outcomes or a new continuation rule), please (re-)submit the relevant sections from the 'Specification for manufacturer/sponsor submission of evidence' (particularly sections 5.5, 6.7 and 6.9). You should complete those sections both with and without the patient access scheme. You must also complete the rest of this template.

The population to whom the scheme applies has been presented in the main submission of evidence.

3.15 If you are submitting the patient access scheme at the end of the technology appraisal process, you should update the economic model to reflect the assumptions that the Appraisal Committee considered to be most plausible. No other changes should be made to the model.

N/A – the patient access scheme is considered alongside the main submission in this technology appraisal.

3.16 Please provide details of how the patient access scheme has been incorporated into the economic model. If applicable, please also provide details of any changes made to the model to reflect the assumptions that the Appraisal Committee considered most plausible.

The patient access scheme has been incorporated into the economic model by utilising the discounted / per mg price for dabrafenib that would apply in the context of the straight discount.

3.17 Please provide the clinical effectiveness data resulting from the evidence synthesis and used in the economic model which includes the patient access scheme.

Table 1 provides the clinical effectiveness data from the pivotal RCT (BREAK-3) which underpins the economic model in the main submission. Results of indirect comparisons of dabrafenib versus vemurafenib are provided in Table 2. These data do not change with implementation of the patient access schemes.

Table 1. Key outcomes from the BREAK-3 trial (ITT populations)

	Dabrafenib monotherapy (BREAK-3 - BRF113683); NCT01227889 **Latest PFS cut-off; 25 Jun 2012** **OS update; 18 Dec 2012**	
	Dabrafenib **150mb b.d.** **(N=187)**	**Dacarbazine** **1000mg/m^2** **(N = 63)**
PFS; months **Median (95% CI)**	6.9 (5.2, 9.0)	2.7 (1.5, 3.2)
HR (95% CI); p-value	0.37 (0.24, 0.58); p<0.0001	
OS; months **Median (95% CI)**	18.2 (16.6, NR)	15.6 (12.7, NR)
ITT HR (95% CI) **P-value**	0.76 (0.48, 1.21) p=not significant	
Crossover (%)	57	
RPSFTM-adjusted HR (95% CI)	0.55 (0.21, 1.43)	

Table 2. ITC PFS and OS HRs for dabrafenib versus vemurafenib

Treatment	**Control**	**PFS HR (95% CI)**	**OS HR* (95% CI)**
Dabrafenib	Vemurafenib	0.97 (0.59-1.60)	0.86 (0.32-2.29)

HR<1 is in favour of treatment
*Analyses use crossover-adjusted OS HRs (RPSFTM method), including for vemurafenib (BRIM-3 allowed patients to crossover from dacarbazine upon progression and RPSFTM adjustment of OS results was undertaken as part of the NICE appraisal)

3.18 Please list any costs associated with the implementation and operation of the patient access scheme (for example, additional pharmacy time for stock management or rebate calculations). A suggested format is presented in table 1. Please give the reference source of these costs. Please refer to section 6.5 of the 'Specification for manufacturer/sponsor submission of evidence'.

There will be no additional costs associated with the implementation and operation of the patient access scheme.

3.19 Please provide details of any additional treatment-related costs incurred by implementing the patient access scheme. A suggested format is presented in table 2. The costs should be provided for the intervention both with and without the patient access scheme. Please give the reference source of these costs.

Implementation of the patient access scheme will not incur additional treatment-related costs. Treatment costs will be reduced while all other elements of the treatment pathway will be unchanged.

Summary results

Base-case analysis

3.20 Please present in separate tables the cost-effectiveness results as follows.[1]

- **the results for the intervention without the patient access scheme**
- **the results for the intervention with the patient access scheme.**

A suggested format is shown below.

Pairwise base case results for dabrafenib, with and without the patient access scheme are presented in the tables below. Discrepancies are due to rounding as actual figures are used in modelling.

[1] For outcome-based schemes, please see section 5.2.8 in appendix B.

