NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Axitinib for the treatment of advanced renal cell carcinoma after failure of prior systemic treatment

Submitted by Pfizer Ltd.

Technology appraisals

Patient access scheme submission template

October 2009

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 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/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 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/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’ (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.

The patient access scheme will apply to axitinib (Inlyta®), which is indicated for adult patients with advanced renal cell carcinoma (RCC) after failure of prior treatment with sunitinib or a cytokine.

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

The patient access scheme aims to improve patient access and cost effectiveness of axitinib use in adult patients with advanced renal cell carcinoma (RCC) after failure of prior treatment with sunitinib or a cytokine.

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

The patient access scheme is a simple discount, which is conditional on the level of discount offered remaining confidential and not being published in NICE guidance. It is proposed that NHS Trust procurement entities which have entered into a contract with Pfizer that contains appropriate confidentiality provisions will purchase axitinib at a discount applied at the point of purchase.

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?

Patient access scheme will apply to the licensed population, which is all adult patients with advanced renal cell carcinoma (RCC) after failure of prior treatment with sunitinib or a cytokine.

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.

The scheme is not dependent upon any criteria and is simply applied as a discount.

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 NHS patients for whom axitinib is indicated and where the NHS procurement entities have entered into an agreement with appropriate confidentiality provisions with Pfizer.

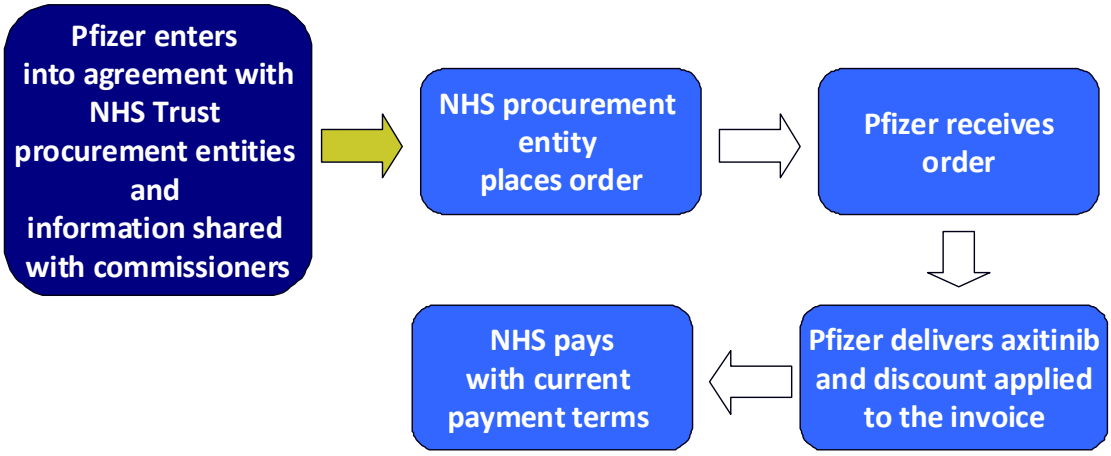
3.7 Please explain in detail the financial aspects of the scheme. How will any rebates be calculated and paid?

The discount will be applied at the point of invoice. [redacted]

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 discount will be applied at the point of invoice.

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



3.10 Please provide details of the duration of the scheme.

The proposed patient access scheme will be conditional upon:

(1) NICE positive guidance for Axitinib use in adult patients with advanced renal cell carcinoma (RCC) after failure of prior treatment with sunitinib or a cytokine;

(2) the relevant NHS procurement entity entering into a contract with Pfizer that contains appropriate confidentiality provisions; and will remain in place so long as NICE positive guidance exists for Axitinib review and subject to Department of Health agreement

This PAS is conditional on the level of discount offered remaining confidential and not being published in NICE guidance.

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 scheme taking into account current legislation.

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.

Not applicable.

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.

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 (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.

Not applicable.

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.

Not applicable.

4.3 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 PAS has been applied by reducing the current NHS list price of axitinib.

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.

The PAS is a simple discount and therefore does not impact the clinical effectiveness data used in the evidence synthesis or in the economic model.

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). 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 PAS is a simple discount introduced at the point of invoice and as a result will not be associated with operational or implementation costs.

4.6 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.

Not applicable.

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
- the results for the intervention with the patient access scheme.

A suggested format is shown below (table 3).

