NATIONAL INSTITUTE FOR HEALTH AND CLINICAL 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/Pharmaceuticalpricerегulationscheme/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/Pharmaceuticalpricerегulationscheme/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.

Lucentis™ (ranibizumab) for the treatment of neovascular (wet) age-related macular degeneration (AMD), for the treatment of visual impairment due to diabetic macular oedema (DMO) and for the treatment of visual impairment due to macular oedema (MO) secondary to retinal vein occlusion (RVO). This submission relates to the cost-effectiveness of ranibizumab in the RVO indication.

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

To provide a cost-effective therapy to the NHS, thereby facilitating patient access to optimal treatment for wet AMD, visual impairment due to DMO and visual impairment due to MO secondary to RVO. The PAS is a mechanism through which the NHS will be able to procure ranibizumab at a price lower than list. There have been informal discussions about the existing scheme for ranibizumab and the response has been to keep the NHS administration burden to a minimum. The new scheme reflects this feedback.

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

Financially-based scheme: simple discount to list price.

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 all supplies and preparation of ranibizumab applicable to all current and future indications.

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 will apply when patients commence treatment. It is not dependent on any criteria.

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

All patients prescribed ranibizumab will meet the scheme criteria.

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

The NHS Trust signs a commercial agreement with Novartis Pharmaceuticals UK Ltd as per the standard NHS pharmacy procurement procedure. The hospital pharmacy then orders ranibizumab through the normal procedure. Ranibizumab is provided to the NHS Trust at list price minus [redacted]*. The amount of discount 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.

No additional information, further to the standard NHS pharmacy procurement procedure, need be collected routinely.

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 scheme will be in place until NICE review of guidance for the treatment of visual impairment due to DMO, and subject to Department of Health agreement.

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

No.

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 draft purchase agreement letter and terms are included in the appendix. These are provided as commercial in confidence.

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 applied has been presented in the main submission of evidence.

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.

A simple discount of [redacted] *is applied to the list price of ranibizumab in 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.

Not applicable.

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 costs associated with the implementation and operation of the patient access scheme. Table 1 has therefore been removed.

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. Table 2 has been removed.

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).

Table 3a BRVO base-case cost-effectiveness results (without PAS)

	Ranibizumab	Laser
Total costs (£)	18,717	11,990
Difference in total costs (£)	6,727	
QALYs	[redacted]	7.705
QALY difference	[redacted]	
ICER (£)	24,610	

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

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

Table 3b BRVO base-case cost-effectiveness results (with PAS)

	Ranibizumab	Laser
Total costs (£)	[redacted]	11,990
Difference in total costs (£)	[redacted]	-
QALYs	[redacted]	7.705
QALY difference	[redacted]	-
ICER (£)	20,494	-

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

Table 3c CRVO base-case cost-effectiveness results (without PAS)

	Ranibizumab	Best supportive care
Total costs (£)	26,327	20,727
Difference in total costs (£)	5,600	-
QALYs	[redacted]	7.061
QALY difference	[redacted]	-
ICER (£)	11,428	-

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

Table 3d CRVO base-case cost-effectiveness results (with PAS)

	Ranibizumab	Best supportive care
Total costs (£)	[redacted]	20,727
Difference in total costs (£)	[redacted]	
QALYs	[redacted]	7.061
QALY difference	[redacted]	-
ICER (£)	8,643	-

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.

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

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.

Note: Limitations of the clinical data available to estimate cost effectiveness of ranibizumab versus dexamethasone implant means that should be interpreted with caution (detailed reasons are described in section 6.6.2 of the manufacturer submission)

Table 4a BRVO base-case incremental results (without PAS)

	Total costs (£)	Total LY	Total QALYs	Ranibizumab vs. laser monotherapy			
				Incremental costs (£)	Incremental QALYs	ICER (£) versus laser (QALYs)	ICER (£) incremental (QALYs)
Laser	11,990	12.56	7.705				
Dexamethasone implant	16,448	12.58	7.769	4,458	0.065	68,742	68,742
Ranibizumab	18,717	[redacted]	[redacted]	2,269	[redacted]	24,610	10,883

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

Table 4b BRVO base-case incremental results (with PAS)

