# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

**Technology appraisals**

Patient access scheme submission template

(October 2009)

# Ipilimumab for previously treated unresectable malignant melanoma

# January 2012

# 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.

# 1 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.

# 2 Details of the patient access scheme

2.1 Please give the name of the technology and the disease area to which the patient access scheme applies.

Ipilimumab for previously treated unresectable malignant melanoma

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

To allow patients within the NHS access to ipilimumab, by improving the cost-effectiveness of ipilimumab compared with best supportive care

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

The patient access scheme is a simple discount scheme

2.4 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:

The patient access scheme applies to all patients treated within the NHS for whom the technology is licensed

2.5 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:

Not applicable – the scheme is available to all patients treated by the NHS

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

Not applicable – the scheme is available to all patients treated by the NHS

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

A financial discount of [redacted] per 50mg vial and [redacted] per 200mg vial ([redacted]) will be applied to the NHS list price of the product. This will be applied on the original invoice.

2.8 Please provide details of how the scheme will be administered. Please specify whether any additional information will need to be collected, explaining when this will be done and by whom.

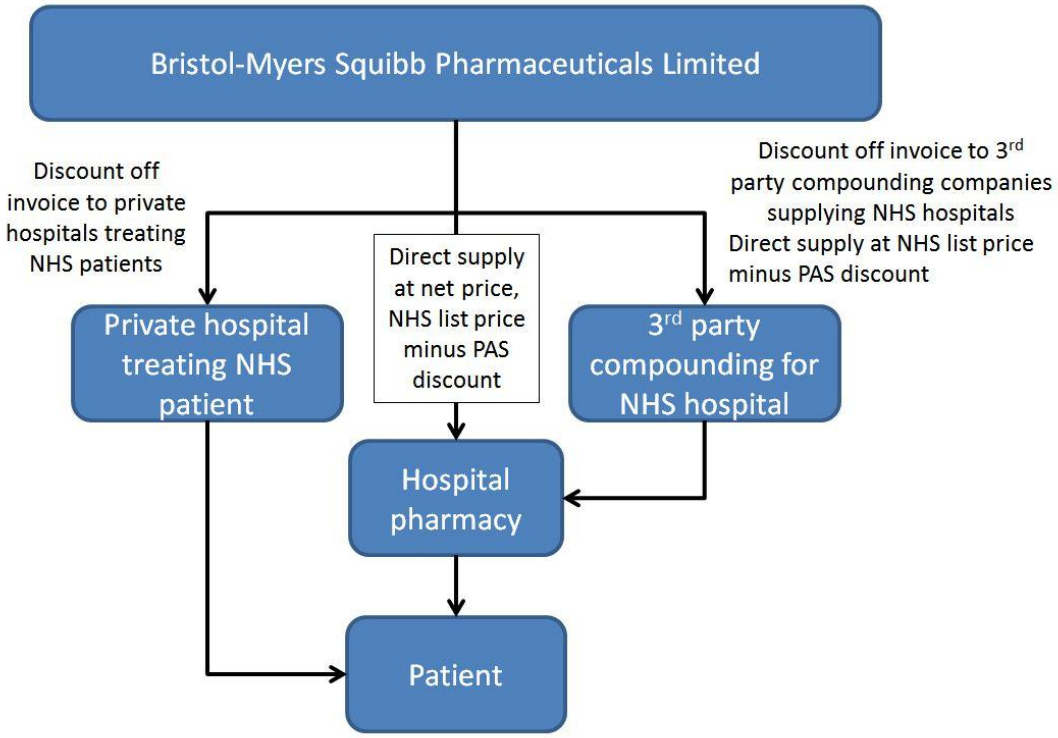
The discount will be a financial discount of applied to the original invoice sent to healthcare providers.

BMS will also sell ipilimumab to Baxter (and third party compounding companies) to compound ipilimumab for hospitals that lack the facilities to do this in house. BMS will discount ipilimumab to the same level as to the NHS which will be applied on the original invoice. Baxter would then sell ipilimumab to NHS hospital pharmacies at NHS list price, minus the discount, including

whatever commercial arrangement exists between Baxter and their customers (e.g. fees for compounding).

BMS will inform all NHS customers of this discount to facilitate transparency around the actual acquisition cost of ipilimumab.

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




2.10 Please provide details of the duration of the scheme.

The scheme will come in to operation immediately on positive NICE recommendation of ipilimumab for previously treated unresectable malignant melanoma.

