NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

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 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.

Brand Name: Giotrif
Approved Name: Afatinib

CHMP positive opinion was received for afatinib (GIOTRIF) from EMA on 25/07/13 and states the following:

GIOTRIF as monotherapy is indicated for the treatment of Epidermal Growth Factor Receptor (EGFR) TKI-naïve adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating EGFR mutation(s)

The patient access scheme (PAS) will apply across this entire licensed indication.

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

The patient access scheme has been developed in order to support the cost effectiveness case for Afatinib.

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

The scheme is a commercial in confidence simple discount patient access scheme which is a type of a financially based scheme.

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 patient access scheme will apply to the entire licensed patient population as per the marketing authorisation for the product.

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 on any criteria and the discounted price will be reflected on all original invoices for the product.

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

100%

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

The approved discounted price in the scheme will be the price paid by the NHS at the point of sale so there is no requirement for the calculation of rebates.

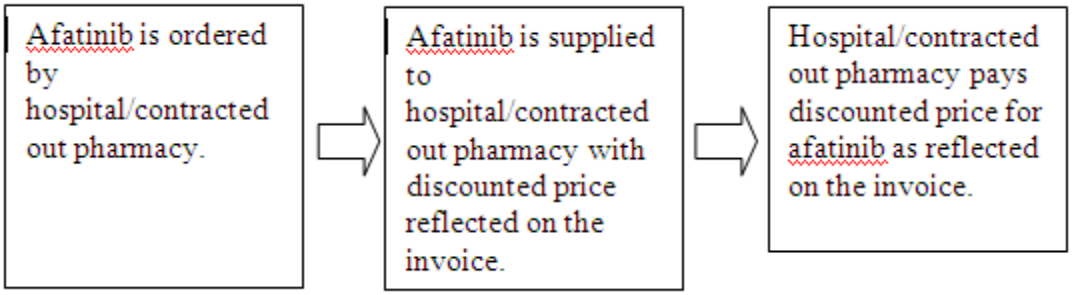
[redacted]

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.

There are no associated administrative processes required with the scheme as stock for the product will be ordered in the usual way and the approved discounted price will be paid at the point of sale by the NHS and will be reflected on all original invoices.

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

Figure 1 Flow diagram showing how the PAS scheme would be implemented in practice



3.10 Please provide details of the duration of the scheme.

The scheme will remain in place until NICE next reviews the guidance on the product.

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 issues have been identified by Boehringer Ingelheim Ltd in this regard.

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.

A confidential disclosure agreement will need to be signed by NHS stakeholders before the discounted price can be shared. A copy is included in the appendices.

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.

The population to whom the scheme applies has been presented in the main manufacturer 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.

The patient access scheme is being submitted simultaneously with the technology appraisal.

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 model provides an option on the main inputs page (sheet 'Exec Sum') for the user to select a cost-effectiveness analysis based on either list prices or PAS prices. The user is able to input the discount value in the sheet 'Custom Inputs'. The economic model then calculates costs by removing the discount from the list price.

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 main drivers in the cost-effectiveness analysis are the relative rates of progression-free survival and of overall survival. These are presented here. Of less importance are the relative adverse event rates, which are not reported here but are included in full in the main submission.

The basis for the clinical effectiveness data used in the economic analysis is the relative effectiveness of afatinib compared to erlotinib and gefitinib as a first line treatment. These are based on a mixed treatment comparison (MTC) incorporating a network meta-analysis.

The data for the MTC was derived from 20 studies identified through a systematic review. The main results of the MTC are shown in xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx and **Error! Reference source not found.**, which show the hazard ratios for progressions free survival (PFS) and overall survival (OS) for afatinib compared to: pemetrexed with cisplatin, gemcitabine with cisplatin, gefitinib, and erlotinib.

xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx show that afatinib has statistically significant better PFS outcomes relative to the combination of pemetrexed with cisplatin and gemcitabine with cisplatin. Relative to gefitinib and erlotinib, there is a non-significant trend in favour of afatinib. **Error! Reference source not found.**, which is based on the current immature OS data for afatinib, shows a trend favouring afatinib compared with all four comparators. Further results from the MTC are presented in the main submission.

[redacted]

[redacted]

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'

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

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.

There are no additional treatment-related costs incurred by implementing the patient access scheme.

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.

The base-case results using the NHS list prices for all three treatments are shown in Table 1. The results in Table 2 are base on the confidential PAS price.

