# 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/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.

Lenalidomide – (Revlimid®)

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

The Patient Access Scheme for lenalidomide has been devised in order that lenalidomide for the treatment of patients with MDS del5(q) is considered a cost-effective use of NHS resources

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

Financially based.

3.4 Please provide specific details of the patient population to which the patient access scheme applies. Does the scheme apply to the whole licensed population or only to a specific subgroup (for example, type of tumour, location of tumour)? If so:

- How is the subgroup defined?
- If certain criteria have been used to select patients, why have these have been chosen?
- How are the criteria measured and why have the measures been chosen?

The scheme applies to the entire license (anticipated) population i.e. patients with transfusion-dependent anaemia due to low- or intermediate-1 risk MDS associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate.

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 proposed scheme will provide free drug to transfusion dependent low or intermediate-1 risk MDS patients with isolated del 5q absnormality after a fixed time point on therapy with lenalidomide (26 cycles). There are no further criteria limiting the PAS.

The proposed scheme is an extension of the existing scheme with TA171 and so from an administration point of view would be familiar to the NHS. In addition, extending the 26 cycle capping scheme to the expected indication in MDS del 5q, renders it to be cost-effective.

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

In the health economic evidence submitted to NICE, the model based on the pivotal trial MDS-004 estimated that approximately 31.9% of patients would reach 26 cycles and be eligible for free lenalidomide thereafter.

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

The proposed scheme is a capping scheme where beyond a certain number of cycles (26), the drug is provided free-of-charge. Celgene administers the patient access scheme alongside the mandatory risk management programme i.e Pregnancy Prevention Programme (PPP) and when a

Prescription Authorisation Form (PAF) is received for the 26th cycle, an alert is automatically generated by Celgene and sent to the prescribing / dispensing centre, to inform that the patient is eligible for lenalidomide free-of-charge from the next cycle onwards. Celgene offers three options with the scheme and NHS organisations can either choose to receive a credit note, free stock or rebate via BACS. Celgene will issues zero cost invoices, a credit note or monetary rebate for those eligible patients.

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.

Lenalidomide is structurally related to thalidomide, a known human teratogenic substance that causes severe life-threatening birth defects. If lenalidomide is taken during pregnancy, a teratogenic effect of lenalidomide cannot be ruled out in humans and for these reasons a risk minimisation plan was mandated and approved by the EMEA and MHRA during the licensing process to ensure that there is no foetal exposure to lenalidomide.

The patient access scheme (PAS), namely the Revlimid® TCS™ operates alongside the existing Pregnancy Prevention Programme (PPP). Completion of a Prescription Authorisation Form (PAF) by a registered pharmacy is a prerequisite of the PPP. The PAF must be sent to Celgene for each lenalidomide treatment cycle. Celgene manages the treatment records and pharmacies have no additional paperwork. Pharmacies are notified when eligible patients have completed 26 cycles of lenalidomide treatment and, thereafter, automatically receive all future cycles of lenalidomide, for that patient, free-of-charge.

Dispensing Pharmacy Registration: (Mandatory Requirement): It is a requirement of the PPP that pharmacies wishing to purchase and dispense lenalidomide are registered with Celgene. Registration involves receiving a Healthcare Professional's Information Pack (HPIP) and faxing (or posting) to Celgene a signed Pharmacy Registration Form to indicate agreement and

compliance with the content. Once a pharmacy has been registered, Celgene will issue a unique Pharmacy Identification Number.

Enrolling on the PAS: Hospitals / Pharmacists wishing to enrol need to complete and return the Revlimid® TCS™ Agreement which sets out the terms under which patients will be eligible for free treatment. Celgene will confirm in writing an acceptance onto the Revlimid® TCS™, and the method of supply of free-of charge lenalidomide.