The scheme will be run at least until NICE reappraise the medicine, or subsequent indications are launched, at which point a re-review may be necessary.

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

No equity or equality concerns have been raised during the course of the appraisal

2.12 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.

No such materials are required – BMS are prepared to apply the discount to the original invoice, eliminating the need for complex claim forms.

2.13 In the exceptional case that you are submitting an outcome-based scheme, as defined by the PPRS, please also refer to appendix B.

Not applicable – the scheme proposed is a simple patient access scheme

# 3 Cost effectiveness

3.1 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 not changed

3.2 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 most plausible ICER listed in the FAD is [redacted]', referring to the revised BMS model following the Appraisal Consultation Document. Results with and without the discount applied are presented from Section 3.7 onwards

3.3 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 patient access scheme has been incorporated into the model as a straight discount of [redacted] per 50mg ([redacted])to the cost of ipilimumab. This reduces the cost per 50mg vial from £3,750 to [redacted].

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

The patient access scheme does not affect the clinical data used within the model. This remains unchanged from the original submission.

3.5 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'.

No additional costs are anticipated, due to the simplicity of the scheme proposed by BMS.

3.6 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.

The scheme is not outcomes or response based, therefore no additional costs are anticipated.

## *Summary results*

### Base-case analysis

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

- the results for the intervention without the patient access scheme
- the results for the intervention with the patient access scheme.

**Table 3 Base-case cost-effectiveness results – without Patient Access Scheme, Discounted**

| | Ipilimumab | BSC |
|---|---|---|
| Intervention cost (£) | [redacted] | £0 |
| Other costs (£) | [redacted] | £11,747 |
| Total costs (£) | [redacted] | £11,747 |
| Difference in total costs (£) | N/A | £81,181 |
| LYG | 2.77 | 1.07 |
| LYG difference | N/A | 1.70 |
| QALYs | 2.06 | 0.82 |
| QALY difference | N/A | 1.24 |
| ICER (£) | N/A | [redacted] |

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

**Table 3 Base-case cost-effectiveness results – with Patient Access Scheme, Discounted**

| | Ipilimumab | BSC |
|---|---|---|
| Intervention cost (£) | [redacted] | £0 |
| Other costs (£) | [redacted] | £11,747 |
| Total costs (£) | [redacted] | £11,747 |
| Difference in total costs (£) | N/A | £61,962 |
| LYG | 2.77 | 1.07 |
| LYG difference | N/A | 1.70 |
| QALYs | 2.06 | 0.82 |
| QALY difference | N/A | 1.24 |
| ICER (£) | N/A | £49,844 |

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

3.8 Please present in separate tables the incremental results as follows.

- 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.

**Table 4 Base-case incremental results – without Patient Access Scheme, Discounted**

| Technologies | Total costs (£) | Total LYG | Total QALYs | Incremental costs (£) | Incremental LYG | Incremental QALYs | ICER (£) incremental (QALYs) |
|---|---|---|---|---|---|---|---|
| BSC | £11,747 | 1.07 | 0.82 | | | | |
| Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |

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

**Table 4 Base-case incremental results – with Patient Access Scheme, Discounted**

| Technologies | Total costs (£) | Total LYG | Total QALYs | Incremental costs (£) | Incremental LYG | Incremental QALYs | ICER (£) incremental (QALYs) |
|---|---|---|---|---|---|---|---|
| BSC | £11,747 | 1.07 | 0.82 | | | | |
| Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £49,844 |

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

## Sensitivity analyses

3.9 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** [redacted]

