

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Technology appraisals

Patient access scheme submission template

Erlotinib monotherapy for the maintenance treatment
of advanced or metastatic non-small cell lung cancer

1 Introduction

The 2009 Pharmaceutical Price Regulation Scheme (PPRS) (www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalalpriceregulationscheme/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 Clinical 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/Pharmaceuticalalpriceregulationscheme/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 Clinical 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'
(www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/guidetothemethodsoftechnologyappraisal.jsp)
- 'Specification for manufacturer/sponsor submission of evidence'
(<http://www.nice.org.uk/aboutnice/howwework/devnicetech/singletechnologypappraisalsubmissiontemplates.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' (www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/guidetothemethodsoftechnologyappraisal.jsp).

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.

Erlotinib monotherapy for the maintenance treatment of advanced or metastatic non-small cell lung cancer

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

The list price of (erlotinib) Tarceva tablets is as follows:-

150 mg (pack of 30) - £1,631.53

100 mg (pack of 30) - £1,324.14

25 mg (pack of 30) - £378.33

Following TA162 Tarceva (erlotinib) is supplied to the NHS at a discount of 14.5% direct to the NHS for the treatment of relapsed NSCLC. This discount arrangement will remain in place and will not discriminate between erlotinib purchased within the upcoming maintenance or existing relapsed indications. Therefore the NHS acquisition cost will be:

150 mg (pack of 30) - £1,394.96

100 mg (pack of 30) - £1,132.96

25 mg (pack of 30) - £323.47

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

The erlotinib Patient Access Scheme is categorised as a financially based scheme and is designed to reduce the total cost of using erlotinib

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?

The PAS applies to the expected entire licensed population. Based on the CHMP opinion published on March 2010, the expected license is as follows: "Tarceva is indicated as monotherapy for maintenance treatment in patients with locally advanced or metastatic non-small cell lung cancer with stable disease after 4 cycles of standard platinum-based first-line chemotherapy".

3.5 Please provide details of when the scheme will apply to the population specified in 3.4.

The scheme will apply to all eligible patients who are suitable for treatment as described in 3.4 and will apply throughout their treatment.

Is the scheme dependent on certain criteria, for example, degree of response, response by a certain time point, number of injections?

No

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 will apply to all eligible patients who are suitable for treatment as described in 3.4.

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

No rebate is involved – the 14.5% discount is deducted from the list price at the time of supply to the NHS.

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.

The proposed discount is already in place and therefore no information needs 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.

As the scheme will not modify existing methods of purchase of drugs by the NHS from Roche, no diagram appears applicable.

3.10 Please provide details of the duration of the scheme.

In the case of positive guidance from NICE the scheme will remain in place at least until any review of this guidance by NICE.

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?

No equity issues have been identified

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.

None required.

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

4 Cost effectiveness

- 4.1 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, please (re-)submit the relevant sections from the 'Specification for manufacturer/sponsor submission of evidence' (particularly sections 5.5, 6.7 and 6.9)..

The population to whom the scheme applies (as described in sections 3.4 and 3.5) has been presented in the main manufacturer/sponsor submission of evidence for the technology appraisal.

- 4.2 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

4.3 Please provide details of how the patient access scheme has been incorporated into the economic model.

A 14.5% discount was applied to the reported list price within the model

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

N/A,

4.5 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.

N/A

4.6 Please provide details of any additional treatment-related costs incurred by implementing the patient access scheme..

There are no additional “treatment-related” costs associated with this PAS.

Summary results

Base-case analysis

4.7 Please present in separate tables the cost-effectiveness results as follows.¹

- the results for the intervention without the patient access scheme (Table 1)
- the results for the intervention with the patient access scheme (Table 2)

Table 1. Base-case cost-effectiveness results without patient access for the SD population

	Erlotinib/BSC	Placebo/BSC
Intervention cost (£)	£7,480.28	£0
Other costs (£)	£17,732.91	£16,381.79
Total costs (£)	£25,213.19	£16,381.79
Difference in total costs (£)	N/A	£8,831.40
LYG	1.385	1.108
LYG difference	N/A	0.277
QALYs	0.750	0.587
QALY difference	N/A	0.162
ICER (£)	N/A	£54,427.54

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

Table 2. Base-case cost-effectiveness results with patient access for the SD population

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

	Erlotinib/BSC	Placebo/BSC
Intervention cost (£)	£6,395.64	£0
Other costs (£)	£17,732.91	£16,381.79
Total costs (£)	£24,128.55	£16,381.79
Difference in total costs (£)	N/A	£7,746.76
LYG	1.385	1.108
LYG difference	N/A	0.277
QALYs	0.750	0.587
QALY difference	N/A	0.162
ICER (£)	N/A	£47,742.95

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

4.8 Please present in separate tables the incremental results as follows.²

- the results for the intervention without the patient access scheme (Table 3)
- the results for the intervention with the patient access scheme (Table 4).