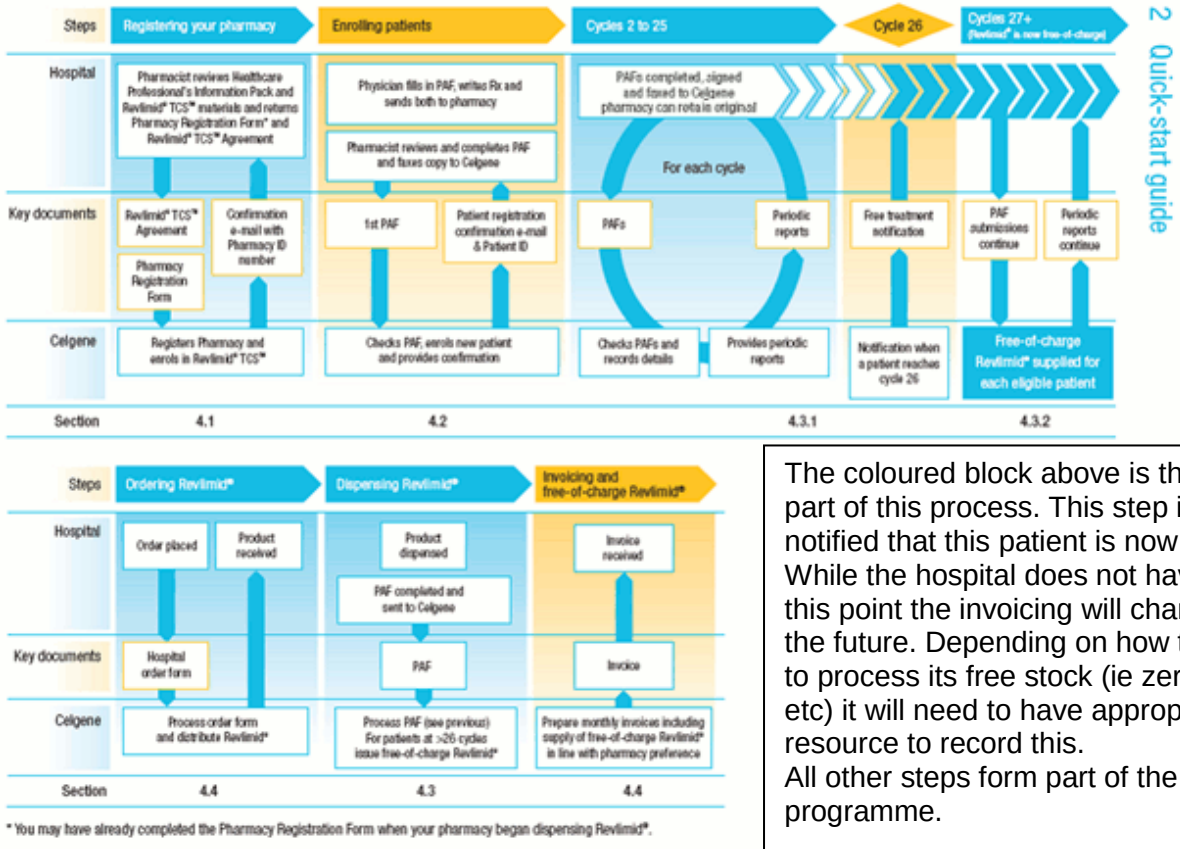
Enrolling patients: Sending in the first PAF for an unregistered, eligible patient to Celgene will automatically trigger patient enrolment. Celgene will confirm in writing that a new patient has been enrolled into the Revlimid® TCS™ and provide a unique Patient Identification Number. This will enable Celgene to track the number of PAFs received for each patient, and to supply free-of-charge Revlimid® for patients continuing treatment beyond cycle 26.

Cycle management: For Cycles 1 to 26, Celgene will use the PAFs to confirm which cycle of treatment a patient is on. When a pharmacist receives a PAF and prescription for lenalidomide from a physician, it needs to be checked for completion and a copy returned to Celgene. The original copy can be retained within the pharmacy.

Celgene will track the number of PAFs received for each patient; receipt of the 26th PAF for an eligible patient will trigger notification from Celgene that the patient will now receive lenalidomide free-of-charge.

Continuing treatment beyond cycle 26: Pharmacies must continue to send all completed PAFs to Celgene in order to receive free-of-charge lenalidomide for eligible patients. Celgene will provide quarterly and annual reports, using anonymised data of patients registered on the Revlimid® TCS™ and those who have become eligible to receive lenalidomide free-of-charge patients' cycle status doses used. The annual report will also summarise patients' PAF histories over the previous calendar year.

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




The coloured block above is the only PAS specific part of this process. This step is when the hospital is notified that this patient is now eligible for free stock. While the hospital does not have to do anything at this point the invoicing will change for this patient in the future. Depending on how the hospital would like to process its free stock (ie zero invoice, credit note, etc) it will need to have appropriate systems and resource to record this.
All other steps form part of the mandatory PPP programme.

Step 4.4 can be replaced by the hospital completing and returning a claim form to receive a monetary rebate.