	Total costs (£)	Total LY	Total QALYs	Ranibizumab vs. laser monotherapy			
				Incremental costs (£)	Incremental QALYs	ICER (£) versus laser (QALYs)	ICER (£) incremental (QALYs)
Laser	11,990	12.56	7.705				
Dexamethasone implant	16,448	12.58	7.769	4,458	0.065	68,742	68,742
Ranibizumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	20,494	5,486

Table 4c CRVO base-case incremental results (without PAS)

	Total costs (£)	Total LY	Total QALYs	Ranibizumab vs. laser monotherapy			
				Incremental costs (£)	Incremental QALYs	ICER (£) versus BSC (QALYs)	ICER (£) incremental (QALYs)
Best supportive care	20,727	12.149	7.061	-	-	-	-
Dexamethasone implant	22,945	12.209	7.270	2,218	0.209	10,622	10,662
Ranibizumab	26,327	[redacted]	[redacted]	3,382	[redacted]	11,428	12,027

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

Table 4d CRVO base-case incremental results (with PAS)

	Total costs (£)	Total LY	Total QALYs	Ranibizumab vs. laser monotherapy			
				Incremental costs (£)	Incremental QALYs	ICER (£) versus BSC (QALYs)	ICER (£) incremental (QALYs)
Best supportive care	20,727	12.149	7.061				
Dexamethasone implant	22,945	12.209	7.270	2,218	0.209	10,622	10,622
Ranibizumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	8,643	7,174

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 5a BRVO one way sensitivity analysis for ranibizumab versus laser (with PAS)

Parameter	Incremental costs	Incremental QALYs	Incremental cost per QALY
Base case	[redacted]	[redacted]	**20,494**
Frequency of ranibizumab treatment in year 1, 3 injections	[redacted]	[redacted]	8,527
Frequency of ranibizumab treatment in year 1, 12 injections	[redacted]	[redacted]	30,067
Frequency of ranibizumab treatment in year 2, 3 injections	[redacted]	[redacted]	21,633
Frequency of ranibizumab treatment in year 2, 6 injections	[redacted]	[redacted]	28,468
Continued ranibizumab treatment in year 3, 1 injection	[redacted]	[redacted]	23,284
Administration costs, £96	[redacted]	[redacted]	16,944
Administration costs, £288	[redacted]	[redacted]	24,044
Follow up costs, £76	[redacted]	[redacted]	19,941
Follow up costs, £227	[redacted]	[redacted]	21,054
Frequency of ranibizumab visits in year 2, 4	[redacted]	[redacted]	20,750
Frequency of ranibizumab visits in year 2, 8	[redacted]	[redacted]	22,798
Frequency of ranibizumab visits in year 3+, 0	[redacted]	[redacted]	11,551
Frequency of ranibizumab visits in year 3+, 4	[redacted]	[redacted]	29,437
Discount rate costs and benefits, 0%	[redacted]	[redacted]	15,049
Discount rate costs and benefits, 6%	[redacted]	[redacted]	24,556
Discount rate costs 3.5% Discount rate benefits, 0%	[redacted]	[redacted]	16,286

Table 5b CRVO one way sensitivity analysis for ranibizumab vs best supportive care (with PAS)