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

Table 1 Base-case cost-effectiveness results – Without the PAS

	Cytokine refractory		Sunitinib refractory	
	Axitinib	**BSC**	**Axitinib**	**BSC**
Intervention cost (£)	[redacted]	[redacted]	[redacted]	[redacted]
Other costs (£)	[redacted]	[redacted]	[redacted]	[redacted]
Total costs (£)	[redacted]	[redacted]	[redacted]	[redacted]
Difference in total costs (£)	N/A	[redacted]	N/A	[redacted]
LYG	[redacted]	[redacted]	[redacted]	[redacted]
LYG difference	N/A		N/A	[redacted]
QALYs	[redacted]	[redacted]	[redacted]	[redacted]
QALY difference	N/A	[redacted]	N/A	[redacted]
ICER (QALYs) (£)	N/A	[redacted]	N/A	[redacted]

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

Table 2 Base-case cost-effectiveness results – With the PAS

	Cytokine refractory		Sunitinib refractory	
	Axitinib	**BSC**	**Axitinib**	**BSC**
Intervention cost (£)	[redacted]	[redacted]	[redacted]	[redacted]
Other costs (£)	[redacted]	[redacted]	[redacted]	[redacted]
Total costs (£)	[redacted]	[redacted]	[redacted]	[redacted]
Difference in total costs (£)	N/A	[redacted]	N/A	[redacted]
LYG	[redacted]	[redacted]	[redacted]	[redacted]
LYG difference	N/A		N/A	[redacted]
QALYs	[redacted]	[redacted]	[redacted]	[redacted]
QALY difference	N/A	[redacted]	N/A	[redacted]
ICER (QALYs) (£)	N/A	£65,326	N/A	£40,933

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
- 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.

Table 3 Base-case incremental results – without PAS

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) incremental (QALYs)
Prior Cytokine							
Axitinib	[redacted]	[redacted]	[redacted]				
BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Prior Sunitinib							
Axitinib	[redacted]	[redacted]	[redacted]				
BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

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

Table 4 Base-case incremental results – with PAS

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) incremental (QALYs)
Prior Cytokine							
Axitinib	[redacted]	[redacted]	[redacted]				
BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£65,326
Prior Sunitinib							
Axitinib	[redacted]	[redacted]	[redacted]				
BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£40,933

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

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

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.