Table 1 Base-case cost-effectiveness using NHS list prices

	Afatinib	Gefitinib	Erlotinib
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
LYG	2.55	2.29	2.22
LYG difference	N/A	0.26	0.33
QALYs	1.59	1.42	1.42
QALY difference	N/A	0.17	0.17
[redacted]	[redacted]	[redacted]	[redacted]

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

Table 2 Base-case cost-effectiveness using PAS prices

	Afatinib	Gefitinib	Erlotinib
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
Total costs	£32,304	£29,191	£30,581
Difference in total costs	N/A	£3,113	£1,723
LYG	2.55	2.29	2.22
LYG difference	N/A	0.26	0.33
QALYs	1.59	1.42	1.42
QALY difference	N/A	0.17	0.17
ICER	N/A	£17,933	£10,079

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.

Incremental cost effectiveness analysis is shown with the list price in Table 3 and with the PAS price in Table 4. Note that the values in these tables may differ slightly to those above due to rounding errors.

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

Table 3 Base-case results using list prices

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYs)
Erlotinib	[redacted]	2.223	1.423	-	-	-	-	-
Gefitinib	[redacted]	2.291	1.421	[redacted]	0.068	-0.002	[redacted]	[redacted]
Afatinib	[redacted]	2.549	1.594	[redacted]	0.258	0.173	[redacted]	[redacted]

Table 4 Base-case results using PAS prices

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYs)
Gefitinib	£29,191	2.291	1.421	-	-	-	-	-
Erlotinib	£30,581	2.223	1.423	£1,390	-0.068	0.002	£695,000	ED
Afatinib	£32,304	2.549	1.594	£1,723	0.326	0.171	£17,994	£10,076

ED = Extended dominance

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.

Presented below are the one-way sensitivity analyses (OWSA) with and without the PAS. The top ten variables that have the greatest impact on the ICERs without the PAS are shown for afatinib compared to gefitinib in **Error! Reference source not found.** and afatinib compared to erlotinib in **Error! Reference source not found.**. These analyses are repeated using the PAS prices in Table 5 and Table 6.

[redacted]

[redacted]

[redacted]

Table 5 OWSA results for afatinib compared to gefitinib using discounted prices

Variable	Low variation				High variation			
	Inc cost	Inc QALY	Inc LY	ICER	Inc cost	Inc QALY	Inc LY	ICER
MTC-based HR for PFS (afa vs. gef)	£1,963	0.2447	0.2581	£8,023	£4,899	0.0894	0.2581	£54,800
MTC-based HR for OS (afa vs. gef)	£8,532	0.4495	0.7876	£18,983	-£3,990	-0.1880	-0.4360	£21,221
Cost/month Progression-free, 1L,	£2,858	0.1736	0.2581	£16,466	£5,854	0.1736	0.2581	£33,724
Cost/month in 3rd Line progressive disease (BSC)	£2,953	0.1736	0.2581	£17,011	£4,568	0.1736	0.2581	£26,315
Weibull model HR for OS (afa vs. pmc) for comparison with erl/gef	£3,316	0.1943	0.3037	£17,069	£2,914	0.1542	0.2156	£18,894
Discounting effect	£3,113	0.1900	0.2873	£16,386	£3,113	0.1635	0.2402	£19,045
Weibull model HR for PFS (afa vs. pmc)	£5,675	0.1851	0.2581	£30,656	£1,171	0.1641	0.2581	£7,135
Cost per Diarrhea AE	£2,740	0.1736	0.2581	£15,786	£3,489	0.1736	0.2581	£20,098
Discounting cost	£3,515	0.1736	0.2581	£20,248	£2,859	0.1736	0.2581	£16,473
Freq of diarrhea (grade 3/4) in 1L afa patients	£2,857	0.1738	0.2581	£16,442	£3,369	0.1734	0.2581	£19,427

OWSA = one way sensitivity analysis; MTC = mixed treatment comparison; HR = hazard ratio; BSC = best supportive care; AE = adverse event.