Table 3. Dabrafenib vs. vemurafenib and dacarbazine (list price)

	Dabrafenib	Dacarbazine	Vemurafenib	Dabrafenib vs. dacarbazine	Dabrafenib vs. Vemurafenib
Effectiveness, Undiscounted					
Progression-Free Life Years	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Post-Progression Life Years	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Life Years	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Quality-Adjusted Life Years	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Effectiveness, Discounted					
Progression-Free Life Years	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Post-Progression Life Years	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Life Years	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Quality-Adjusted Life Years	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Costs, Discounted					
Direct Medical	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Medication	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Administration	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Adverse Events	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Diagnostic Testing	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Other, Progression-Free	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Other, Post-Progression	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Total	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost-Effectiveness					
Cost per Progression-Free Life Year	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost per Life Year	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost per Quality-Adjusted Life Year	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Table 4. Dabrafenib vs. vemurafenib and dacarbazine (PAS price)

	Dabrafenib	Dacarbazine	Vemurafenib	Dabrafenib vs. dacarbazine	Dabrafenib vs. Vemurafenib
Effectiveness, Undiscounted					
Progression-Free Life Years	[redacted]				
Post-Progression Life Years					
Life Years					
Quality-Adjusted Life Years					
Effectiveness, Discounted					
Progression-Free Life Years	[redacted]				
Post-Progression Life Years					
Life Years					
Quality-Adjusted Life Years					
Costs, Discounted					
Medication	[redacted]				
Administration					
Adverse Events					
Diagnostic Testing					
Other, Progression-Free					
Other, Post-Progression					
Total					
Cost-Effectiveness					
Cost per Progression-Free Life Year				100,204	122,046
Cost per Life Year				34,962	7,531
Cost per Quality-Adjusted Life Year				49,019	11,028

3.21 Please present in separate tables the incremental results as follows

- **the results for the intervention without the patient access scheme**
- **the results for the intervention with the patient access scheme.**

List the interventions and comparator(s) from least to most expensive. Present the incremental cost-effectiveness ratios (ICERs) in comparison with baseline (usually standard care), and the incremental analysis ranking technologies in terms of dominance and extended dominance.

Table 5: Incremental analyses (list price)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYs)
Dacarbazine	[redacted]							
Vemurafenib								
Dabrafenib								

Table 6: Incremental analyses (PAS price)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Inc LYG	Inc QALYs	ICER (£) vs baseline (QALYs)	ICER (£) incremental (QALYs)
Dacarbazine	[redacted]			-	-	-	-	-
Vemurafenib								Extended dominance
Dabrafenib							49,019	49,019

Sensitivity analyses

3.22 Please present deterministic sensitivity analysis results as described for the main manufacturer/sponsor submission of evidence for the technology appraisal. Consider using tornado diagrams.

Results of the deterministic sensitivity analyses for each of the three interventions (incorporating the PAS) are presented fully in the tables below. The ten scenarios that impact most on the base case result (in either direction) are highlighted in each table for each pairwise comparison.

Table 7. Results of deterministic sensitivity analyses on cost-effectiveness of dabrafenib (list price) vs. vemurafenib and dacarbazine

		Strategies						Dabrafenib vs.					
		Dabrafenib		Dacarbazine		Vemurafenib		Dacarbazine			Vemurafenib		
		QALYs	Cost	QALYs	Cost	QALYs	Cost	QALYs	Cost	Cost/QALY	QALYs	Cost	Cost/QALY
0	Base case	[redacted]											
1	Time horizon set to 10 years												
2	BRAF class effect												
3	PFS for dabrafenib and dacarbazine – Weibull												
4	PFS for dabrafenib and dacarbazine – gamma												
5	PFS for dabrafenib and dacarbazine - KM data												
6	OS for dabrafenib – Weibull												
7	OS for dabrafenib - log-logistic												
8	OS for dabrafenib – gamma												
9	OS for dabrafenib based on Kaplan-Meier data												
10	OS for dacarbazine (trial segment) based on RPSFT-adjusted Kaplan-Meier data												
11	OS for dacarbazine (trial segment) based on proportional hazards versus dabrefnib using ITT HR from BREAK-3												
12	Survival for dacarbazine based on AJCC survival for entire model timeframe, dabrafenib												

