NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Technology appraisals

Patient access scheme submission template

Trametinib in combination with dabrafenib for treating advanced (unresectable or metastatic) BRAF V600 mutation-positive melanoma

December 2015

File name	Version	Contains confidential information	Date
		Yes	17/12/2015

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.

Mekinist®(trametinib) in combination with dabrafenib for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.

Following a positive recommendation by NICE for trametinib for the treatment of unresectable or metastatic melanoma with a BRAF V600 mutation, the patient access scheme (PAS) will be applied to all supplies and preparations of trametinib and dabrafenib and is applicable to all current and future indications.

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

The simple discount PAS is a mechanism through which the NHS will be able to procure both trametinib and dabrafenib at net prices lower than the current list prices. Together these discounts result in a price for the combination that is cost-effective versus current treatment alternatives.

The proposed patient access scheme is a simple discount to the trametinib list price and a reduction to the existing net PAS price for dabrafenib monotherapy. The discounts will apply at the point of invoicing for trametinib and dabrafenib. Both the scheme for trametinib and the revised scheme for dabrafenib will only be implemented upon publication of positive NICE guidance.

Should the list prices of either trametinib or dabrafenib change, the percentage discount will change accordingly to maintain a fixed net price.

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

Financially-based scheme: simple discount to list price. The amount of discount and net price will remain commercial in confidence.

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 entire population for whom the combination of dabrafenib and trametinib has been licensed, namely adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.

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.

Following positive NICE guidance for trametinib+dabrafenib combination the PAS will apply to all supplies and preparations of trametinib+dabrafenib and is applicable to all current and future indications. 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 the combination of dabrafenib and trametinib 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?

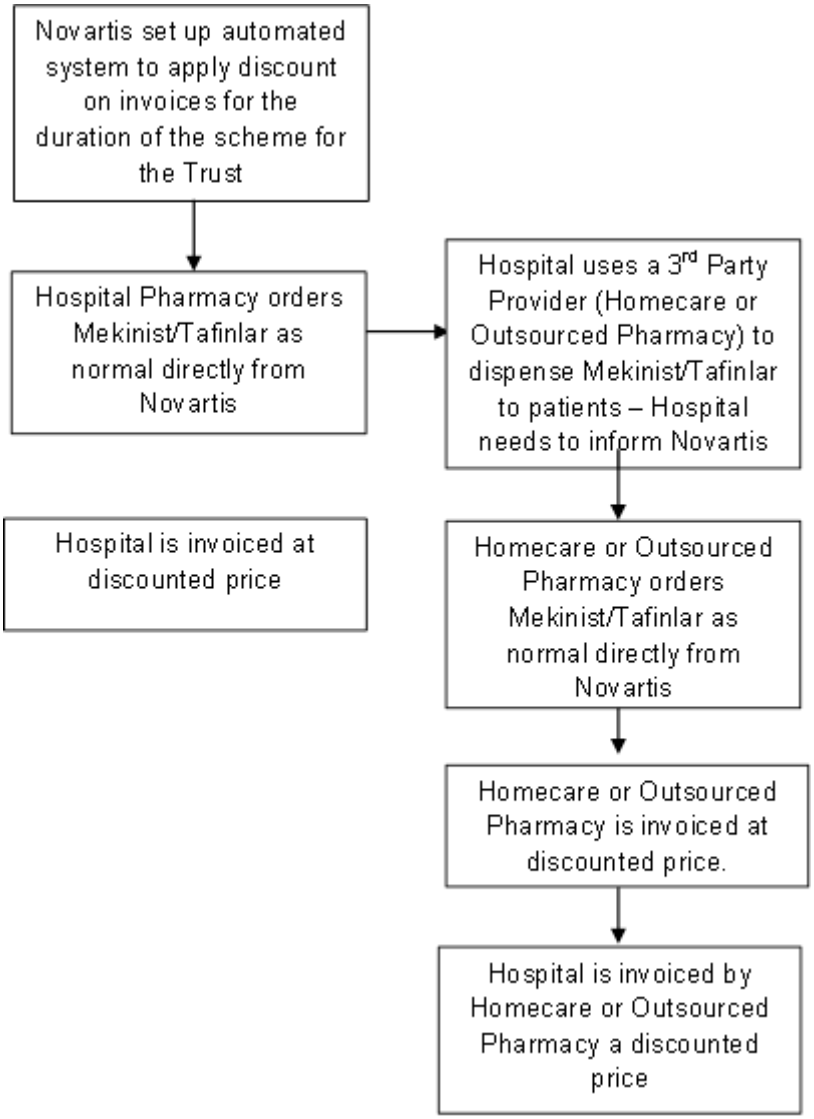
The discount will be applied at the point of invoicing for purchases of trametinib and dabrafenib packs made by NHS Providers on behalf of NHS patients. The proposed discount will be reflected in the invoice. The amount of discount and net price will remain commercial in confidence.