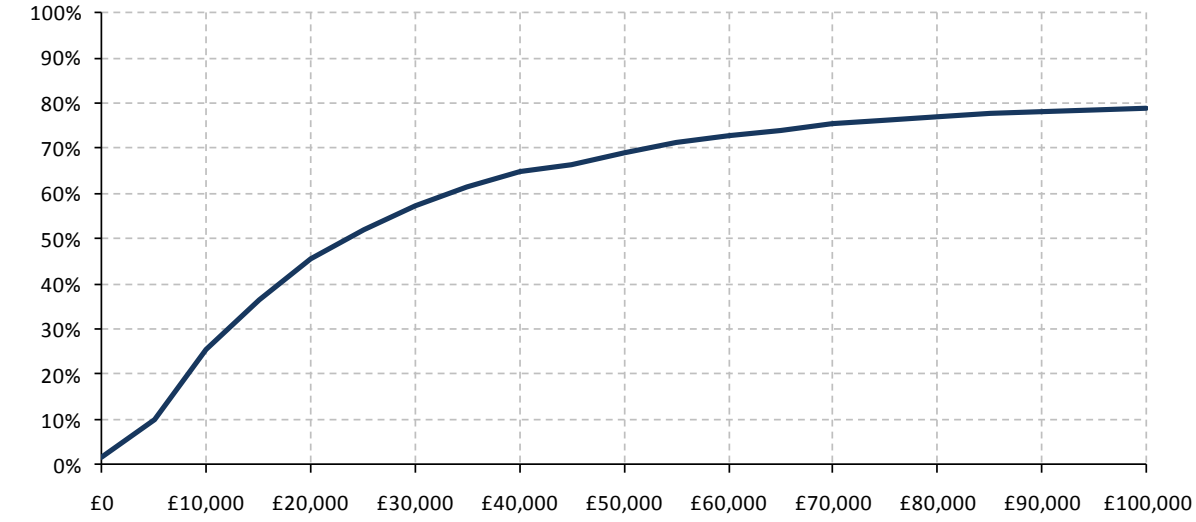
Variable	Incremental Costs	Incremental QALYs	Cost per QALY
Base case	[redacted]	[redacted]	**8,643**
Frequency of ranibizumab treatment in year 1, 3	[redacted]	[redacted]	644
Frequency of ranibizumab treatment in year 1, 12	[redacted]	[redacted]	12,643
Frequency of ranibizumab treatment in year 2, 0	[redacted]	[redacted]	3,834
Frequency of ranibizumab treatment in year 2, 6	[redacted]	[redacted]	11,428
Continued treatment in year 3, 1 injection	[redacted]	[redacted]	10,193
Administration costs, £96	[redacted]	[redacted]	6,242
Administration costs, £288	[redacted]	[redacted]	11,045
Follow up costs, £76	[redacted]	[redacted]	8,721
Follow up costs, £227	[redacted]	[redacted]	8,565
Frequency of ranibizumab visits in year 2, 6	[redacted]	[redacted]	8,586
Frequency of ranibizumab visits in year 2, 12	[redacted]	[redacted]	10,293
Frequency of ranibizumab visits in year 3+, 2	[redacted]	[redacted]	8,586
Frequency of ranibizumab visits in year 3+, 6	[redacted]	[redacted]	18,274
Discount rate costs 0% and discount rate benefits 0%	[redacted]	[redacted]	5,135
Discount rate costs 6% and discount rate benefits 6%	[redacted]	[redacted]	11,302
Discount rates cost 3.5% and discount rates benefits 0%	[redacted]	[redacted]	6,810

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

Table 6: Probability of cost effectiveness (with PAS)

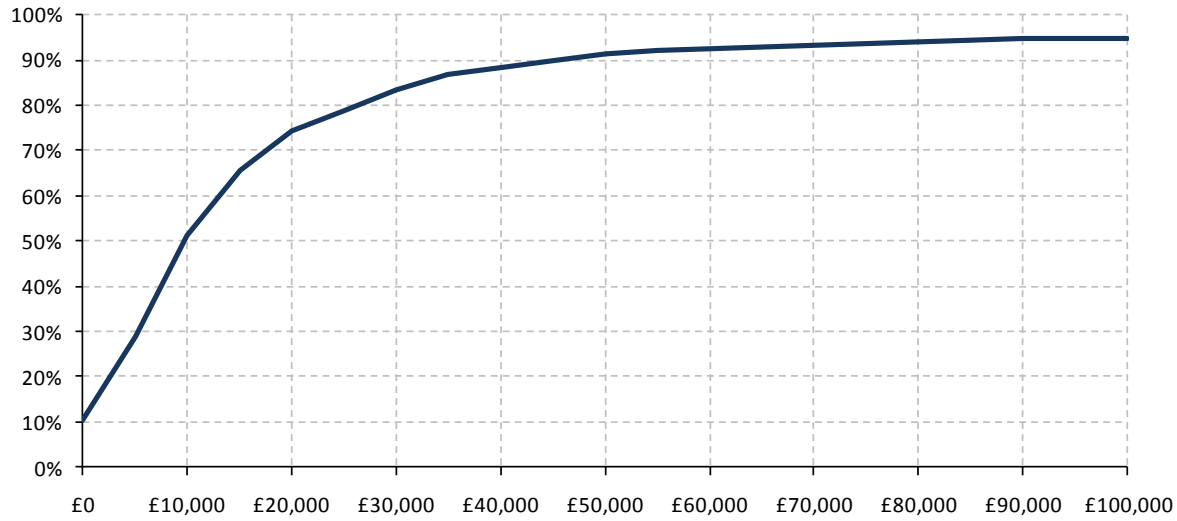
	WTP = £0	WTP= £ 20,000	WTP= £ 30,000
BRVO: ranibizumab vs laser	1.6%	45.5%	57.2%
CRVO: ranibizumab vs best supportive care	10.3%	74.5%	83.3%