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.

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

Table 3 Base-case incremental results without patient access scheme for the SD population

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYs)
Placebo/BSC	£16,381.79	1.108	0.587	£0	-	-	-	
Erlotinib/BSC	£25,213.19	1.385	0.750	£8,831.40	0.277	0.162	£54,427.54	£54,427.54

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

Table 4 Base-case incremental results with patient access scheme for the SD population

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYs)
Placebo/BSC	£16,381.79	1.108	0.587	£0	-	-	-	
Erlotinib/BSC	£24,128.55	1.385	0.750	£7,746.76	0.277	0.162	£47,427.54	£47,427.54

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

Sensitivity analyses

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

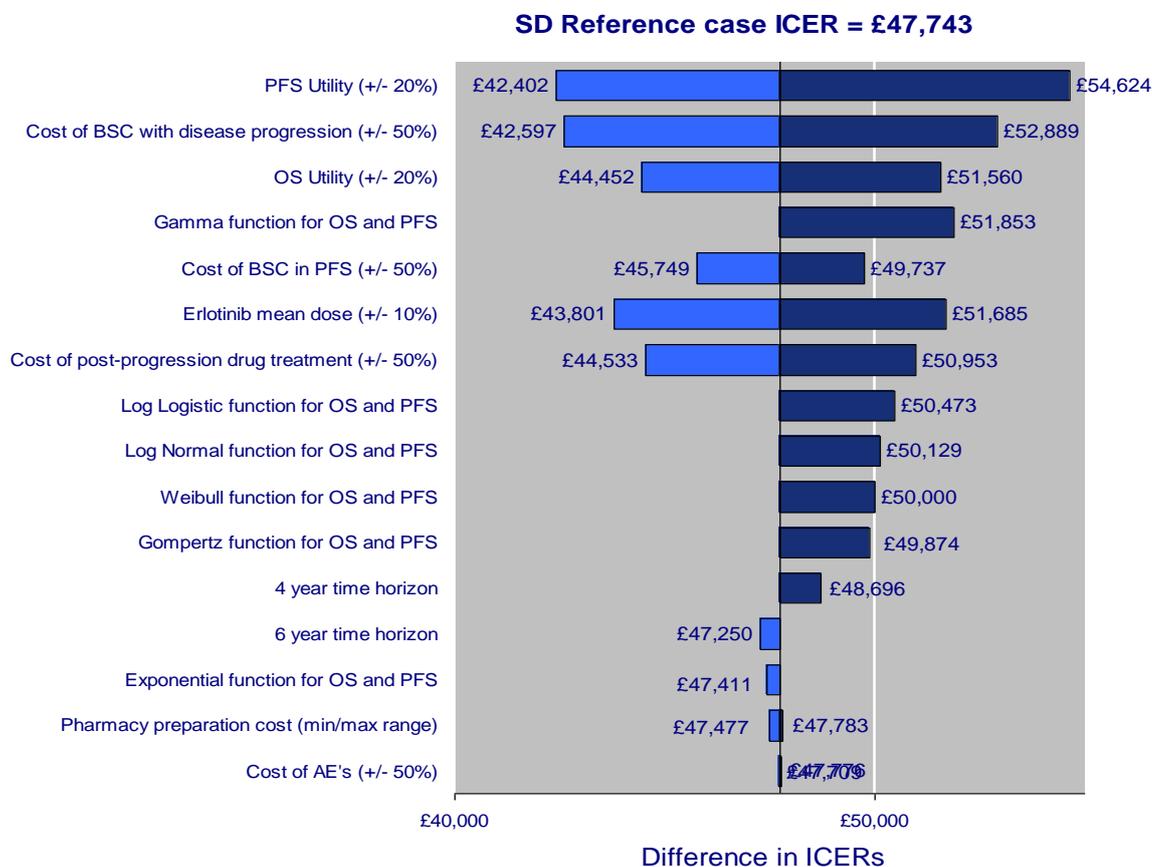
Table 5. One-way sensitivity analyses for the stable disease population