## Figure 2 Tornado Diagram – With PAS

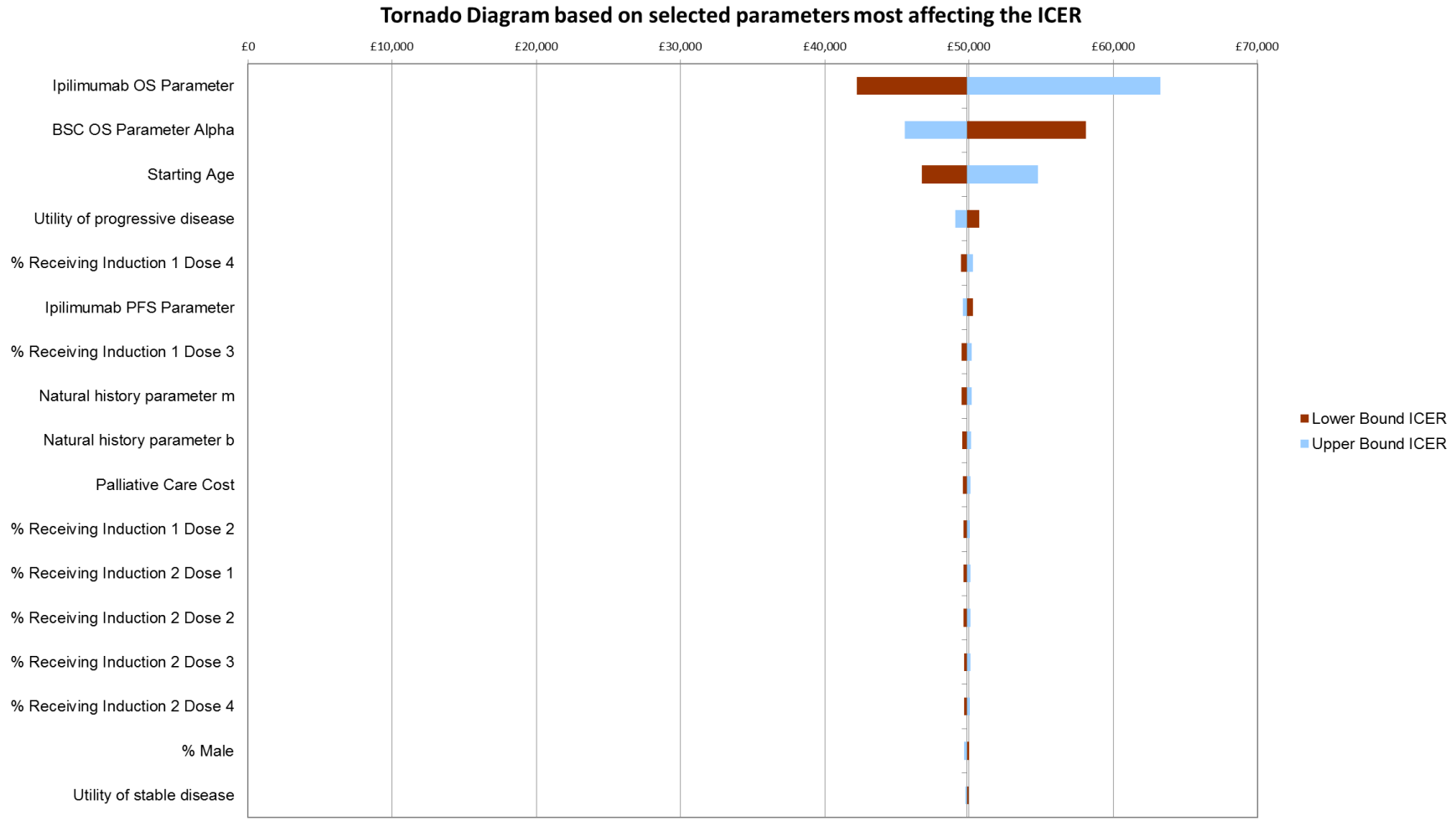


**Table 1: Impact of Dose Required**

| Number of Vials | ICER without PAS | ICER with PAS |
|---|---|---|
| 3 x 50mg | [redacted] | £31,810 |
| 1 x 200mg | [redacted] | £39,970 |
| 1 x 200mg + 1 x 50mg | [redacted] | £48,171 |
| **5.21 x 50mg** | [redacted] | **£49,844** |
| 1 x 200mg + 2 x 50mg | [redacted] | £56,291 |
| 1 x 200mg + 3 x 50mg | [redacted] | £64,451 |
| 2 x 200mg | [redacted] | £72,611 |

**Table 2: Impact of Vial Sharing**

| % of patients sharing vials | ICER without PAS | ICER with PAS |
|---|---|---|
| **0%** | [redacted] | **£49,844** |
| 25% | [redacted] | £48,864 |
| 50% | [redacted] | £47,885 |

**Table 3: Impact of the Utility of Progressive Disease**

| Utility of Progressive Disease | ICER without PAS | ICER with PAS |
|---|---|---|
| 0.6 | [redacted] | £61,149 |
| 0.65 | [redacted] | £57,180 |
| 0.7 | [redacted] | £53,694 |
| 0.75 | [redacted] | £50,609 |
| **0.763** | [redacted] | **£49,844** |
| 0.8 | [redacted] | £47,859 |