Figure 1a BRVO cost effectiveness acceptability curve – ranibizumab versus laser (with PAS)



[redacted]

Figure 2a CRVO cost effectiveness acceptability curve – ranibizumab versus laser (PAS)



[redacted]

[redacted]

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

See section 4.13

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.

Table 5 Results showing the impact of patient access scheme on ICERs

	BRVO: ICER for ranibizumab versus laser		CRVO: ICER for ranibizumab versus best supportive care	
	Without PAS	**With PAS**	**Without PAS**	**With PAS**
Scenario 1 (base-case)	24,610	20,494	11,428	8,643
Scenario 2 (source of utilities[a])	19,841	16,522	9,723	7,353
Scenario 3 (potential stopping rule)	22,404	15,011	9,909	7,352
Scenario 4 (WSE analysis with trial based BSE proportion)	See figure 3a and 3b		See figure 5a and 5b	
Scenario 5 (WSE analysis with assumption based BSE proportion)	See figure 4a and 4b		See figure 6a and 6b	

PAS: patient access scheme.
A: Sharma 2000 utilities (univariate analysis)

-0.019

Figure 3a: BRVO scenario 4 (without PAS)

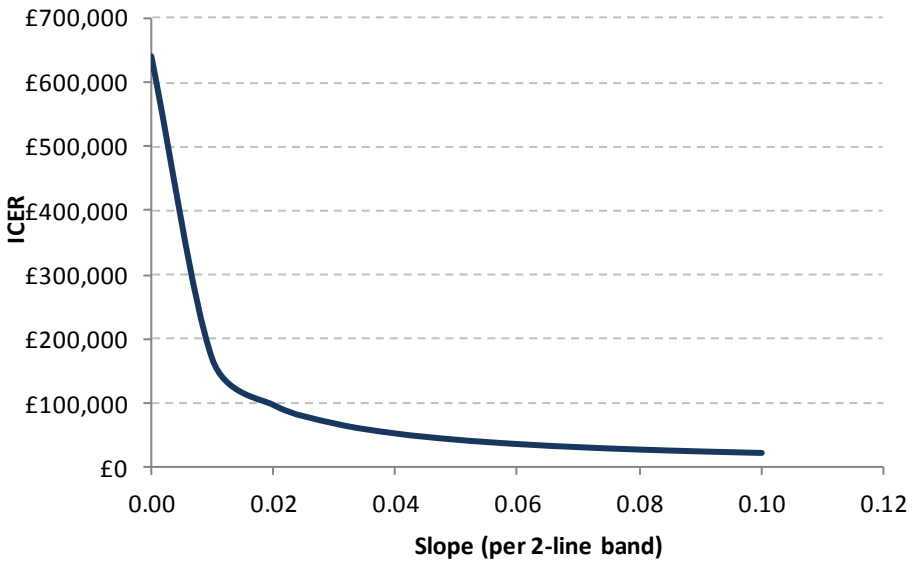


Figure 3b: BRVO scenario 4 (with PAS)