Sensitivity analyses	SD population (erlotinib vs placebo) ICERs
Base case	£47,743
PFS utility decreased by 20%	£54,624
PFS utility increased by 20%	£42,402
OS utility decreased by 20%	£51,560
OS utility increased by 20%	£44,452
Pharmacy preparation decreased to minimum values	£47,477

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Pharmacy preparation increased to maximum values	£47,783
Cost of BSC PFS health state decreased by 50%	£45,749
Cost of BSC PFS health state increased by 50%	£49,737
Cost of BSC progressed health state decreased by 50%	£42,597
Cost of BSC progressed OS health state increased by 50%	£52,889
Cost of post-progression drug treatment decreased by 50%	£50,953
Cost of post-progression drug treatment increased by 50%	£44,533
Cost of treating AE decreased by 50%	£47,709
Cost of treating AE increased by 50%	£47,776
Treatment dose decreased by 10%	£43,801
Treatment dose increased by 10%	£51,685
4 years time horizon	£48,696
6 years time horizon	£47,250
Gamma function for both PFS and OS	£51,853
Log Logistic function for both PFS and OS	£50,473
Log Normal function for both PFS and OS	£50,129
Gompertz function for both PFS and OS	£49,874
Weibull function for both PFS and OS	£50,000
Exponential function for both PFS and OS	£47,411

Figure 1. Tornado diagram of one-way sensitivity analyses erlotinib vs placebo for the stable disease population



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

Table 6. Probabilistic Cost Effectiveness results for erlotinib vs placebo (1000 runs). Stable disease population

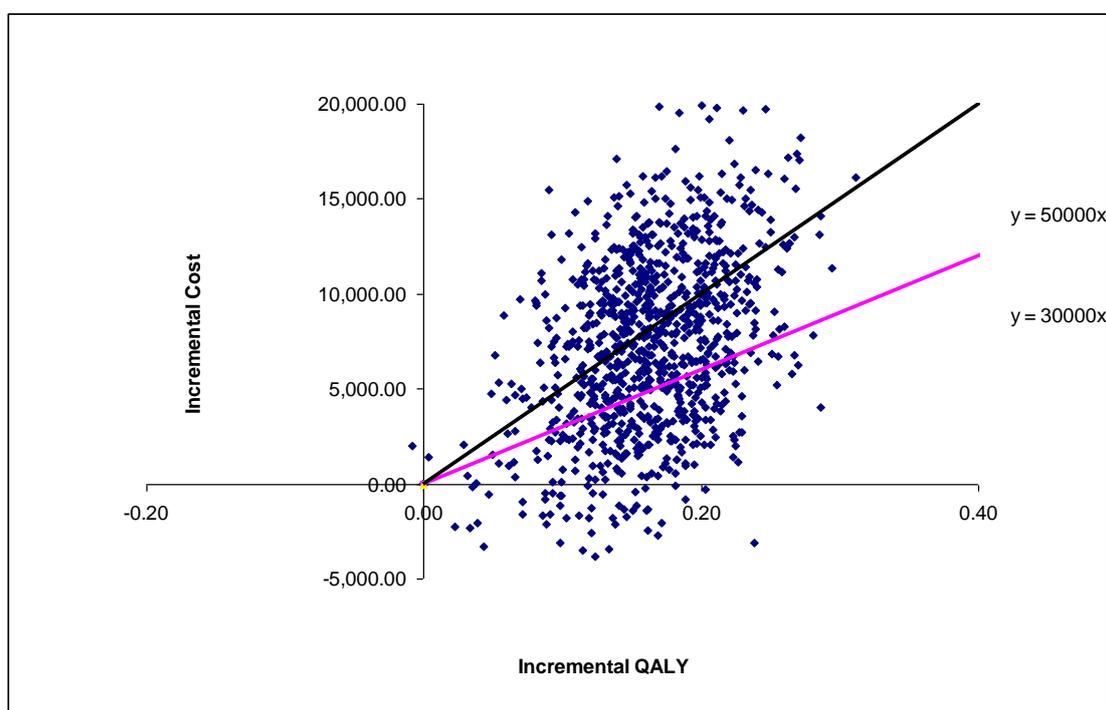
Cost-utility results	Erlotinib	Placebo	Δ erlotinib vs placebo
Mean Life Years (yrs)	1.387	1.109	0.279
Mean QALYs	0.751	0.588	0.163
Mean Total Cost	£23,843	£16,463	£7,380