3.10 Please provide details of the duration of the scheme.

The scheme provides free drug beyond 26 cycles of use. There are no other limiting criteria for this PAS.

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?

MDS predominantly affects elderly patients, many of whom have concomitant conditions. This patient population may also have mobility issues; that is, patients who are frail and live at long distances from a hospital may find difficulty in commuting to receive blood transfusions. Lenalidomide is an oral therapy which can be taken at home.

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.

Please see attached.

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.

N/A

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.

Model provided with an option (button) to apply PAS. The following changes have been made to the initial model, based upon the appraisal process:

- In line with Committee recommendations, the present analysis assumes routine monitoring appointments to be performed by a haematologist in a hospital outpatient setting. The initial analysis had assumed that such visits were performed by a general practitioner.
- In line with Committee recommendations, the rate of progression to acute myeloid leukaemia (AML) is no longer dependent upon whether a patient is dependent on blood transfusions. The rate of progression to AML has been set to the rate associated with transfusion independent patients for all patients.
- The ERG provided an updated cost for iron chelation therapy which includes the use of deferiprone. This was not included in Celgene's initial analysis, and so the cost per cycle of iron chelation therapy was different to that suggested by the ERG. In the present analysis the cost of iron chelation therapy has been changed to match the cost presented by the ERG, reflecting the use of deferiprone in UK practice.

- Based upon feedback from the ERG, a half-cycle correction was fully implemented into the model.
- The number of cycles required before the threshold for iron chelation therapy is reached has been set to 2, in keeping with the initial analysis. Celgene have clarified, and the ERG accepted that, an initial assessment that this value should in fact be 4 was a result of a labelling error within the cost-effectiveness model.

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.

Patient Access Scheme sets cost to £0 for all patients still receiving Revlimid after cycle 26.

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.

Same as without patient access scheme, as presented in manufacturer submission.

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 **Error! Reference source not found.**. Please give the reference source of these costs. Please refer to section 6.5 of the 'Specification for manufacturer/sponsor submission of evidence'.

The proposed scheme will function on the back of the PPP which is a mandatory requirement for prescribing lenalidomide. This approach, incorporating the implementation of the price capping scheme within PPP would be expected to have neutral burden on the NHS.

4.6 Please provide details of any additional treatment-related costs incurred by implementing the patient access scheme. A suggested format is presented. The costs should be provided for the intervention both with

and without the patient access scheme. Please give the reference source of these costs.

**Table 1 Additional treatment-related costs for the intervention both with and without the patient access scheme (PAS)**

| | Intervention without PAS | | Intervention with PAS | | Reference source |
|---|---|---|---|---|---|
| | **Unit cost (£)** | **Total cost e.g. per cycle, per patient (£)** | **Unit cost (£)** | **Total cost e.g. per cycle, per patient (£)** | |
| Interventions | £180 per 10mg tablet<br>£170 per 5mg tablet | £3,780 per cycle receiving 10mg<br>(£180 * 21 days per cycle)<br><br>£4,760 per cycle receiving 5mg at 28 days per cycle<br>(£170 * 28 days per cycle)<br><br>£2,380 per cycle receiving 5mg at 14 days per cycle<br>(£170 * 14 days per cycle) | Same as without PAS then £0 after cycle 26 | Same as without PAS then £0 after cycle 26 | British National Formulary v64 |
| Monitoring tests | £159.56 per outpatient haematologist visit (£134.25,£186.68)<br>Weekly for first 56 days, 2 weekly until 84 days, every 28 days thereafter | | Same as without PAS | Same as without PAS | NHS Reference Costs 2011-12 |
| Diagnostic tests | £3.09 for full blood count (£2.60,£3.61)<br>One of each with every monitoring visit | | Same as without PAS | Same as without PAS | NHS Reference Costs 2011-2012 |
| Total treatment-related costs | ≤£4,080 per cycle depending on the proportion of patients | | Same as without PAS then £163 after cycle 26 | | |

| | | | | | |
|---|---|---|---|---|---|
| | receiving each dosing regime within the trial | | | | |