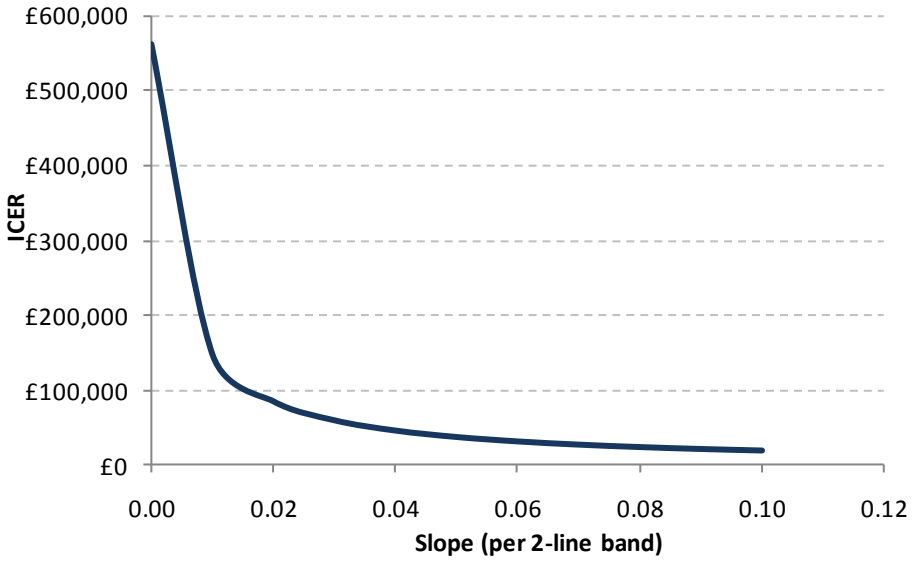


Figure 4a: BRVO scenario 5 (without PAS)

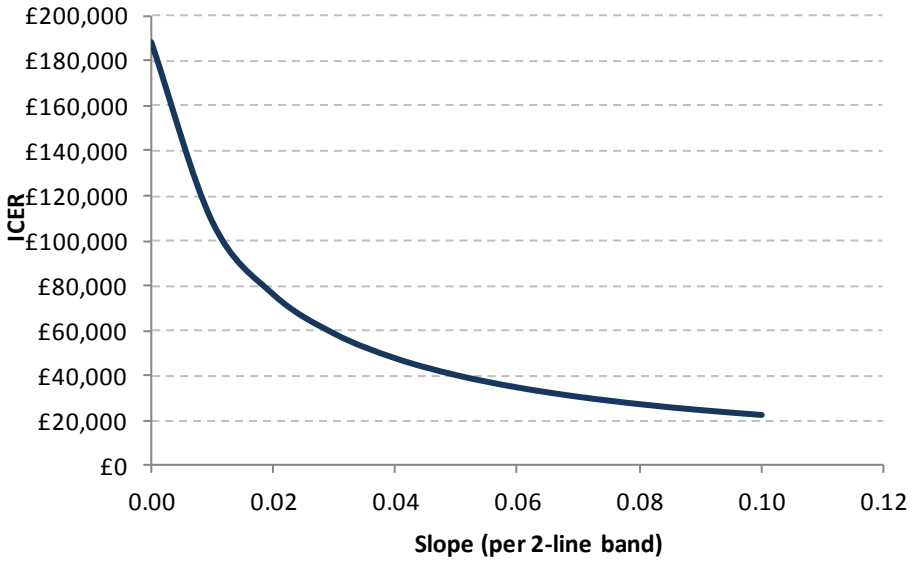


Figure 4b: BRVO scenario 5 (with PAS)