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.

There will be no need to collect any additional information.

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

The scheme will not require any additional NHS resource to access the PAS net price as hospital pharmacy will operate the standard NHS pharmacy procurement procedure to order trametinib and dabrafenib directly from Novartis.



3.10 Please provide details of the duration of the scheme.

Subject to positive NICE guidance for the combination of dabrafenib and trametinib, the proposed scheme will be in place until NICE review of the guidance, subject to the usual NICE review process.

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 this scheme.

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 discount will apply automatically and will not require any additional documentation.

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 trametinib scheme and the existing dabrafenib scheme are financial schemes (simple 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 – this patient access scheme is being submitted for consideration 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.

In the main submission document, list prices are used for trametinib, dabrafenib and vemurafenib. This is in keeping with NICE's recent proposed approach for addressing a comparator associated with a confidential patient access scheme.

Discounts for interventions and comparators can be incorporated into the economic model by utilising the functionality on the 'run analyses' sheet. Here the actual discount values (which apply to the per mg price) can be entered directly for each treatment.

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 below describe the clinical data that have been used in the base case of the economic model. These data do not change with implementation of the patient access scheme.

Table 1: Key outcomes from the COMBI-D and COMBI-D trials

	COMBI-D (datacut Jan 2015)		COMBI-V (datacut Mar 2015)	
	T+D	Dabrafenib	T+D	Vemurafenib
PFS; months Median (95% CI)	11.0 (8.0 – 13.9)	8.8 (5.9 – 9.3)	12.6 (10.7-15.5)	7.3 (5.8-7.8)
HR (95% CI); p value	0.67 (0.53 – 0.84), p=0.0004		0.61 (0.51 – 0.73), p<0.001	
OS; months Median (95% CI); p value	25.1 (19.2 – NR)	18.7 (15.2 – 23.7)	25.6 (22.6 – NR)	18.0 (15.6 – 20.7)
ITT HR (95% CI); p value	0.71 (0.55 – 0.92), p=0.011		0.66 (0.53 – 0.81), p<0.001	
Cross over (%)	Not applicable		21 / 352 (6%)	
RPSFTM-adjusted HR (95% CI)	Not applicable		0.63 (0.50, 0.79)	

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'.

The proposed scheme consists of simple discounts, and therefore there will be no additional costs associated with its implementation and operation in NHS England and Wales.

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 this scheme will not incur additional treatment-related costs. Treatment costs for the NHS in England and Wales will in fact be reduced whilst all other elements of the treatment pathway will remain 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 (table 3).

Pairwise base case results for the combination of dabrafenib and trametinib versus dabrafenib monotherapy and versus vemurafenib with and without the patient access scheme are presented below.

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

Table 2: Base-case cost-effectiveness results (all treatments at list prices)

Discounted costs and benefits	Dabrafenib-trametinib combination	Vemurafenib	Dabrafenib monotherapy
Intervention cost (£)	[redacted]	[redacted]	[redacted]
Other costs (£)	[redacted]	[redacted]	[redacted]
Total costs (£)	[redacted]	[redacted]	[redacted]
Difference in total costs (£)	-	129,707	135,058
LYG	4.586	2.933	2.933
LYG difference	-	1.653	1.653
QALYs	3.443	2.098	2.146
QALY difference		1.345	1.298
ICER (£)	**-**	**96,437**	**104,069**

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

Table 3: Base-case cost-effectiveness results (all treatments including actual/estimated net prices)