***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.

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

**Table 2 Base-case cost-effectiveness results without PAS**

| | Intervention | Best supportive care |
|---|---|---|
| Technology acquisition cost | £74,196 | £2,243 |
| Other costs | £98,111 | £120,999 |
| Total costs | £172,307 | £123,241 |
| Difference in total costs | N/A | £49,065 |
| LYG | 6.06 | 5.17 |
| LYG difference | N/A | 0.88 |
| QALYs | 3.67 | 2.95 |
| QALY difference | N/A | 0.72 |
| ICER | N/A | £68,125 |
| LYG, life years gained; QALY(s), quality-adjusted life year(s); ICER, incremental cost-effectiveness ratio<br>QALYs and Costs are presented with a 3.5% discount rate. LYG are undiscounted. | | |

**Table 3 Base-case cost-effectiveness results with PAS**

| | Intervention | Best supportive care |
|---|---|---|
| Technology acquisition cost | £42,808 | £2,243 |
| Other costs | £98,111 | £120,999 |
| Total costs | £140,919 | £123,241 |
| Difference in total costs | N/A | £17, 677 |
| LYG | 6.06 | 5.17 |
| LYG difference | N/A | 0.88 |
| QALYs | 3.67 | 2.95 |
| QALY difference | N/A | 0.72 |
| ICER | N/A | £24,544 |
| LYG, life years gained; QALY(s), quality-adjusted life year(s); ICER, incremental cost-effectiveness ratio<br>QALYs and Costs are presented with a 3.5% discount rate. LYG are undiscounted. | | |

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

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

- 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.

**Table 4 Base-case incremental results**

| Technologies | Total costs (£) | Total LYG | Total QALYs | Incremental costs (£) | Incremental LYG | Incremental QALYs | ICER (£) versus baseline (QALYs) | ICER (£) incremental (QALYs) |
|---|---|---|---|---|---|---|---|---|
| Best supportive care | £123,241 | 5.17 | 2.95 | - | - | - | £41,767 | - |
| Revlimid | £140,919 | 6.06 | 3.67 | £17,677 | 0.88 | 0.72 | £38,388 | £24,544 |

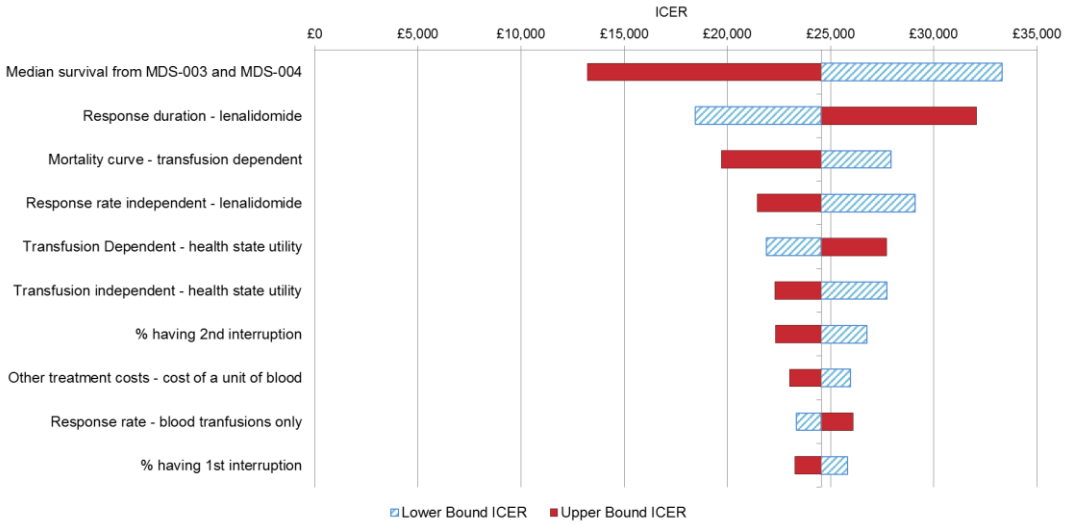
LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

## 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.

Figure 1 shows the top 10 parameters affecting the ICER. The most influential parameter is the median survival from the MDS-003 and MDS-004 studies, while the lenalidomide response duration is also an important determinant of the ICER. The ICER is also sensitive to curve parameters used for mortality and also the health state utilities assumed. The maximum ICER under deterministic sensitivity analysis is £33,309.

**Figure 1 Tornado diagram – top 10 parameters affecting the ICER with PAS**




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

Probabilistic sensitivity analysis was conducted using 1,000 model runs. The mean ICER using probabilistic analysis (£25,468 per QALY) was similar to the deterministic ICER. Some 65.8% of observations were cost-effective at a £30,000 per QALY threshold. In all cases Revlimid was more effective than Best Supportive Care..