	and vemurafenib based on proportional hazards vs. dacarbazine	[redacted]
13	Survival for dacarbazine and vemurafenib based on approach taken for vemurafenib NICE submission, dabrafenib based on proportional hazards vs. vemurafenib	
14	HR for PFS for dabrafenib vs. dacarbazine (lower CI)	
15	HR for PFS for dabrafenib vs. dacarbazine (upper CI)	
16	HR for PFS for dabrafenib vs. vemurafenib (lower CI)	
17	HR for PFS for dabrafenib vs. vemurafenib (upper CI)	
18	HR for OS for dabrafenib vs. dacarbazine (lower CI)	
19	HR for OS for dabrafenib vs. dacarbazine (upper CI)	
20	HR for OS for dabrafenib vs. vemurafenib (lower CI)	
21	HR for OS for dabrafenib vs. vemurafenib (upper CI)	
22	Perfect dose intensity for all comparators	
23	Admin costs set to +50% of base case value	

24	Admin costs set to -50% of base case value	[redacted]
25	PF costs set to +50% of base case value	
26	PF costs set to -50% of base case value	
27	PP costs set to +50% of base case value	
28	PP costs set to -50% of base case value	
29	Testing costs set to +50% of base case value	
30	Testing costs set to -50% of base case value	
31	PSACT cost set to +50% of base case value	
32	PSACT cost set to -50% of base case value	
33	PSACT cost set to zero	
34	Terminal care cost set to +50% of base case value	
35	Terminal care cost set to -50% of base case value	
36	Costs of all AEs simultaneously set to +50% of base case value	
37	Costs of all AEs simultaneously set to -50% of base case value	
38	Set cost of all adverse events to zero	

39	Disutility of PFS vs. perfect health set to -50% of the base case value	[redacted]
40	Disutility of PFS vs. perfect health set to +50% of the base case value	
41	Disutility of PPS vs. PFS for dacarbazine assumed to be same as Dabrafenib	
42	Disutility of PPS vs. PFS set to -50% of the base case value	
43	Disutility of PPS vs. PFS set to -50% of the base case value	

Table 8. Results of deterministic sensitivity analyses on cost-effectiveness of dabrafenib (PAS price) vs. vemurafenib and dacarbazine

		Strategies						Dabrafenib vs.					
		Dabrafenib		Dacarbazine		Vemurafenib		Dacarbazine			Vemurafenib		
		QALYs	Cost	QALYs	Cost	QALYs	Cost	QALYs	Cost	Cost/QALY	QALYs	Cost	Cost/QALY
0	Base case	[redacted]								49,019	[redacted]		11,028
1	Time horizon set to 10 years	[redacted]								68,520	[redacted]		13,464
2	BRAF class effect	[redacted]								49,019	[redacted]		Dominated
3	PFS for dabrafenib and dacarbazine – Weibull	[redacted]								43,759	[redacted]		Dominant
4	PFS for dabrafenib and dacarbazine – gamma	[redacted]								21,597	[redacted]		Dominant
5	PFS for dabrafenib and dacarbazine KM data	[redacted]								53,820	[redacted]		25,112
6	OS for dabrafenib - Weibull	[redacted]								55,050	[redacted]		16,723
7	OS for dabrafenib - log-logistic	[redacted]								51,360	[redacted]		12,522
8	OS for dabrafenib - gamma	[redacted]								46,104	[redacted]		9,754
9	OS for dabrafenib based on Kaplan-Meier data	[redacted]								43,573	[redacted]		8,951
10	OS for dacarbazine (trial segment) based on RPSFT-adjusted Kaplan-Meier data	[redacted]								91,808	[redacted]		11,028
11	OS for dacarbazine (trial segment) based on proportional hazards versus dabrefnib using ITT HR from BREAK-3	[redacted]								95,225	[redacted]		11,028