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

**Figure 3:** [redacted]

**Figure 4: Scatterplot of PSA results (1,000 simulations), With PAS**

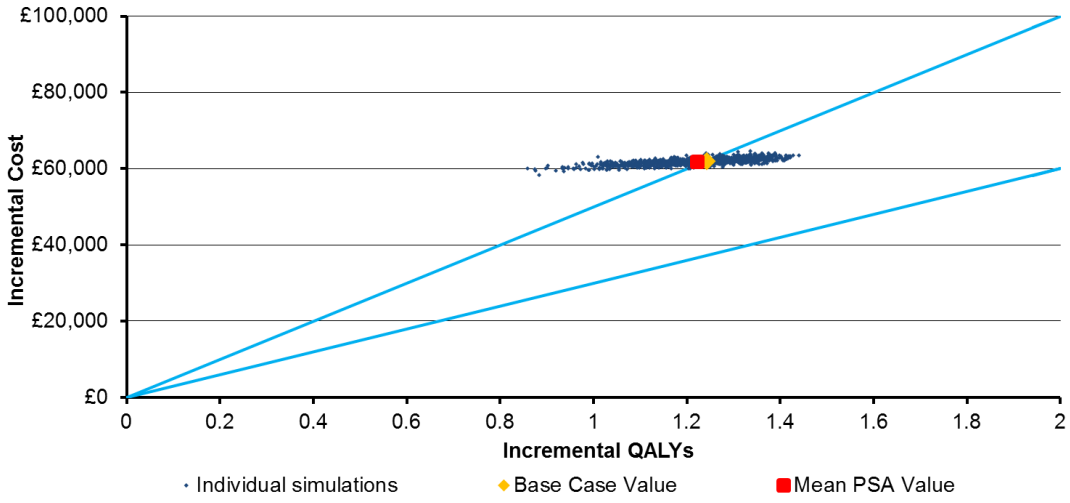
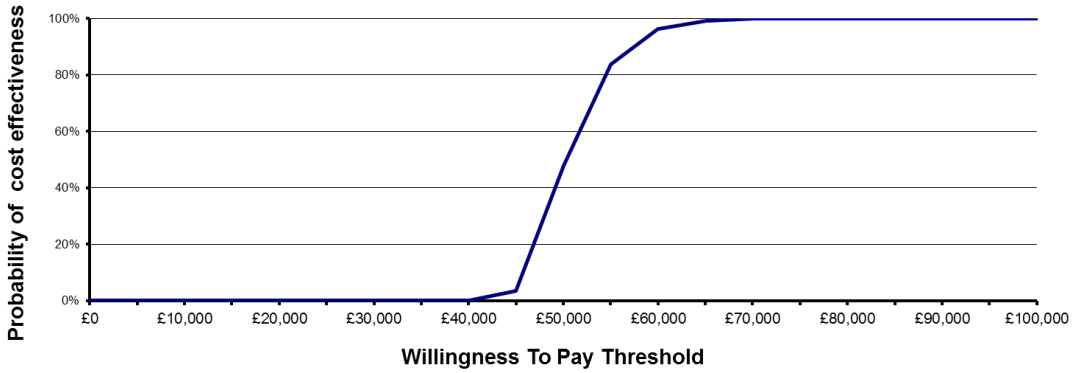


**Figure 5:** [redacted]

**Figure 6: CEAC Curve, With PAS**




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

### Scenario 1: No discounting

**Table 4: Scenario 1: No discounting, results of structural sensitivity analysis and scenario analysis, without PAS**

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) versus baseline |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| Discount 0% | BSC | £12,372 | 1.18 | 0.90 | | | | |
| | Ipilimumab | [redacted] | 3.68 | 2.69 | [redacted] | 2.50 | 1.80 | [redacted] |

## Table 5: Scenario 1: No discounting, results of structural sensitivity analysis and scenario analysis, with PAS

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) versus baseline |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £49,844 |
| Discount 0% | BSC | £12,372 | 1.18 | 0.90 | | | | |
| | Ipilimumab | [redacted] | 3.68 | 2.69 | [redacted] | 2.50 | 1.80 | £36,887 |