**Table 5 Output from PSA**

| | **With PAS** |
|---|---|
| Mean Incremental Costs | £17,573 |
| Mean Incremental QALYs | 0.690 |
| Mean ICER | £25,468 |
| % of observations cost-effective at £20,000 threshold | 24.6% |
| % of observations cost-effective at £30,000 threshold | 65.8% |

**Figure 2. Cost Effectiveness Scatter Plot with PAS**

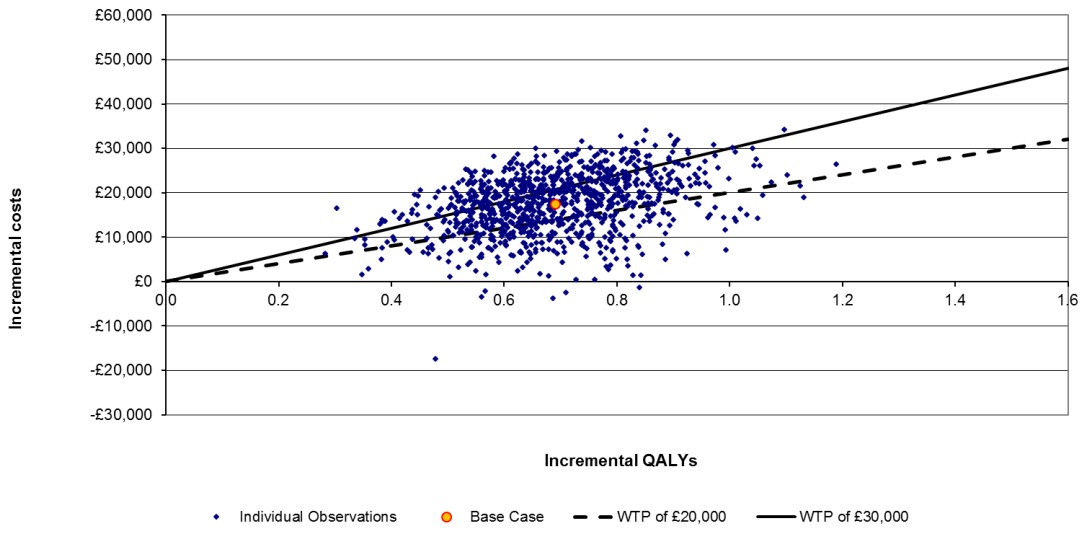
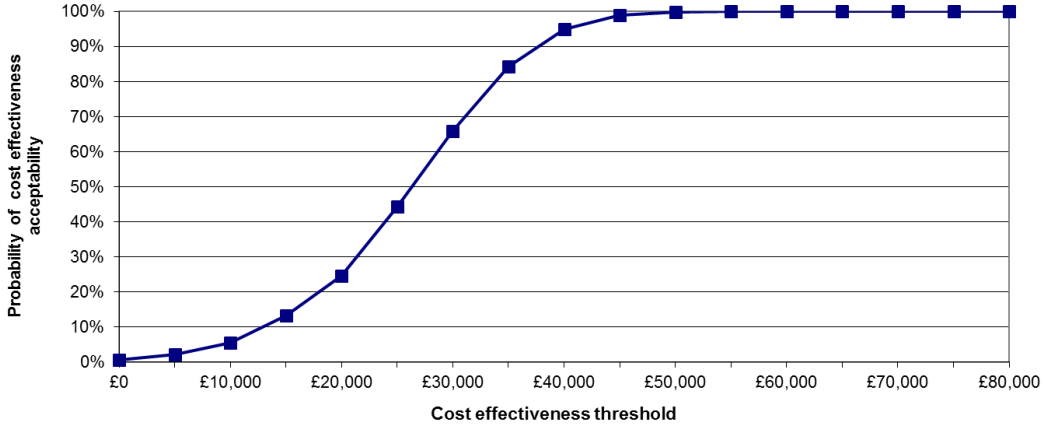


**Figure 3. Cost Effectiveness Acceptability Curve with PAS**




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

**Table 6 All trial patients rather than UK patients with PAS**

| Technology | Total costs (£) | Total LYG | Total QALYs | Incremental costs (£) | Incremental LYG | Incremental QALYs | ICER |
|---|---|---|---|---|---|---|---|
| Best supportive care | £126,613 | 5.23 | 2.99 | - | - | - | - |
| Revlimid | £145,337 | 6.06 | 3.68 | £18,725 | 0.83 | 0.69 | £27,114 |