Figure 1: Cytokine refractory tornado diagram - With PAS

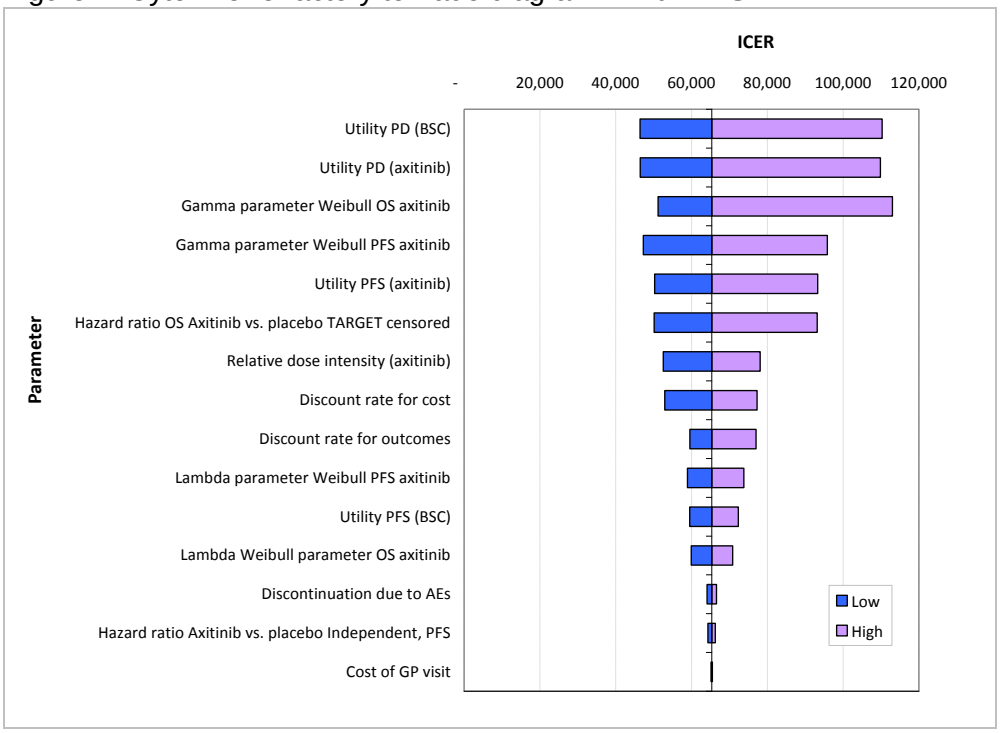
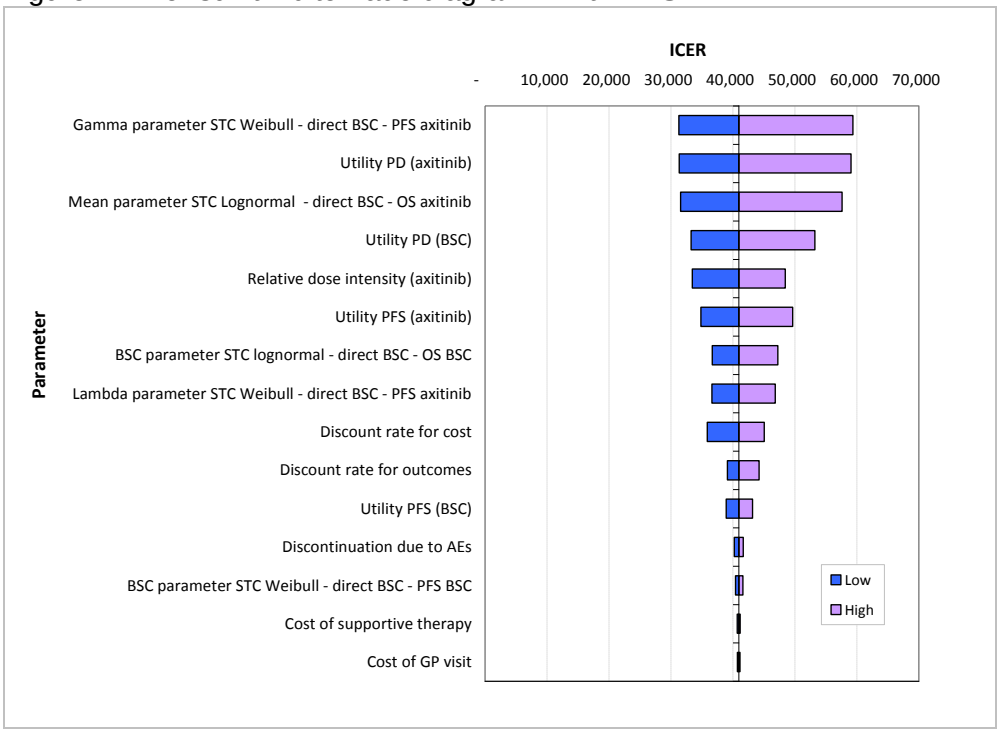