## Scenario 2: Alternative comparators

## Table 6: Scenario 2: Alternative comparators, results of structural sensitivity analysis and scenario analysis, without PAS

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| Collinson | Current Practice | £19,103 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| IMS | Current Practice | £13,473 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| MELODY | Current Practice | £13,020 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| Oxford Outcomes | Current Practice | £15,221 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| Paclitaxel | Paclitaxel | £23,423 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| Paclitaxel + Carboplatin | Paclitaxel + Carboplatin | £35,825 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| Carboplatin | Carboplatin | £17,973 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |

## Table 7: Scenario 2: Alternative comparators, results of structural sensitivity analysis and scenario analysis, with PAS

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £49,844 |
| Collinson | Current Practice | £19,103 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £43,926 |
| IMS | Current Practice | £13,473 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £48,455 |
| MELODY | Current Practice | £13,020 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £48,819 |
| Oxford Outcomes | Current Practice | £15,221 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £47,049 |
| Paclitaxel | Paclitaxel | £23,423 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £40,451 |
| Paclitaxel + Carboplatin | Paclitaxel + Carboplatin | £35,825 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £30,475 |

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Carboplatin | Carboplatin | £17,973 | 1.07 | 0.82 | | | | |
| | Ipilimumab | | 2.77 | 2.06 | | 1.70 | 1.24 | £44,835 |

## Scenario 3: Alternative utility estimates

### Table 8: Scenario 3: Alternative utility estimates, results of structural sensitivity analysis and scenario analysis, without PAS

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | | 2.77 | 2.06 | | 1.70 | 1.24 | |
| Time to death utilities | BSC | £11,747 | 1.07 | 0.81 | | | | |
| | Ipilimumab | | 2.77 | 2.14 | | 1.70 | 1.32 | |
| Beusterien et al UK Utilities | BSC | £11,747 | 1.07 | 0.68 | | | | |
| | Ipilimumab | | 2.77 | 1.65 | | 1.70 | 0.98 | |
| SF-6D Utilities | BSC | £11,747 | 1.07 | 0.66 | | | | |
| | Ipilimumab | | 2.77 | 1.65 | | 1.70 | 0.99 | |
| Drug Specific EORTC Utilities | BSC | £11,747 | 1.07 | 0.78 | | | | |
| | Ipilimumab | | 2.77 | 2.09 | | 1.70 | 1.31 | |
| EORTC Utilities with additional decrement for AEs and no AEs for BSC | BSC | £11,590 | 1.07 | 0.82 | | | | |
| | Ipilimumab | | 2.77 | 2.05 | | 1.70 | 1.23 | |
| EORTC Utilities unadjusted for age | BSC | £11,747 | 1.07 | 0.83 | | | | |
| | Ipilimumab | | 2.77 | 2.14 | | 1.70 | 1.31 | |

### Table 9: Scenario 3: Alternative utility estimates, results of structural sensitivity analysis and scenario analysis, with PAS

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | | 2.77 | 2.06 | | 1.70 | 1.24 | £49,844 |
| Time to death utilities | BSC | £11,747 | 1.07 | 0.81 | | | | |
| | Ipilimumab | | 2.77 | 2.14 | | 1.70 | 1.32 | £46,845 |
| Beusterien et al UK Utilities | BSC | £11,747 | 1.07 | 0.68 | | | | |
| | Ipilimumab | | 2.77 | 1.65 | | 1.70 | 0.98 | £63,317 |
| SF-6D Utilities | BSC | £11,747 | 1.07 | 0.66 | | | | |
| | Ipilimumab | | 2.77 | 1.65 | | 1.70 | 0.99 | £62,436 |
| Drug Specific EORTC Utilities | BSC | £11,747 | 1.07 | 0.78 | | | | |
| | Ipilimumab | | 2.77 | 2.09 | | 1.70 | 1.31 | £47,316 |
| EORTC Utilities with additional decrement for AEs and no AEs for BSC | BSC | £11,590 | 1.07 | 0.82 | | | | |
| | Ipilimumab | | 2.77 | 2.05 | | 1.70 | 1.23 | £50,474 |
| EORTC Utilities unadjusted for age | BSC | £11,747 | 1.07 | 0.83 | | | | |
| | Ipilimumab | | 2.77 | 2.14 | | 1.70 | 1.31 | £47,287 |

## Scenario 4: Maximum dosing assumption

### Table 10: Scenario 4: Maximum dosing assumption, results of structural sensitivity analysis and scenario analysis, without PAS