Table 6 OWSA results for afatinib compared to erlotinib using discounted prices

	Low variation				High variation			
Variable	Inc cost	Inc QALY	Inc LY	ICER	Inc cost	Inc QALY	Inc LY	ICER
Cost/month Progressive disease, 3&4L, both arms	£1,254	0.171	0.326	£7,339	£5,977	0.171	0.326	£34,970
MTC-based HR for PFS (afa vs. erl)	£3,501	0.252	0.326	£13,893	-£648	0.063	0.326	-£10,302
MTC-based HR for OS (afa vs. erl)	£6,560	0.405	0.768	£16,206	-£4,152	-0.113	-0.211	£36,718
Cost/month Progression-free, 1L, both arms	£1,621	0.171	0.326	£9,482	£2,820	0.171	0.326	£16,500
Freq of diarrhea (grade	£1,467	0.171	0.326	£8,572	£1,979	0.171	0.326	£11,589

3/4) in 1L afa patients								
Cost per Diarrhea AE	£1,484	0.171	0.326	£8,685	£1,963	0.171	0.326	£11,485
Discounting cost	£1,997	0.171	0.326	£11,681	£1,556	0.171	0.326	£9,104
Discounting effect	£1,723	0.189	0.362	£9,098	£1,723	0.160	0.304	£10,796
PD Utility in 3rd Line, progressive disease	£1,723	0.160	0.326	£10,767	£1,723	0.182	0.326	£9,473
No episodes diarrhea per 1L pt suffering diarrhea (grade 3/4)	£1,625	0.171	0.326	£9,505	£1,820	0.171	0.326	£10,653

OWSA = one way sensitivity analysis; MTC = mixed treatment comparison; HR = hazard ratio; BSC = best supportive care; AE = adverse event.

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

The probabilities of cost effectiveness using list prices at different willingness to pay thresholds for the pair wise comparisons are shown in Table 7.

Table 7 Probability of cost-effectiveness using list prices

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]

The comparison between the determinist and probabilistic results for afatinib vs. gefitinib using list prices is shown in Table 8.

Table 8 Deterministic and probabilistic ICERs for afatinib vs. gefitinib using list prices

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

The cost-effectiveness planes and acceptability curves for afatinib vs. gefitinib using list prices are displayed in Figure 2 and Figure 3.

Figure 2 Incremental cost-effectiveness scatter plot for afatinib as compared to gefitinib using list prices

[redacted]

Figure 3 CEAC for afatinib compared to gefitinib using list prices

[redacted]

The comparison between determinist and probabilistic results for afatinib vs. erlotinib using list prices is shown in Table 9.

Table 9 Deterministic and probabilistic ICERs for afatinib vs. erlotinib using list prices

	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

The cost-effectiveness planes and acceptability curves for afatinib vs. erlotinib using list prices are displayed Figure 4 and Figure 5.

Figure 4 Incremental cost-effectiveness scatter plot for afatinib as compared to erlotinib using list prices

[redacted]

Figure 5 CEAC for afatinib as compared to erlotinib using list prices

[redacted]

The probabilities of cost effectiveness at different willingness to pay thresholds for the pair wise comparisons under the confidential PAS are shown in Table 10.

Table 10 Probability of cost-effectiveness using the confidential PAS

Intervention	Comparator	£20,000 per QALY	£30,000 per QALY
Afatinib	Erlotinib	100%	100%
	Gefitinib	72%	81%

The comparison between the determinist and probabilistic results for afatinib vs. gefitinib under the confidential PAS is shown in Table 11.

Table 11 Deterministic and probabilistic ICERs for afatinib vs. gefitinib using the confidential PAS

	Incremental cost	Incremental QALY	ICER
Deterministic Values	£3,113	0.17	£17,933
Average value for PSA	£2,390	0.16	£15,027

The cost-effectiveness planes and acceptability curves for afatinib vs. gefitinib are displayed in Figure 6 and Figure 7.

Figure 6 Incremental cost-effectiveness scatter plot for afatinib as compared to gefitinib using the confidential PAS