	Dabrafenib-trametinib combination [redacted]	**Assumed vemurafenib discounts**			
		Vemurafenib (35% discount)	**Vemurafenib (45% discount)**	**Vemurafenib (55% discount)**	**Dabrafenib monotherapy** [redacted]
Intervention cost (£)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Other costs (£)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Total costs (£)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Difference in total costs (£)	-	[redacted]	[redacted]	[redacted]	[redacted]
LYG	4.586	2.933	2.933	2.933	2.933
LYG difference	-	1.653	1.653	1.653	1.653
QALYs	3.443	2.098	2.098	2.098	2.146
QALY difference	-	1.345	1.345	1.345	1.298
ICER (£)		[redacted]	[redacted]	[redacted]	[redacted]

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

3.21 Please present in separate tables the incremental results as follows. [2]

- 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. A suggested format is presented in table 4.

[2] For outcome-based schemes, please see section 5.2.9 in appendix B.

Table 4: Base-case incremental results (intervention and comparators at list price)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) pure dominance (QALYs)	ICER (£) extended dominance (QALYs)
Dabrafenib	[redacted]	2.933	2.146	-	-	-	-	-
Vemurafenib	[redacted]	2.933	2.098	5,351	1.653	-0.047	dominated	dominated
Dabrafenib-trametinib combination	[redacted]	4.586	3.443	129,707	1.653	1.345	104,069	104,069

ICER, incremental cost-effectiveness ratio; LYG, life years gained; QALYs, quality-adjusted life years

Costs and benefits are discounted

Table 5: Base-case incremental results (dabrafenib in combination: [redacted] | trametinib [redacted] | vemurafenib -35% | dabrafenib monotherapy [redacted])

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) pure dominance (QALYs)	ICER (£) extended dominance (QALYs)
Vemurafenib	[redacted]	2.933	2.098	-	-	-	-	-
Dabrafenib	[redacted]	2.933	2.146	[redacted]	0	0.047	[redacted]	[redacted]
Dabrafenib-trametinib combination	[redacted]	4.586	3.443	[redacted]	1.653	1.298	[redacted]	[redacted]

Table 6: Base-case incremental results (dabrafenib in combination: [redacted] | trametinib [redacted] | vemurafenib -45% | dabrafenib monotherapy [redacted])

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) pure dominance (QALYs)	ICER (£) extended dominance (QALYs)
Vemurafenib	[redacted]	2.933	2.098	-	-	-	-	-
Dabrafenib	[redacted]	2.933	2.146	[redacted]	0.000	0.047	[redacted]	[redacted]
Dabrafenib-trametinib combination	[redacted]	4.586	3.443	[redacted]	1.653	1.298	[redacted]	[redacted]

Table 7: Base-case incremental results (dabrafenib in combination: [redacted] | trametinib [redacted] | vemurafenib -55% | dabrafenib monotherapy [redacted]

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) pure dominance (QALYs)	ICER (£) extended dominance (QALYs)
Vemurafenib	[redacted]	2.933	2.098	-	-	-	-	-
Dabrafenib	[redacted]	2.933	2.146	[redacted]	0.000	0.047	[redacted]	[redacted]
Dabrafenib-trametinib combination	[redacted]	4.586	3.443	[redacted]	1.653	1.298	[redacted]	[redacted]

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.

Table 8 below details the scenarios investigated in deterministic sensitivity analyses along with a rationale for each set of changes.

Table 8: Deterministic sensitivity analyses

1	Model timeframe 20-40 years	Horizon is a potential sensitivity in the economic model, particularly given the accrual of benefit post progression
2	No continuing benefit assumed for PFS	To determine the impact of this clinically conservative assumption
3	Varying additional pre- and post-progression monthly costs and terminal care costs by +/- 50%	These costs accrue alongside treatment costs and may be important contributors in the assessment of ICERs
4	Varying utility decrement of pre-progression and post-progression versus perfect health to their upper and lower 95%CI bounds	The valuation of the individual health states is likely to have an impact on the overall cost-effectiveness

The results of deterministic sensitivity analyses are presented in the tornado plots below, incorporating the specified discounts.