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| Patients Receive all 4 Doses of Ipilimumab | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| 50% more patients receive each reinduction | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| 50% less patients receive each reinduction | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |

### Table 11: Scenario 4: Maximum dosing assumption, results of structural sensitivity analysis and scenario analysis, with PAS

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £49,844 |
| Patients Receive all 4 Doses of Ipilimumab | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £54,131 |
| 50% more patients receive each reinduction | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £51,845 |
| 50% less patients receive each reinduction | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £47,843 |

## Scenario 5: Alternative curve fits

**Table 12: Scenario 5: Alternative curve fits, results of structural sensitivity analysis and scenario analysis, without PAS**

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| One Curve Fit Both Arms – Best AIC | BSC | £11,023 | 0.92 | 0.71 | | | | |
| | Ipilimumab | [redacted] | 1.66 | 1.26 | [redacted] | 0.74 | 0.55 | [redacted] |
| One Curve Fit Both Arms – Weibull | BSC | £10,840 | 0.89 | 0.69 | | | | |
| | Ipilimumab | [redacted] | 1.40 | 1.08 | [redacted] | 0.51 | 0.39 | [redacted] |
| One Curve Fit BSC Arm – Best AIC | BSC | £11,023 | 0.92 | 0.71 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.85 | 1.35 | [redacted] |
| One Curve Fit BSC Arm – Weibull | BSC | £10,840 | 0.89 | 0.69 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.88 | 1.37 | [redacted] |
| Two Part Curve Fit – Best AIC without Melanoma Mortality (assumes cure after 5 years) | BSC | £12,157 | 1.17 | 0.88 | | | | |
| | Ipilimumab | [redacted] | 3.34 | 2.45 | [redacted] | 2.18 | 1.57 | [redacted] |
| Two Part Curve Fit – Mortality Hazard one between arms | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.61 | 1.95 | [redacted] | 1.54 | 1.13 | [redacted] |
| Two Part Curve Fit – Mortality Hazard 0.5 between arms | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.98 | 2.20 | [redacted] | 1.91 | 1.38 | [redacted] |

**Table 13: Scenario 5: Alternative curve fits, results of structural sensitivity analysis and scenario analysis, with PAS**

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £49,844 |
| One Curve Fit Both Arms – Best AIC | BSC | £11,023 | 0.92 | 0.71 | [redacted] | | | |
| | Ipilimumab | [redacted] | 1.66 | 1.26 | [redacted] | 0.74 | 0.55 | £101,955 |
| One Curve Fit Both Arms – Weibull | BSC | £10,840 | 0.89 | 0.69 | [redacted] | | | |
| | Ipilimumab | [redacted] | 1.40 | 1.08 | [redacted] | 0.51 | 0.39 | £142,704 |
| One Curve Fit BSC Arm – Best AIC | BSC | £11,023 | 0.92 | 0.71 | [redacted] | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.85 | 1.35 | £46,394 |
| One Curve Fit BSC Arm – Weibull | BSC | £10,840 | 0.89 | 0.69 | [redacted] | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.88 | 1.37 | £45,843 |
| Two Part Curve Fit – Best AIC without Melanoma Mortality (assumes cure after 5 years) | BSC | £12,157 | 1.17 | 0.88 | [redacted] | | | |
| | Ipilimumab | [redacted] | 3.34 | 2.45 | [redacted] | 2.18 | 1.57 | £40,861 |
| Two Part Curve Fit – Mortality Hazard one between arms | BSC | £11,747 | 1.07 | 0.82 | [redacted] | | | |
| | Ipilimumab | [redacted] | 2.61 | 1.95 | [redacted] | 1.54 | 1.13 | £54,003 |
| Two Part Curve Fit – Mortality Hazard 0.5 between arms | BSC | £11,747 | 1.07 | 0.82 | [redacted] | | | |
| | Ipilimumab | [redacted] | 2.98 | 2.20 | [redacted] | 1.91 | 1.38 | £45,435 |

## Scenario 6: Use of alternative data for ipilimumab

**Table 14: Scenario 6: Use of alternative data for ipilimumab, without PAS**

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| Data for Ipilimumab only arm | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 3.24 | 2.44 | [redacted] | 2.17 | 1.62 | [redacted] |
| Data for Ipilimumab + GP100 arm | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.31 | 1.73 | [redacted] | 1.24 | 0.91 | [redacted] |