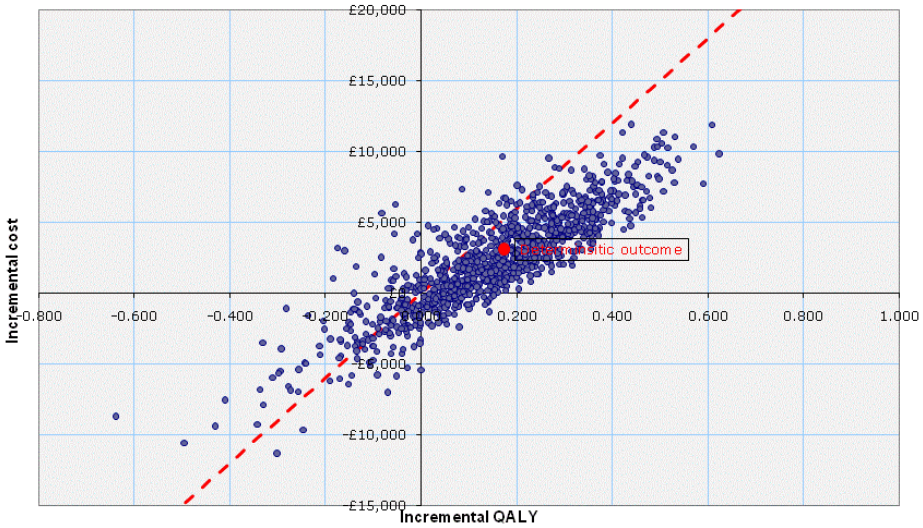
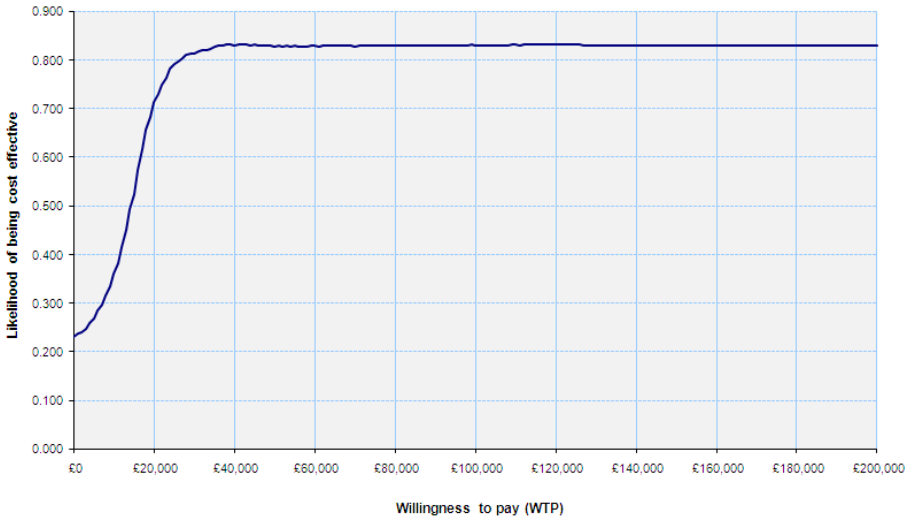


Figure 7 CEAC for afatinib as compared to gefitinib using the confidential PAS



The comparison between the determinist and probabilistic results for afatinib vs. erlotinib using the confidential PAS is shown in Table 12.

Table 12 Deterministic and probabilistic ICERs for afatinib vs. erlotinib using the confidential PAS

	Incremental cost	Incremental QALY	ICER
Deterministic Values	£1,723	0.17	£10,079
Average value for PSA	£1,058	0.16	£6,671

The cost-effectiveness planes and acceptability curves for afatinib vs. erlotinib using the confidential PAS are displayed Figure 8 and Figure 9.

Figure 8 Incremental cost-effectiveness scatter plot for afatinib as compared to erlotinib using the confidential PAS