12	Survival for dacarbazine based on AJCC survival for entire model timeframe, dabrafenib and vemurafenib based on proportional hazards vs. dacarbazine	[redacted]	47,180	[redacted]	11,592
13	Survival for dacarbazine and vemurafenib based on approach taken for vemurafenib NICE submission, dabrafenib based on proportional hazards vs. vemurafenib	[redacted]	36,802	[redacted]	8,993
14	HR for PFS for dabrafenib vs. dacarbazine (lower CI)	[redacted]	48,551	[redacted]	11,028
15	HR for PFS for dabrafenib vs. dacarbazine (upper CI)	[redacted]	48,738	[redacted]	11,028
16	HR for PFS for dabrafenib vs. vemurafenib (lower CI)	[redacted]	49,019	[redacted]	67,220
17	HR for PFS for dabrafenib vs. vemurafenib (upper CI)	[redacted]	49,019	[redacted]	Dominant
18	HR for OS for dabrafenib vs. dacarbazine (lower CI)	[redacted]	26,470	[redacted]	11,028
19	HR for OS for dabrafenib vs. dacarbazine (upper CI)	[redacted]	Dominated	[redacted]	11,028
20	HR for OS for dabrafenib vs. vemurafenib (lower CI)	[redacted]	49,019	[redacted]	6,422

21	HR for OS for dabrafenib vs. vemurafenib (upper CI)	[redacted]	49,019	[redacted]	4,276 †
22	Perfect dose intensity for all comparators	[redacted]	48,210	[redacted]	10,956
23	Admin costs set to +50% of base case value	[redacted]	48,399	[redacted]	11,037
24	Admin costs set to -50% of base case value	[redacted]	49,640	[redacted]	11,020
25	PF costs set to +50% of base case value	[redacted]	49,392	[redacted]	11,097
26	PF costs set to -50% of base case value	[redacted]	48,646	[redacted]	10,959
27	PP costs set to +50% of base case value	[redacted]	50,841	[redacted]	13,771
28	PP costs set to -50% of base case value	[redacted]	47,197	[redacted]	8,286
29	Testing costs set to +50% of base case value	[redacted]	49,123	[redacted]	11,028
30	Testing costs set to -50% of base case value	[redacted]	48,915	[redacted]	11,028
31	PSACT cost set to +50% of base case value	[redacted]	47,479	[redacted]	11,024
32	PSACT cost set to -50% of base case value	[redacted]	50,560	[redacted]	11,033
33	PSACT cost set to zero	[redacted]	52,100	[redacted]	11,038
34	Terminal care cost set to +50% of base case value	[redacted]	48,841	[redacted]	10,841
35	Terminal care cost set to -50% of base case value	[redacted]	49,198	[redacted]	11,215

36	Costs of all AEs simultaneously set to +50% of base case value	[redacted]	49,239	[redacted]	11,485
37	Costs of all AEs simultaneously set to -50% of base case value	[redacted]	48,800	[redacted]	10,571
38	Set cost of all adverse events to zero	[redacted]	48,580	[redacted]	10,115
39	Disutility of PFS vs. perfect health set to -50% of the base case value	[redacted]	45,090	[redacted]	13,299
40	Disutility of PFS vs. perfect health set to +50% of the base case value	[redacted]	53,698	[redacted]	9,420
41	Disutility of PPS vs. PFS for dacarbazine assumed to be same as Dabrafenib	[redacted]	49,343	[redacted]	11,028
42	Disutility of PPS vs. PFS set to -50% of the base case value	[redacted]	51,998	[redacted]	11,751
43	Disutility of PPS vs. PFS set to -50% of the base case value	[redacted]	46,363	[redacted]	10,389

3.23 **Please present any probabilistic sensitivity analysis results, and include scatter plots and cost-effectiveness acceptability curves.**

<u>Probabilistic sensitivity analyses (scatter plots and CEAC) at dabrafenib list price</u>