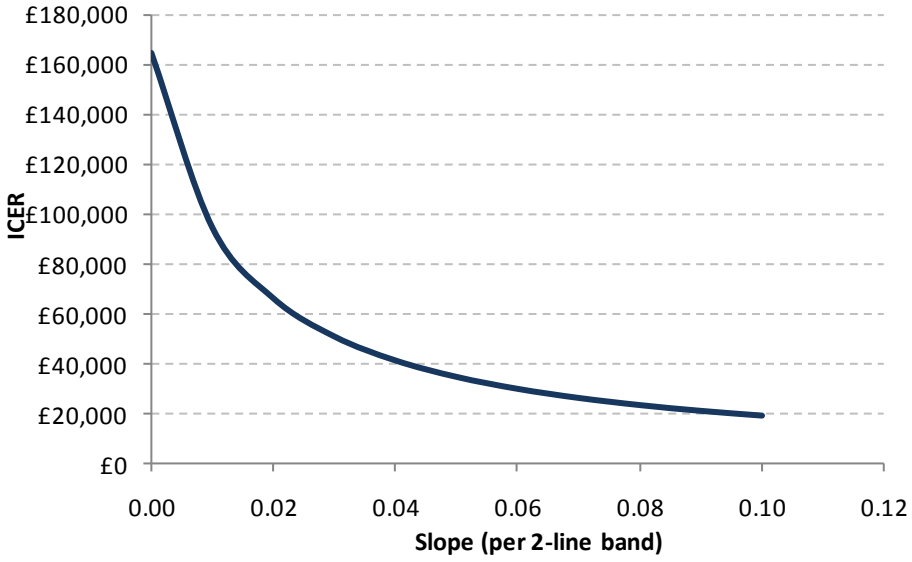


Figure 5a: CRVO scenario 4 (without PAS)

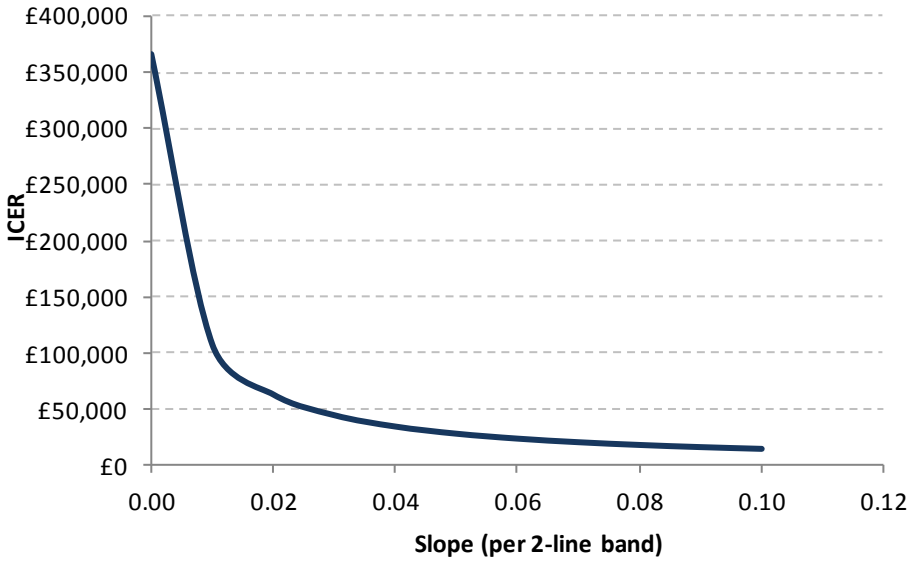


Figure 5b: CRVO scenario 4 (with PAS)

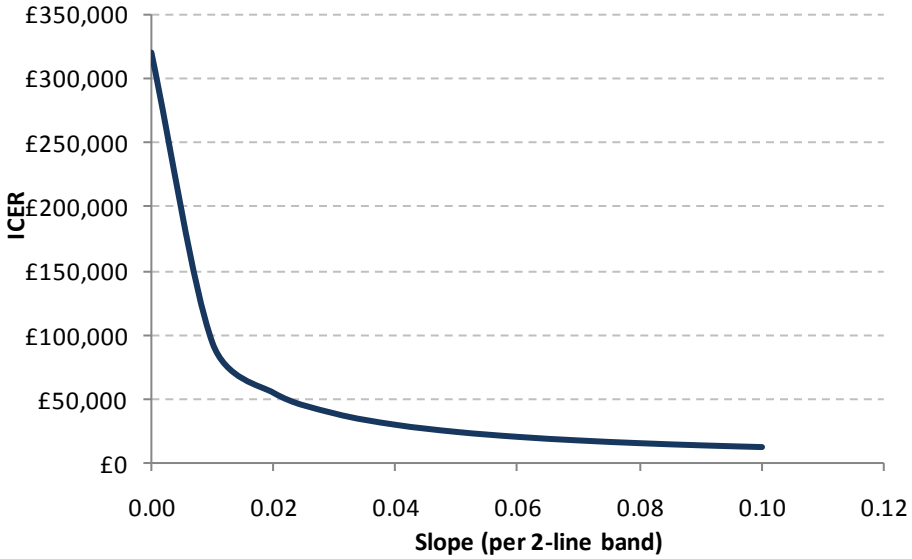


Figure 6a: CRVO scenario 5 (without PAS)