Figure 1: Trametinib [redacted] + dabrafenib [redacted] combination versus dabrafenib monotherapy [redacted]

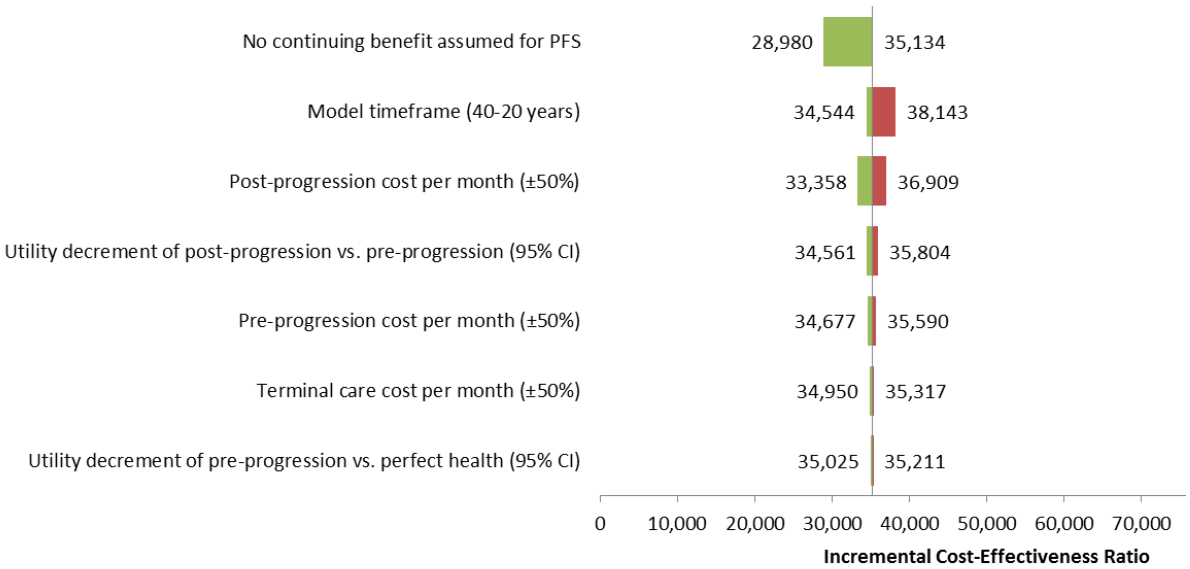


Figure 2: Trametinib [redacted] + dabrafenib [redacted] combination versus vemurafenib monotherapy (-35%)

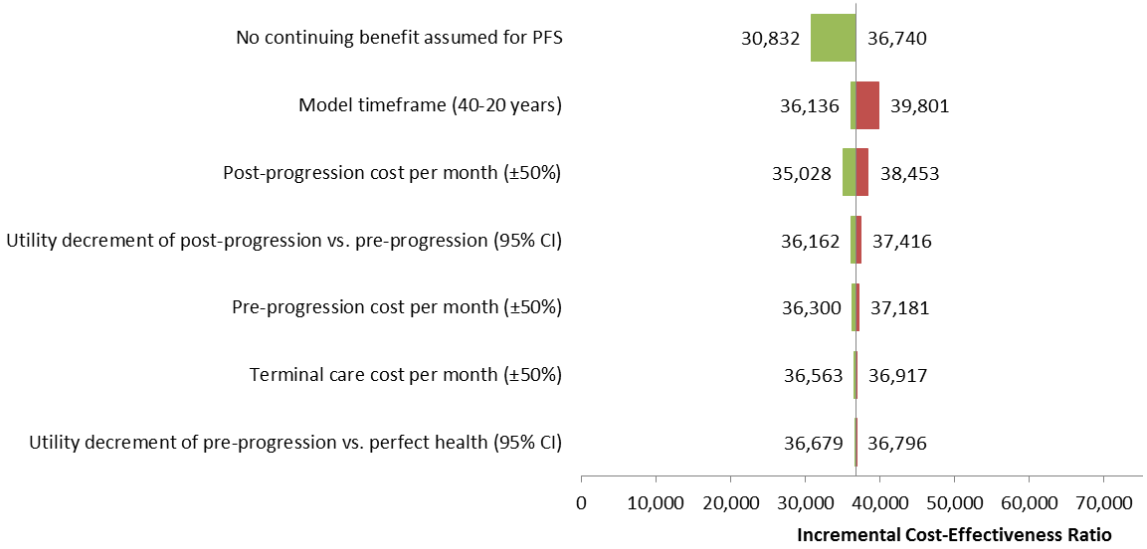


Figure 3: Trametinib [redacted] + dabrafenib [redacted] combination versus vemurafenib monotherapy (-45%)