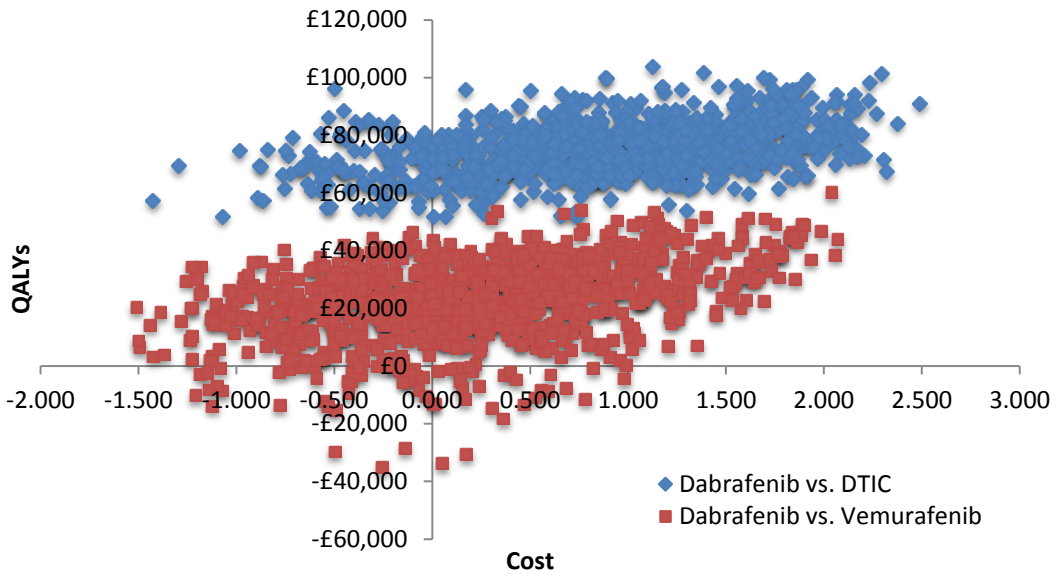

Figure 1. ICER scatterplot for dabrafenib (list price) comparisons

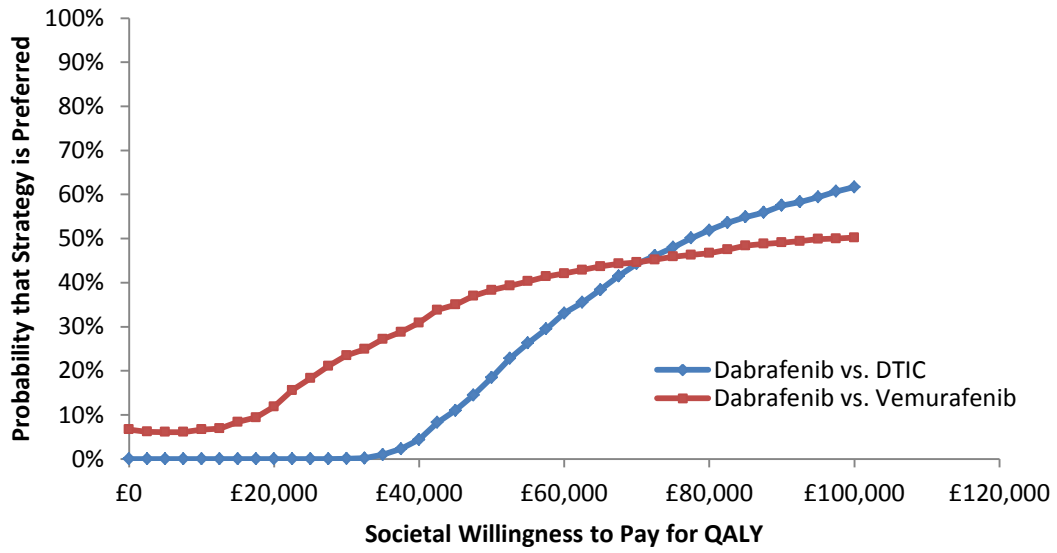

Figure 2. Pairwise acceptability plot for dabrafenib versus comparators (list price)