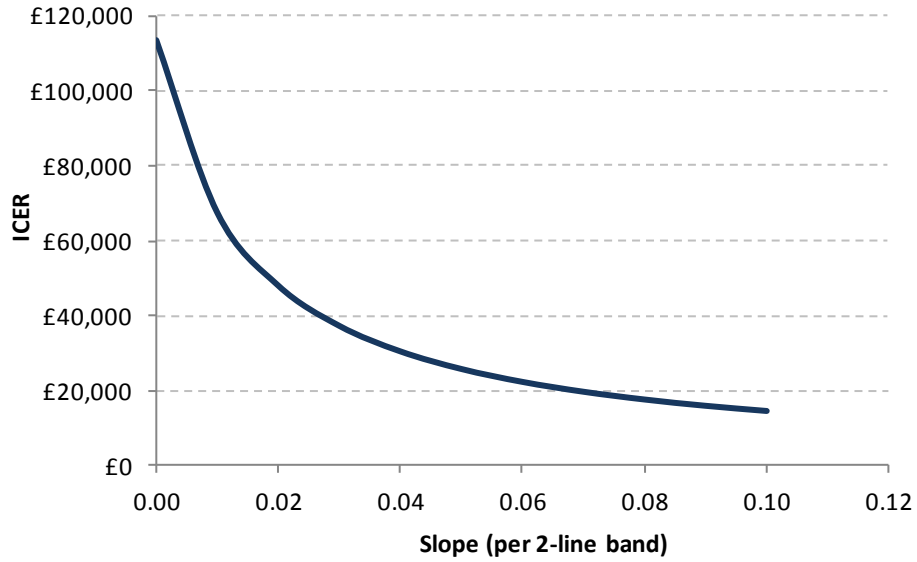
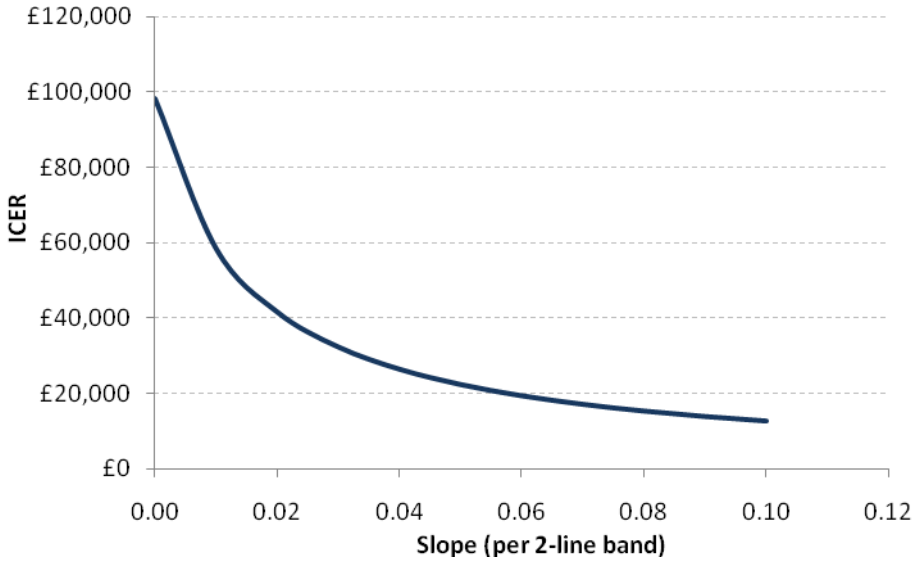


Figure 6b: CRVO scenario 5 (with PAS)



Appendices

4.14 Appendix A: Additional documents

4.14.1 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.

Refer to associated file Lucentis Net Price Agreement Feb 2011 – DRAFT v3.pdf.

4.15 Appendix B: Details of outcome-based schemes

4.15.1 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

4.15.2 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

4.15.3 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

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

4.15.4 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

4.15.5 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

4.15.6 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

4.15.7 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.

4.15.8 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.