Figure 2: Prior sunitinib tornado diagram - With PAS



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

Cytokine refractory analysis

Figure 3: Cytokine refractory scatter plot - With PAS

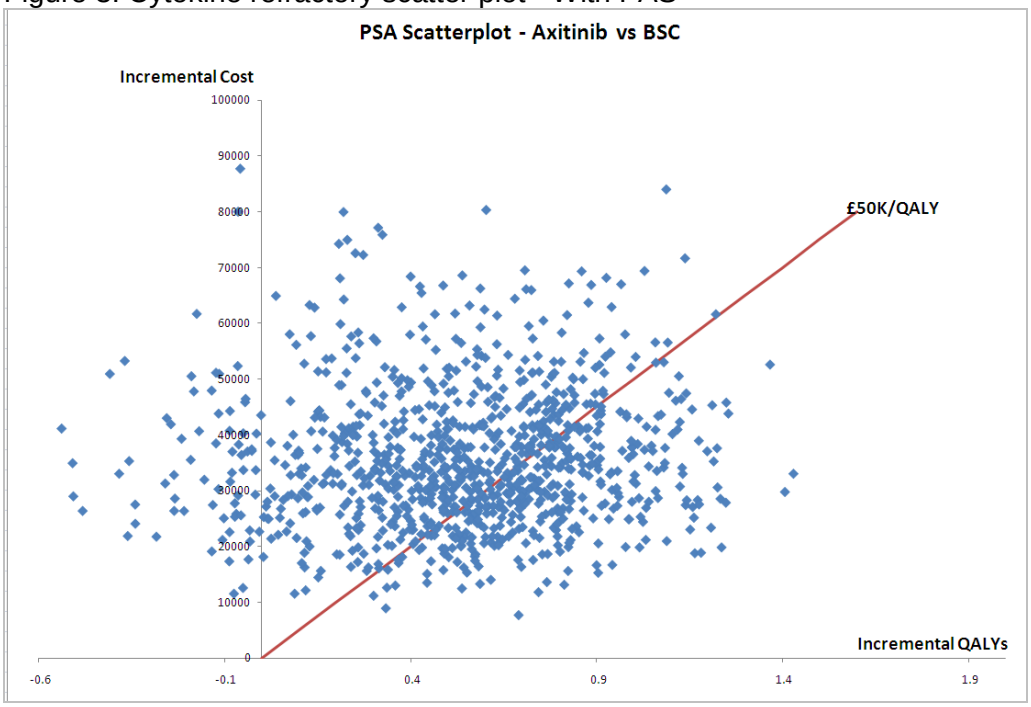
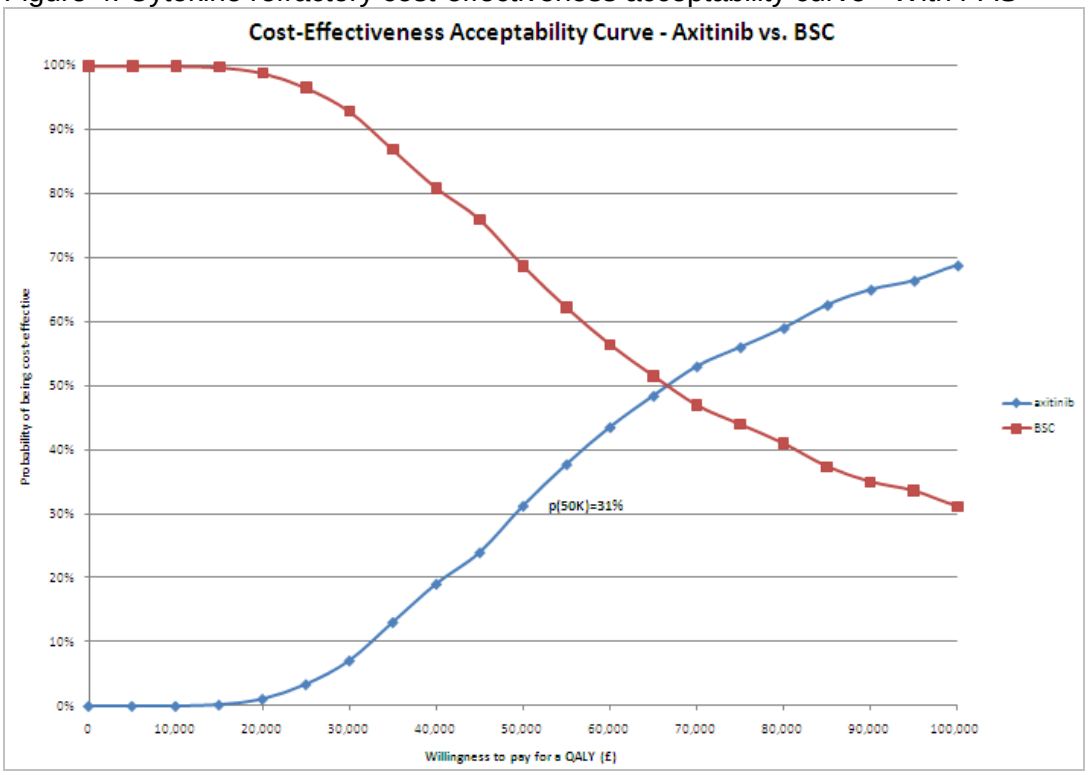