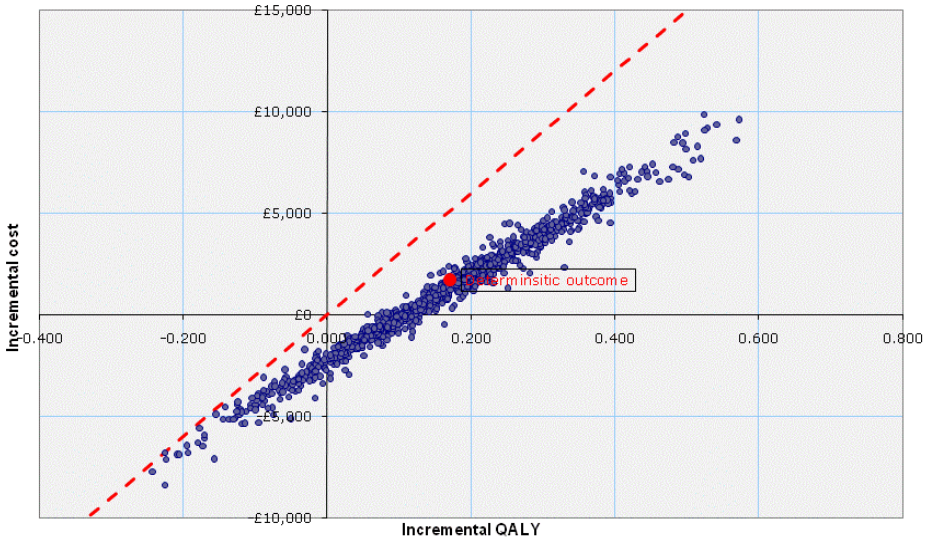
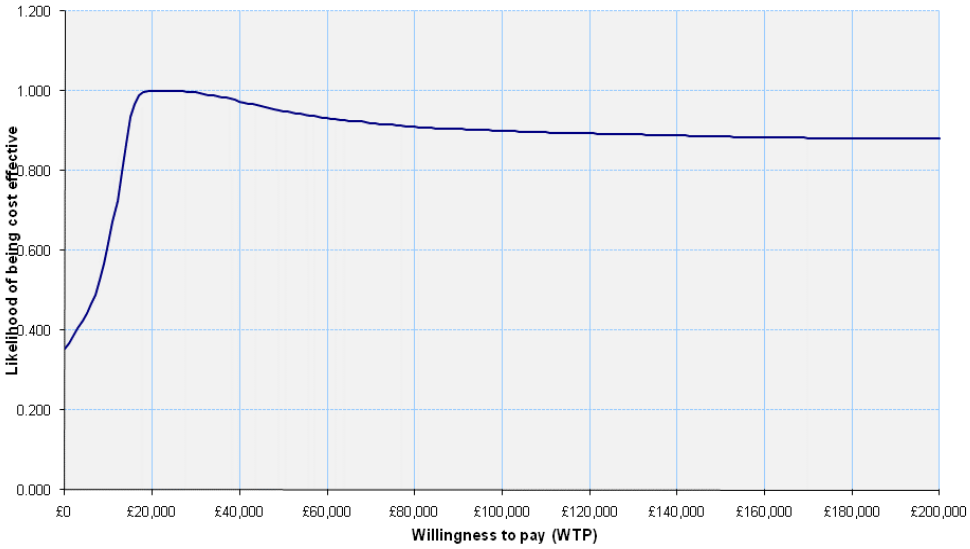


Figure 9 CEAC for afatinib as compared to erlotinib using the confidential PAS



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

In the base case, following treatment with any of the TKIs (afatinib, erlotinib or gefitinib), all patients are assumed to receive docetaxel as 2nd line treatment, before proceeding to best supportive care. To test the impact of this assumption on the cost-effectiveness results, a scenario analysis was conducted in which patients received another possible 2nd line treatment, pemetrexed, instead of docetaxel. The results for this scenario analysis are compared with the base case analysis in Table 13.

Table 13 Alternate 2nd line treatment scenario analysis using list prices

	Docetaxel (base case)	Pemetrexed
Afatinib vs. gefitinib		
ICER (QALY)	[redacted]	[redacted]

ICER (LY)	[redacted]	[redacted]
ICER (PFLY)	[redacted]	[redacted]
Afatinib vs. erlotinib		
ICER (QALY)	[redacted]	[redacted]
ICER (LY)	[redacted]	[redacted]
ICER (PFLY)	[redacted]	[redacted]

This same analysis using the PAS is shown in Table 14.

Table 14 Alternate 2nd line treatment scenario analysis using PAS prices

	Docetaxel (base case)	Pemetrexed
Afatinib vs. gefitinib		
ICER (QALY)	£17,933	£17,925
ICER (LY)	£12,062	£12,076
ICER (PFLY)	£18,021	£18,043
Afatinib vs. erlotinib		
ICER (QALY)	£10,079	£10,084
ICER (LY)	£5,286	£5,297
ICER (PFLY)	£24,909	£24,963

The results for the scenario analysis outlined in the second part of Section 7.6.1 in the main submission are shown in Table 15, including a scenario in which both the 2nd line treatment regimen and the 2nd line treatment duration are changed from the base case.

Table 15 Alternate 2nd line treatment duration scenario analysis using list prices

	2nd line treatment duration		
	Constant (base case)	Proportionate	Proportionate
2nd line treatment →	Docetaxel	Docetaxel	Pemetrexed
Afatinib vs. gefitinib			
ICER (QALY)	[redacted]	[redacted]	[redacted]
ICER (LY)	[redacted]	[redacted]	[redacted]
ICER (PFLY)	[redacted]	[redacted]	[redacted]
Afatinib vs. erlotinib			
ICER (QALY)	[redacted]	[redacted]	[redacted]
ICER (LY)	[redacted]	[redacted]	[redacted]
ICER (PFLY)	[redacted]	[redacted]	[redacted]

This same analysis using the PAS is shown in Table 16.