**Table 7 Comparator with PAS**

| Curve | Technology | Total costs (£) | Total LYG | Total QALYs | Incremental costs (£) | Incremental LYG | Incremental QALYs | ICER |
|---|---|---|---|---|---|---|---|---|
| All patients using ESA | Best Supportive Care | £131,509 | 5.34 | 3.04 | - | - | - | - |
| | Revlimid | £140,919 | 6.06 | 3.67 | £9,409 | 0.71 | 0.63 | £15,030 |
| All patients receiving only transfusions as required | Best Supportive Care | £120,521 | 5.11 | 2.92 | - | - | - | - |
| | Revlimid | £140,919 | 6.06 | 3.67 | £20,398 | 0.95 | 0.76 | £27,005 |

**Table 8 Iron chelation threshold with PAS**

| Threshold | Technology | Total costs (£) | Total LYG | Total QALYs | Incremental costs (£) | Incremental LYG | Incremental QALYs | ICER |
|---|---|---|---|---|---|---|---|---|
| 20 | Best Supportive Care | £121,964 | 5.17 | 2.95 | - | - | - | - |
| | Revlimid | £141,103 | 6.06 | 3.67 | £19,139 | 0.88 | 0.72 | £26,551 |
| 30 | Best Supportive Care | £123,767 | 5.17 | 2.95 | - | - | - | - |
| | Revlimid | £144,632 | 6.06 | 3.67 | £20,864 | 0.88 | 0.72 | £28,881 |

**Table 9 Source of Utilities with PAS**

| Threshold | Technology | Total costs (£) | Total LYG | Total QALYs | Incremental costs (£) | Incremental LYG | Incremental QALYs | ICER |
|---|---|---|---|---|---|---|---|---|
| Goss | Best Supportive Care | £123,241 | 5.17 | 2.31 | - | - | - | - |
| | Revlimid | £140,919 | 6.06 | 3.23 | £17,677 | 0.88 | 0.92 | £19,135 |
| Buckstein | Best Supportive Care | £123,241 | 5.17 | 2.99 | - | - | - | - |
| | Revlimid | £140,919 | 6.06 | 4.19 | £17,677 | 0.88 | 0.68 | £25,861 |

**Table 10 Curve selection – response duration with PAS**

| Curve | Technology | Total costs (£) | Total LYG | Total QALYs | Incremental costs (£) | Incremental LYG | Incremental QALYs | ICER |
|---|---|---|---|---|---|---|---|---|
| Exponential | Best Supportive Care | £123,235 | 5.17 | 2.95 | - | - | - | - |
| | Revlimid | £140,955 | 6.06 | 3.67 | £17,720 | 0.88 | 0.72 | £24,776 |
| Weibull | Best Supportive Care | £123,328 | 5.17 | 2.95 | - | - | - | - |
| | Revlimid | £142,954 | 6.06 | 3.65 | £19,626 | 0.88 | 0.70 | £27,899 |
| Log-logistic | Best Supportive Care | £123,265 | 5.17 | 2.95 | - | - | - | - |
| | Revlimid | £141,561 | 6.06 | 3.67 | £18,295 | 0.88 | 0.71 | £25,597 |
| Extreme Value | Best Supportive Care | £123,349 | 5.17 | 2.95 | - | - | - | - |
| | Revlimid | £144,120 | 6.06 | 3.64 | £20,771 | 0.88 | 0.69 | £30,022 |

**Table 11 Curve selection – AML Progression with PAS**

| Curve | Technology | Total costs (£) | Total LYG | Total QALYs | Incremental costs (£) | Incremental LYG | Incremental QALYs | ICER |
|---|---|---|---|---|---|---|---|---|
| Exponential | Best Supportive Care | £124,863 | 5.26 | 2.98 | - | - | - | - |
| | Revlimid | £143,647 | 6.24 | 3.74 | £18,785 | 0.98 | 0.76 | £24,808 |
| Log-logistic | Best Supportive Care | £125,283 | 5.28 | 2.99 | - | - | - | - |
| | Revlimid | £144,254 | 6.25 | 3.75 | £18,971 | 0.98 | 0.76 | £25,083 |
| Lognormal | Best Supportive Care | £127,893 | 5.40 | 3.05 | - | - | - | - |
| | Revlimid | £147,831 | 6.46 | 3.84 | £19,938 | 1.05 | 0.79 | £25,218 |
| Extreme Value | Best Supportive Care | £121,208 | 5.07 | 2.91 | - | - | - | - |
| | Revlimid | £137,618 | 5.86 | 3.59 | £16,410 | 0.79 | 0.68 | £23,979 |