Figure 4: Cytokine refractory cost-effectiveness acceptability curve - With PAS



Sunitinib refractory analysis

Figure 5: Sunitinib refractory scatter plot - With PAS

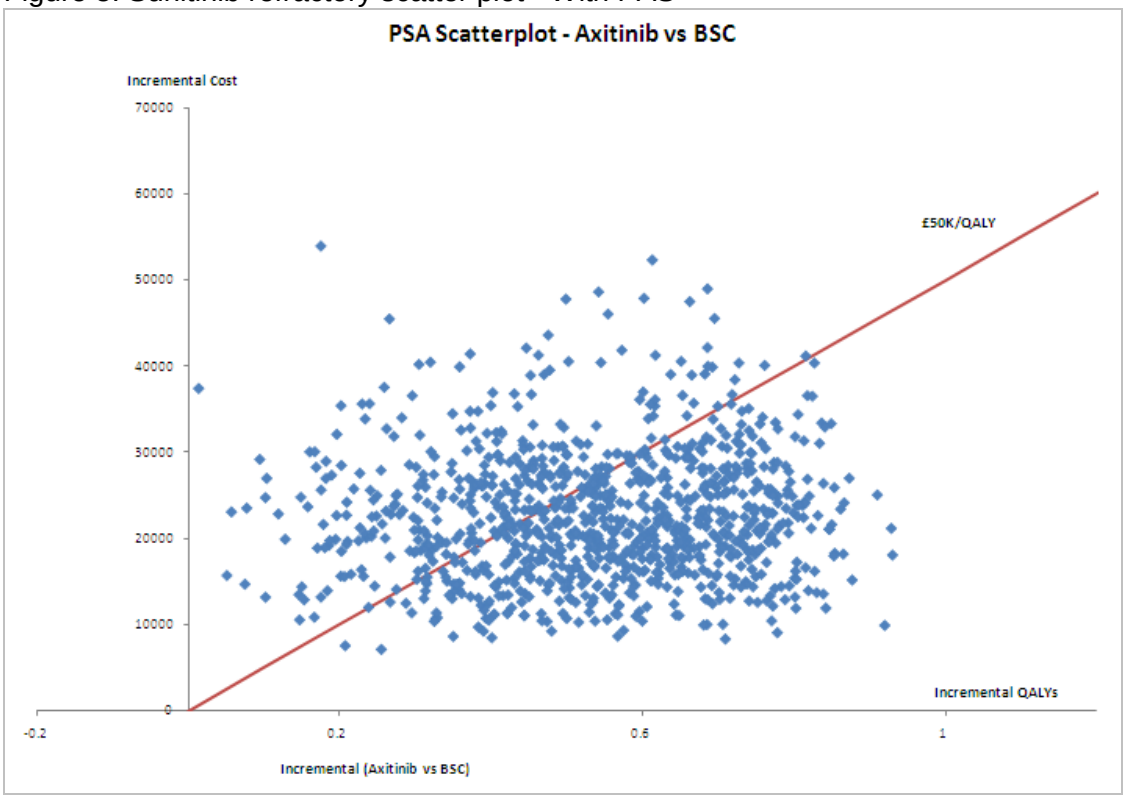
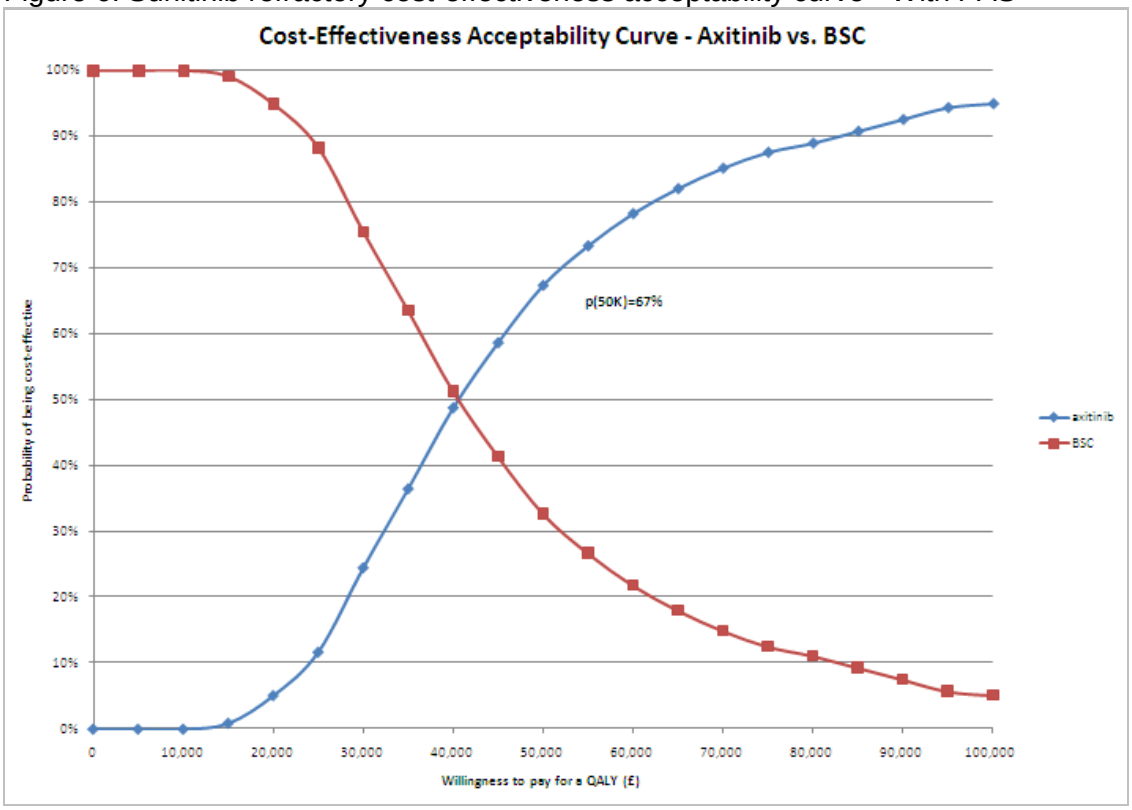