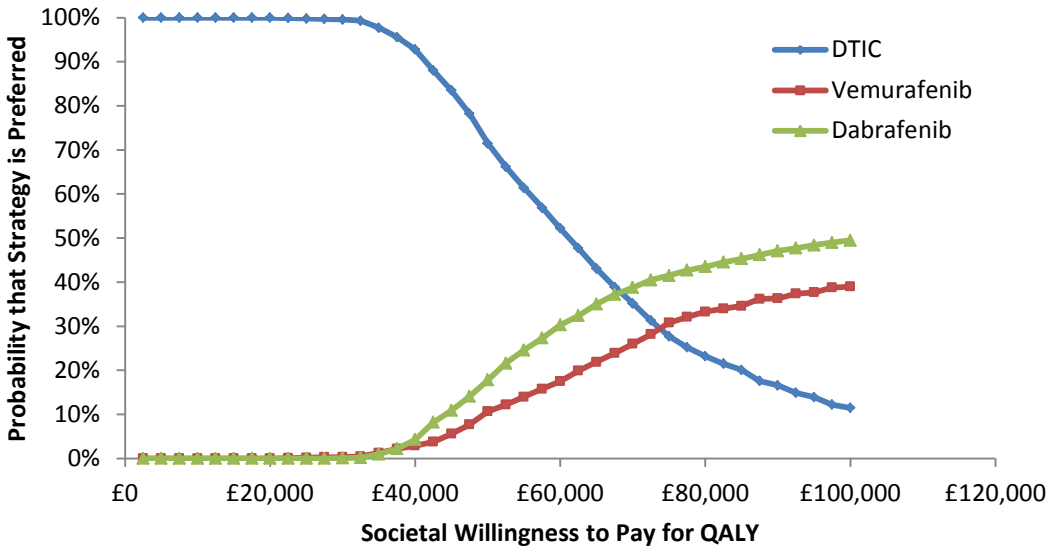

Figure 3. Incremental acceptability plot (list price)

<u>Probabilistic sensitivity analyses (scatter plots and CEAC) at dabrafenib PAS price</u>