Table 16 Alternate 2nd line treatment duration scenario analysis using PAS prices

	2nd line treatment duration		
	Constant (base case)	Proportionate	Proportionate
2nd line treatment →	Docetaxel	Docetaxel	Pemetrexed
Afatinib vs. gefitinib			
ICER (QALY)	£17,933	£19,904	£19,952
ICER (LY)	£12,062	£13,789	£13,727
ICER (PFLY)	£18,021	£20,603	£20,509
Afatinib vs. erlotinib			
ICER (QALY)	£10,079	£15,664	£15,718
ICER (LY)	£5,286	£8,871	£8,722
ICER (PFLY)	£24,909	£41,805	£41,105

The variation in structural assumptions has little impact on the ICERs as demonstrated the results above.

The ICERs using the three sets of utility values are shown in Table 17 and with the PAS prices in Table 18.

Table 17 ICERs for sensitivity analysis with different utility values using list prices

	Afatinib vs. gefitinib	Afatinib vs. erlotinib
LUX-Lung trial data (basecase)	[redacted]	[redacted]
LUCEOR data (Chouaid et al. 2012)	[redacted]	[redacted]
Literature (Nafees et al. 2008)	[redacted]	[redacted]

Table 18 ICERs for sensitivity analysis with different utility values using PAS prices

	Afatinib vs. gefitinib	Afatinib vs. erlotinib
LUX-Lung trial data (basecase)	£17,933	£10,079
LUCEOR data (Chouaid et al. 2012)	£19,359	£10,390
Literature (Nafees et al. 2008)	£20,256	£10,588

The ICERs using only the afatinib data from LUX-Lung 3 in the MTC are shown in Table 19 and with the PAS prices in Table 20.

Table 19 ICERs for sensitivity analysis using only afatinib data from LUX-Lung 3 in the MTC using list prices

	Afatinib vs. gefitinib	**Afatinib vs. erlotinib**
LUX-Lung 3 and LUX-Lung 6 data (basecase)	[redacted]	[redacted]
Only LUX-Lung 3 data	[redacted]	[redacted]

Table 20 ICERs for sensitivity analysis using only afatinib data from LUX-Lung 3 in the MTC using PAS prices

	Afatinib vs. gefitinib	**Afatinib vs. erlotinib**
LUX-Lung 3 and LUX-Lung 6 data (basecase)	£17,933	£10,079
Only LUX-Lung 3 data	£24,339	Dominant

The ICERs using data from OPTIMAL in the MTC are shown Table 21 and with the PAS prices in Table 22.

Table 21 ICERs for sensitivity analysis using only afatinib data from LUX-Lung 3 in the MTC

	Afatinib vs. gefitinib	**Afatinib vs. erlotinib**
Basecase with OPTIMAL data excluded	[redacted]	[redacted]
Results with OPTIMAL data included	[redacted]	[redacted]

Table 22 ICERs for sensitivity analysis using only afatinib data from LUX-Lung 3 in the MTC

	Afatinib vs. gefitinib	**Afatinib vs. erlotinib**
Basecase with OPTIMAL data excluded	£17,933	£10,079
Results with OPTIMAL data included	£15,257	£13,013

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.

The patient access scheme has no impact on clinical criteria. The only affect it has on the cost-effectiveness calculation is to reduce treatment costs.

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.

The impact of the PAS on the ICERs for the two comparators is shown in Table 13.

Table 23 Results showing the impact of the proposed PAS on ICERs

	Afatinib vs. Gefitinib		Afatinib vs. Erlotinib	
	Without PAS	With PAS	Without PAS	With PAS
Base Case	[redacted]	£17,933	[redacted]	£10,079
PSA	[redacted]	£15,027	[redacted]	£6,671

PSA = probability sensitivity analysis

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.

A copy of the confidential disclosure agreement to be signed by NHS stakeholders before the discounted price can be shared is attached.

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.

N/A as the scheme is a financially based scheme.

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.

N/A

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.

N/A

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).

N/A

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.

N/A

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.

N/A

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.

N/A

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.

N/A

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.

N/A