**Table 12 Curve selection – overall survival with PAS**

| Curve | Technology | Total costs (£) | Total LYG | Total QALYs | Incremental costs (£) | Incremental LYG | Incremental QALYs | ICER |
|---|---|---|---|---|---|---|---|---|
| Exponential | Best Supportive Care | £133,596 | 5.76 | 3.17 | - | - | - | - |
| | Revlimid | £148,842 | 6.60 | 3.87 | £15,247 | 0.84 | 0.70 | £21,881 |
| Log-logistic | Best Supportive Care | £127,292 | 5.39 | 3.04 | - | - | - | - |
| | Revlimid | £147,579 | 6.44 | 3.85 | £20,287 | 1.05 | 0.81 | £25,130 |
| Lognormal | Best Supportive Care | £130,724 | 5.57 | 3.12 | - | - | - | - |
| | Revlimid | £151,144 | 6.65 | 3.94 | £20,419 | 1.08 | 0.82 | £24,775 |
| Extreme Value | Best Supportive Care | £120,419 | 5.02 | 2.89 | - | - | - | - |
| | Revlimid | £135,647 | 5.75 | 3.53 | £15,229 | 0.73 | 0.64 | £23,614 |

The most influential parameters within the model were survival inputs and the duration of response to Revlimid. The ICER is also relatively sensitive to the health state utilities assumed. The maximum ICER under deterministic sensitivity analysis is £33,309.

Table 6**Error! Reference source not found.** to Table 11 present the results of structural sensitivity analyses. The model is not overly sensitive to the curve fits assumed, the source of the utilities, the comparator used, the use of all patients rather than UK patients, or the iron chelation threshold used. Only one analysis raises the ICER above £30,000, with the extreme value distribution used to model response duration. However this distribution is unlikely to be a good fit to the data as it had the highest AIC of the distributions tested and provides a poor visual fit to the 5mg (therefore overestimating the benefits of best supportive care). The lowest ICER (£15,030) is obtained by assuming that all patients receive ESA as part of BSC.

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.

Sensitivity analyses provided in 4.11

***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. 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 13 Results showing the impact of patient access scheme on ICERs**

| | **ICER for intervention versus: Best Supportive Care** | |
|---|---|---|
| | **Without PAS** | **With PAS** |
| Base Case | £68,125 | £24,544 |
| All trial patients rather than UK patients | £72,565 | £27,114 |
| All patients using ESA | £65,165 | £15,030 |
| All patients receiving only transfusions as required | £68,560 | £27,005 |
| Iron chelation threshold - 20 | £70,095 | £26,551 |
| Iron chelation threshold - 30 | £72,328 | £28,881 |
| Source of Utilities - Goss | £53,112 | £19,135 |
| Source of Utilities - Buckstein | £71,780 | £25,861 |
| Curve selection – response duration - Exponential | £67,865 | £24,776 |
| Curve selection – response duration – Weibull | £67,377 | £27,889 |
| Curve selection – response duration – Log-Logistic | £67,904 | £25,597 |
| Curve selection – response duration – Extreme Value | £66,861 | £30,022 |
| Curve selection – AML Progression - Exponential | £67,034 | £24,808 |
| Curve selection – AML Progression - Log-Logistic | £67,190 | £25,083 |
| Curve selection – AML Progression – Lognormal | £66,393 | £25,218 |
| Curve selection – response duration – Extreme Value | £69,162 | £23,979 |
| Curve selection – Overall Survival - Exponential | £68,696 | £21,881 |
| Curve selection – Overall Survival - Log-Logistic | £65,706 | £25,130 |
| Curve selection – Overall Survival – Lognormal | £65,330 | £24,775 |

| | | |
|---|---|---|
| Curve selection – Overall Survival – Extreme Value | £70,741 | £23,614 |

PAS: patient access scheme.

## 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.

Please see attached – PAF, Pharmacy registration form and TCS agreement form. These are only provided for reference and may need updating subject to final license and a final NICE guidance.

### *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

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

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

5.2.4 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

5.2.5 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.

N/A

5.2.6 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.

N/A

5.2.7 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.

5.2.8 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.