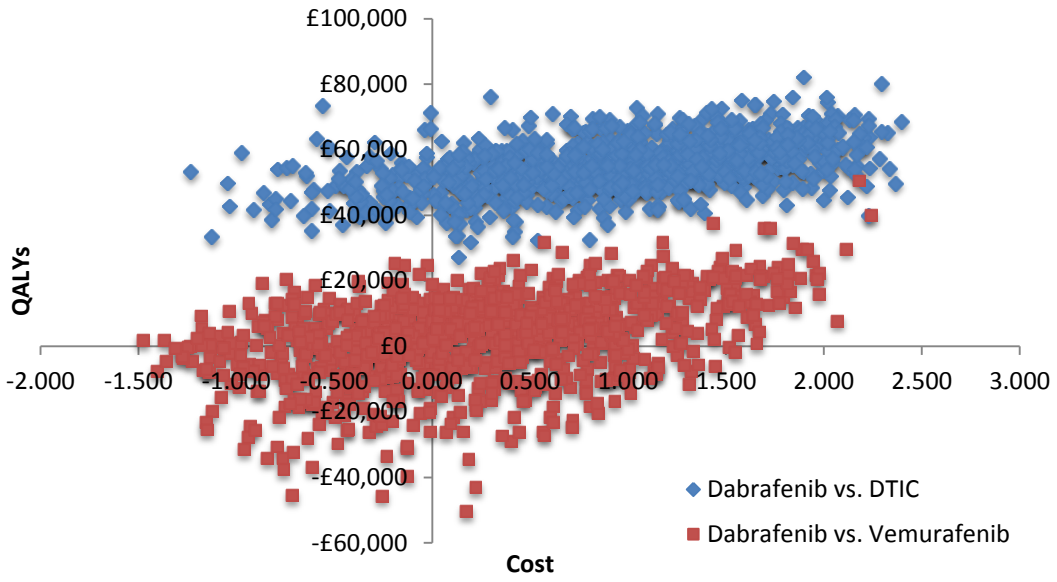

Figure 4. ICER scatterplot for dabrafenib (PAS price) comparisons

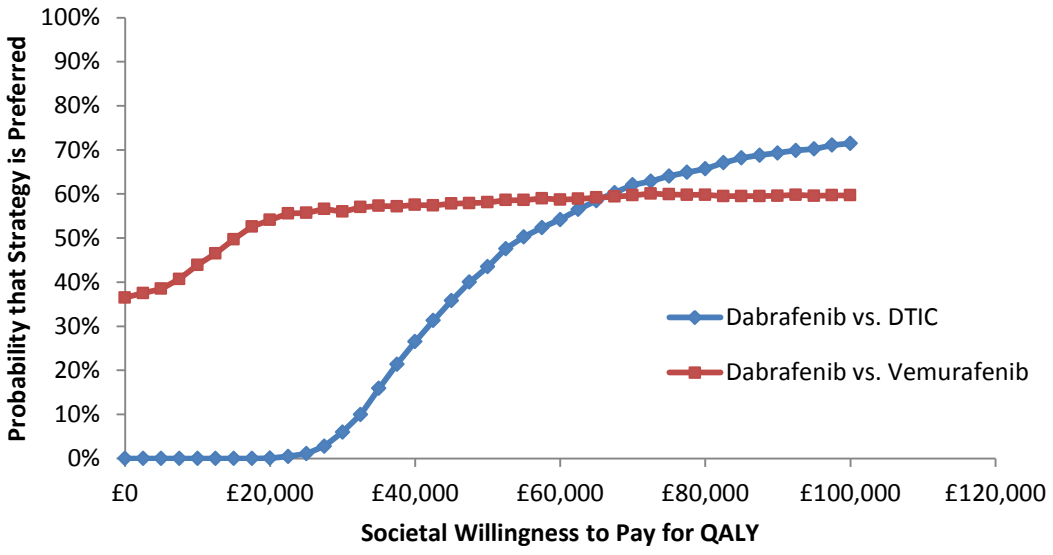

Figure 5. Acceptability curves for pairwise comparisons for dabrafenib (PAS price) vs. vemurafenib and dacarbazine

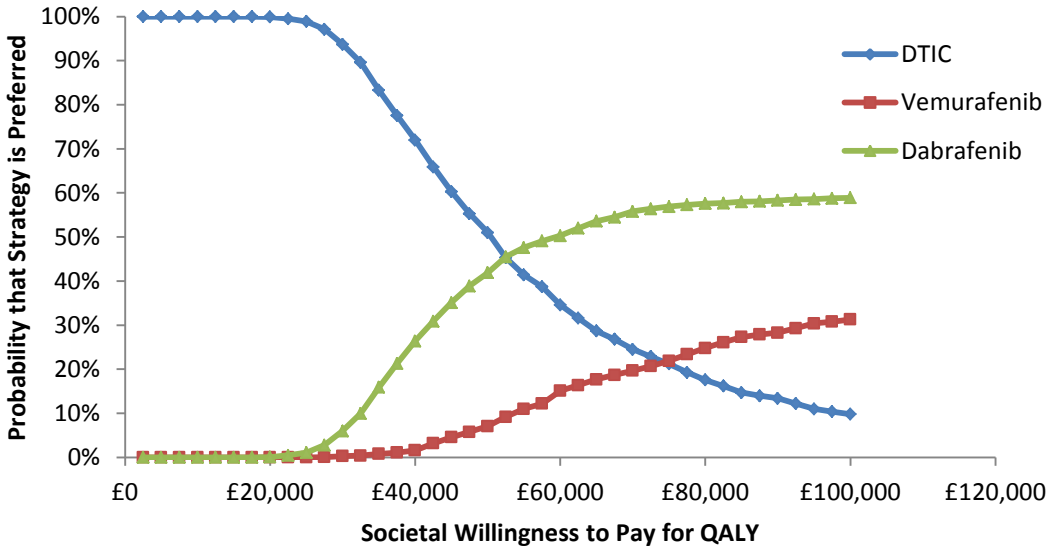

Figure 6. Acceptability curves for incremental analysis of dabrafenib (PAS price) vs. vemurafenib and dacarbazine

3.24 Please present scenario analysis results as described for the main manufacturer/sponsor submission of evidence for the technology appraisal.

No specific additional scenario analyses are presented in the main submission. The base case is as defined in Section B and a number of scenarios are run as part of the deterministic sensitivity analyses.

3.25 If any of the criteria on which the patient access scheme depends are clinical variable (for example, choice of response measure, level of response, duration of treatment), sensitivity analyses around the individual criteria should be provided, so that the Appraisal Committee can determine which criteria are the most appropriate to use.

Implementation of the patient access scheme does not depend upon any clinical variables.