Cost per Life Year Gained (£)			£26,489
Cost per QALY Gained (£)			£45,270

Scatter plots

The cost-effectiveness plane presented below illustrates the distribution of incremental cost per QALY ratios in relation to an assumed willingness to pay (WTP) ceiling ratio of £30,000 per QALY and £50,000 per QALY.

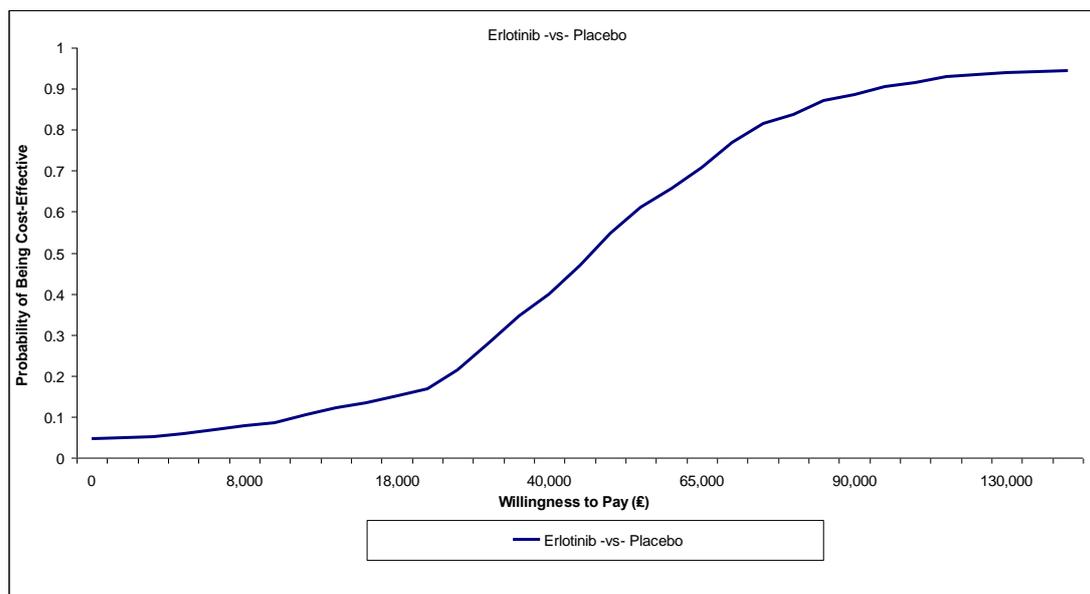
Figure 2: Scatter plot of cost per QALY for erlotinib vs placebo (example:1,000 Monte Carlo simulations). Stable disease population



Cost-effectiveness acceptability curve (CEAC)

The CEAC graph presented below shows the likelihood of erlotinib treatment being cost-effective at different WTP per QALY thresholds.

Figure 3: Cost-effectiveness acceptability curve of erlotinib vs. placebo SD population



The probability of erlotinib being cost effective (compared to placebo) at a threshold of £50,000 is 55%.

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

N/A

4.12 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.

N/A

Impact of patient access scheme on ICERs

4.13 For financially based schemes, please present the results showing the impact of the patient access scheme on the ICERs for the PAS submission, Erlotinib 1LM for advanced or metastatic NSCLC – April 2010

base-case and any scenario analyses.. 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.

Results showing the impact of the patient access scheme on the ICERs for the base-case are shown in point 4.7 above.

Sensitivity analyses which includes the PAS were performed in the main NICE STA submission and are shown in point 4.9 above. There were no scenarios analyses presented in the submission.

5 Appendices

5.1 *Appendix A: Additional documents*

5.1.1 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.

N/A

Appendix B: Details of outcome-based schemes

N/A

5.1.2 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

5.1.3 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.

N/A

5.1.4 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)

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

N/A

5.1.5 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).

N/A

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

N/A

5.1.7 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.

N/A

5.1.8 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.

N/A

5.1.9 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.

See section 4.7

- 5.1.10 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.

N/A