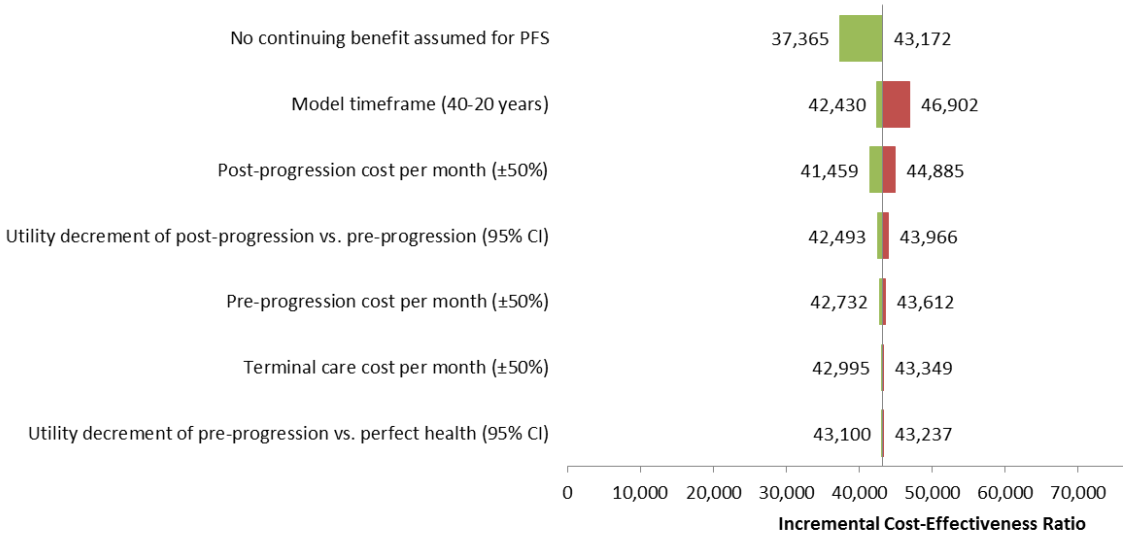
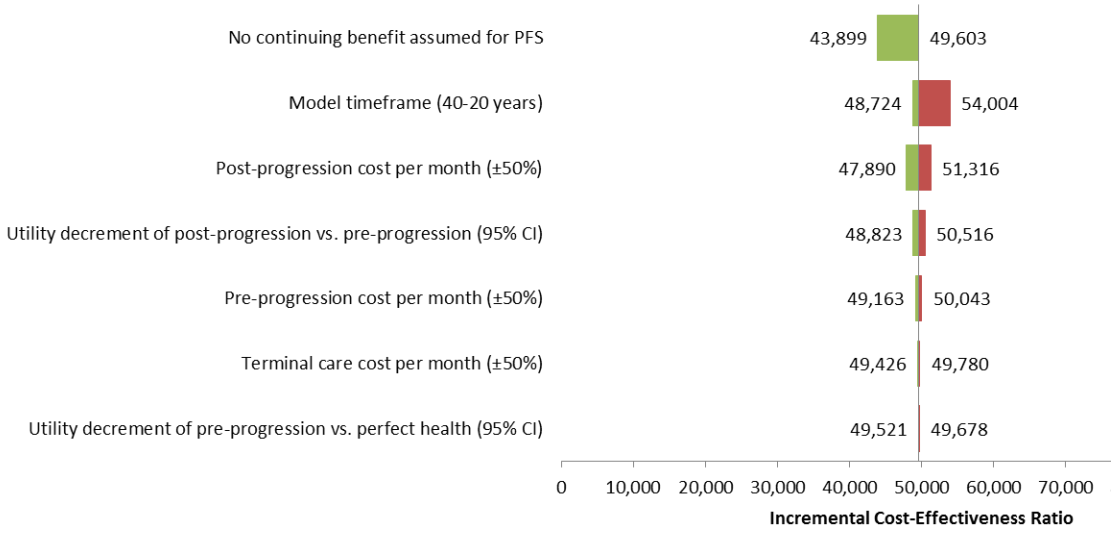


Figure 4: Trametinib [redacted] + dabrafenib [redacted] combination versus vemurafenib monotherapy (-55%)



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

PSA was conducted as described in Section 5.8 in the main submission document. The mean ICERs at the various discount levels are presented below.