Figure 6: Sunitinib refractory cost-effectiveness acceptability curve - With PAS



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

Table 5: Scenario analysis results – Prior cytokine population

Parameter	Base case	Scenario analysis	ICER with PAS
Base Case			£65,326
Method of PFS extrapolation	Weibull	Log-normal Gompertz	£71,535 £63,702
Method of OS extrapolation	Weibull	Log-logistic Gompertz	£52,260 £84,255
Axitinib and BSC utility estimates	AXIS study	2nd-line utilities (mRCC MTA and everolimus appraisal)	£59,654
Axitinib relative dosing intensity	AXIS study	Estimated real-world dosing intensity (Everolimus appraisal)	£51,546
Ongoing medical management in pre-progression state	GP Management	Oncologist Management	£66,410
Time horizon	10 years	5 years 15 years	£83,752 £64,359
Discount Rate	3.5% costs and QALYs	0% 6%	£60,015 £69,164

Abbreviations: BSC, best supportive care; GP, general practitioner; ICER, incremental cost-effectiveness ratio; mRCC< metastatic renal cell carcinoma; MTA multiple technology appraisal; OS, overall survival; PFS, progression-free survival.

Table 6: Scenario analysis results – Prior sunitinib population

Parameter	Base case	Scenario analysis		ICER with PAS
Base Case				£40,933
Method of PFS comparison	STC Weibull via ITT RECORD-1 BSC population	STC lognormal via RECORD-1 BSC		£42,428
		STC Weibull via everolimus prior sunitinib – BSC PFS		£40,509
Method of OS comparison	STC lognormal via RECORD-1 ITT BSC population	STC Weibull via RECORD-1 BSC		£39,906
		STC Weibull via everolimus prior sunitinib – BSC RPSFT		£33,268
		RENCOMP	Weibull	£56,113
			Lognormal	£43,384
			Gompertz	£54,851
Axitinib and BSC utility estimates	AXIS study	2nd-line utilities (mRCC MTA and everolimus appraisal)		£37,059
Axitinib relative dosing intensity	AXIS study	Estimated real-world dosing intensity (Everolimus appraisal)		£32,846

Parameter	Base case	Scenario analysis	ICER with PAS
Medical management pre-progression	GP Management	Oncologist Management	£42,074
Time horizon	10 years	5 years 15 years	£48,283 £39,207
Discount Rate	3.5% costs and QALYs	0% 6%	£38,254 £42,806

Abbreviations: BSC, best supportive care; GP, general practitioner; ICER, incremental cost-effectiveness ratio; mRCC, metastatic renal cell carcinoma; MTA, multiple technology appraisal; OS, overall survival; PFS, progression-free survival; RPSFT, rank preserving structural time failure; STC, simulated treatment comparison.

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.

Not applicable.

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 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.

Please see section 4.9.

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.

5.2 Appendix B: Details of outcome-based schemes

5.2.1 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.

Response

5.2.2 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.

Response

5.2.3 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.

Response

5.2.4 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).

Response

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

Response

5.2.6 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.

Response

5.2.7 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.

Response

5.2.8 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.

5.2.9 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.