Impact of patient access scheme on ICERs

3.26 **For financially based schemes, please present the results showing the impact of the patient access scheme on the ICERs for the base-case and any scenario analyses. A suggested format is shown below (see table 5). If you are submitting the patient access scheme at the end of the appraisal process, you must include the scenario with the assumptions that the Appraisal Committee considered to be most plausible.**

Table 9. Results showing the impact of patient access scheme on ICERs for dabrafenib

	ICER for dabrafenib versus:			
	Vemurafenib		Dacarbazine	
	Without PAS	With PAS	Without PAS	With PAS
Base case	[redacted]	£11,028	[redacted]	£49,019

4 Appendices

4.1 Appendix A: Additional documents

4.1.1 If available, please include copies of patient access scheme agreement forms, patient registration forms, pharmacy claim forms/rebate forms, guides for pharmacists and physicians, patient information documents.

The scheme will operate as simple discounts at the point of invoice, requiring no additional documentation for the NHS.

4.2 Appendix B: Details of outcome-based schemes

4.2.1 If you are submitting a proven value: price increase scheme, as defined in the PPRS, please provide the following information:

- **the current price of the intervention**
- **the proposed higher price of the intervention, which will be supported by the collection of new evidence**
- **a suggested date for when NICE should consider the additional evidence.**

N/A, the scheme is a financially-based scheme.

4.2.2 If you are submitting an expected value: rebate scheme, as defined in the PPRS, please provide the following details:

- **the current price of the intervention (the price that will be supported by the collection of new evidence)**
- **the planned lower price of the intervention in the event that the additional evidence does not support the current price**
- **a suggested date for when NICE should consider the additional evidence.**

Not applicable, the scheme is a financially-based scheme.

4.2.3 If you are submitting a risk-sharing scheme, as defined in the PPRS, please provide the following details:

- **the current price of the intervention (the price that will be supported by the collection of new evidence)**

- **the proposed relationship between future price changes and the evidence to be collected.**

Not applicable, the scheme is a financially-based scheme.

4.2.4 For outcome-based schemes, as defined in the PPRS, please provide the full details of the new information (evidence) planned to be collected, who will collect it and who will carry the cost associated with this planned data collection. Details of the new information (evidence) may include:

- **design of the new study**
- **patient population of the new study**
- **outcomes of the new study**
- **expected duration of data collection**
- **planned statistical analysis, definition of study groups and reporting (including uncertainty)**
- **expected results of the new study**
- **planned evidence synthesis/pooling of data (if applicable)**
- **expected results of the evidence synthesis/pooling of data (if applicable).**

Not applicable, the scheme is a financially-based scheme and does not require that new information is collected.

4.2.5 If you are submitting a risk-sharing scheme, please specify the period between the time points when the additional evidence will be considered.

Not applicable, as above.

4.2.6 Please provide the clinical effectiveness data resulting from the evidence synthesis and used in the economic modelling of the patient access scheme at the different time points when the additional evidence is to be considered.

Not applicable, as above.

4.2.7 Please provide the other data used in the economic modelling of the patient access scheme at the different time points when the additional evidence is to be considered. These data could include cost/resource use, health-related quality of life and utilities.

Not applicable, as above.

4.2.8 Please present the cost-effectiveness results as follows.

- **For proven value: price increase schemes, please summarise in separate tables:**
  - **the results based on current evidence and current price**
  - **the anticipated results based on the expected new evidence and the proposed higher price.**
- **For expected value: rebate schemes, please summarise in separate tables:**
  - **the results based on the expected new evidence and the current price (which will be supported by the additional evidence collection)**
  - **the results based on the current evidence and the lower price (if the new evidence is not forthcoming).**
- **For risk-sharing schemes, please summarise in separate tables:**
  - **the results based on current evidence and current price**
  - **the results based on the expected new evidence and the current price (which will be supported by the additional evidence collection)**
  - **the results based on the current evidence and the lower price (if the new evidence is not forthcoming)**
  - **the anticipated results based on the expected new evidence and the proposed higher price.**

Not applicable, as above.

4.2.9 Please present in separate tables the incremental results for the different scenarios as described above in section 5.2.8 for the type of outcome-based scheme being submitted.

List the interventions and comparator(s) from least to most expensive. Present the incremental cost-effectiveness ratios (ICERs)

in comparison with baseline (usually standard care), and the incremental analysis ranking technologies in terms of dominance and extended dominance. A suggested format is presented in table 4, section 4.8.

Not applicable, as above.