Table 9: Mean PSA results at discounted prices

Trametinib [redacted] + dabrafenib [redacted] combination	Mean ICER (£)	Lower 95% CI	Upper 95% CI
Versus vemurafenib (-35%)	[redacted]	[redacted]	[redacted]
Versus vemurafenib (-45%)	[redacted]	[redacted]	[redacted]
Versus vemurafenib (-55%)	[redacted]	[redacted]	[redacted]
Versus dabrafenib [redacted]	[redacted]	[redacted]	[redacted]

Scatterplots resulting from the PSA for trametinib+dabrafenib versus vemurafenib (at -35%, -45% and -55% discount to list price) and dabrafenib monotherapy [redacted] are presented below.

Figure 5: [redacted]

[redacted]

Figure 6: [redacted]

[redacted]

Figure 7: [redacted]

[redacted]

Acceptability curves of pairwise comparisons for trametinib+dabrafenib versus vemurafenib (at -35%, -45% and -55%) and dabrafenib monotherapy [redacted] are presented below.

Figure 8: [redacted]

[redacted]

In this analysis, the probability of trametinib + dabrafenib's cost-effectiveness at £50,000/QALY are:

[redacted]

Figure 9: [redacted]

[redacted]

In this analysis, the probability of trametinib + dabrafenib's cost-effectiveness at £50,000/QALY are:

[redacted]

Figure 10: [redacted]

[redacted]

In this analysis, the probability of trametinib + dabrafenib's cost-effectiveness at £50,000/QALY are:

[redacted]

Incremental acceptability curves for trametinib + dabrafenib versus vemurafenib (at -35%, -45% and -55%) and dabrafenib monotherapy [redacted] are presented below.

Figure 11: [redacted]

[redacted]

Figure 12: [redacted]

[redacted]

Figure 13: [redacted]

[redacted]

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

As described in Section 5.8.8. of the main submission, one scenario analysis was undertaken which explored the underlying assumption of trametinib + dabrafenib's continuing benefit in progression free survival beyond the study follow up. In this scenario analysis it is assumed that the monotherapy exponential projection applies to the combination arm from the end of follow up, i.e. treatment effect of combination on progression disappears after the end of the trial period and monthly hazards of progression for the trametinib-dabrafenib combination in the projection phase become equivalent to the hazards in the BRAF monotherapy arm.

Table 10: Scenario analysis (assuming no continuing PFS benefit) cost-effectiveness results (all treatments including actual/estimated net prices)

	Dabrafenib-trametinib combination ([redacted] discount for dabrafenib | [redacted] discount for trametinib)	**Assumed vemurafenib discounts**			
		Vemurafenib (35% discount)	**Vemurafenib (45% discount)**	**Vemurafenib (55% discount)**	**Dabrafenib monotherapy ([redacted] discount)**
Intervention cost (£)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Other costs (£)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Total costs (£)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Difference in total costs (£)	-	[redacted]	[redacted]	[redacted]	[redacted]
LYG	4.586	2.933	2.933	2.933	2.933
LYG difference	-	1.653	1.653	1.653	1.653
QALYs	3.422	2.098	2.098	2.098	2.146
QALY difference	-	1.324	1.324	1.324	1.277
ICER (£)	**-**	[redacted]	[redacted]	[redacted]	[redacted]

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 11: Results showing the impact of patient access scheme on ICERs

	ICER for trametinib [redacted] + dabrafenib [redacted] versus:					
	Vemurafenib				**Dabrafenib**	
	List prices	**PAS (-35%)**	**PAS (-45%)**	**PAS (-55%)**	**List prices**	**PAS [redacted]**
Base case	96,437	[redacted]	[redacted]	[redacted]	104,069	[redacted]
Scenario analysis	84,492	[redacted]	[redacted]	[redacted]	91,807	[redacted]

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.

Not applicable.

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.

Not applicable

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

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

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

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

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

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

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.

A suggested format is shown in table 3, section 4.7.

Not applicable

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