### Table 15: Scenario 6: Use of alternative data for ipilimumab, with PAS

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £49,844 |
| Data for Ipilimumab only arm | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 3.24 | 2.44 | [redacted] | 2.17 | 1.62 | £43,162 |
| Data for Ipilimumab + GP100 arm | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.31 | 1.73 | [redacted] | 1.24 | 0.91 | £65,091 |

## Scenario 7: Use of alternative time horizons

### Table 16: Scenario 7: Use of alternative time horizons, without PAS

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case – 40 years | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| Lifetime for all patients | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| 15 years | BSC | £11,523 | 1.03 | 0.79 | | | | |
| | Ipilimumab | [redacted] | 2.33 | 1.76 | [redacted] | 1.30 | 0.97 | [redacted] |
| 20 years | BSC | £11,639 | 1.05 | 0.80 | | | | |
| | Ipilimumab | [redacted] | 2.54 | 1.91 | [redacted] | 1.49 | 1.10 | [redacted] |
| 25 years | BSC | £11,701 | 1.06 | 0.81 | | | | |
| | Ipilimumab | [redacted] | 2.67 | 1.99 | [redacted] | 1.61 | 1.18 | [redacted] |
| 30 years | BSC | £11,731 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.73 | 2.04 | [redacted] | 1.67 | 1.22 | [redacted] |

### Table 17: Scenario 7: Use of alternative time horizons, with PAS

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case – 40 years | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £49,844 |
| Lifetime for all patients | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £49,815 |
| 15 years | BSC | £11,523 | 1.03 | 0.79 | | | | |
| | Ipilimumab | [redacted] | 2.33 | 1.76 | [redacted] | 1.30 | 0.97 | £61,592 |
| 20 years | BSC | £11,639 | 1.05 | 0.80 | | | | |
| | Ipilimumab | [redacted] | 2.54 | 1.91 | [redacted] | 1.49 | 1.10 | £55,106 |
| 25 years | BSC | £11,701 | 1.06 | 0.81 | | | | |
| | Ipilimumab | [redacted] | 2.67 | 1.99 | [redacted] | 1.61 | 1.18 | £52,026 |
| 30 years | BSC | £11,731 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.73 | 2.04 | [redacted] | 1.67 | 1.22 | £50,591 |

### Scenario 8: Use of alternative weight data

**Table 18: Scenario 8: Use of alternative weight data, without PAS**

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| UK Patients from MDX010-20 trial only | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |
| Compassionate use programme patients only | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | [redacted] |

**Table 19: Scenario 8: Use of alternative weight data, with PAS**

| Scenario | Technologies | Total | | | Incremental | | | ICER (£) |
|---|---|---|---|---|---|---|---|---|
| | | Costs (£) | LYG | QALYs | Costs (£) | LYG | QALYs | |
| Base Case | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £49,844 |
| UK Patients from MDX010-20 trial only | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £51,584 |
| Compassionate use programme patients only | BSC | £11,747 | 1.07 | 0.82 | | | | |
| | Ipilimumab | [redacted] | 2.77 | 2.06 | [redacted] | 1.70 | 1.24 | £49,487 |

3.12 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

3.13 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 20: Results showing the impact of patient access scheme on ICERs**

| | BSC | |
|---|---|---|
| | **Without PAS** | **With PAS** |
| Base Case | [redacted] | £49,844 |
| Scenario 1 - Undiscounted | [redacted] | £36,887 |
| Scenario 2 - Collinson | [redacted] | £43,926 |
| Scenario 2 - IMS | [redacted] | £48,455 |
| Scenario 2 - MELODY | [redacted] | £48,819 |
| Scenario 2 – Oxford Outcomes | [redacted] | £47,049 |
| Scenario 2 - Paclitaxel | [redacted] | £40,451 |
| Scenario 2 – Paclitaxel + Carboplatin | [redacted] | £30,475 |
| Scenario 2 – Carboplatin | [redacted] | £44,835 |
| Scenario 3 - Beuerstein | [redacted] | £63,317 |
| Scenario 3 – SF6D | [redacted] | £62,436 |
| Scenario 3 – drug specific | [redacted] | £47,316 |
| Scenario 3 - with additional decrement for AEs and no AEs for BSC | [redacted] | £50,474 |
| Scenario 3 – unadjusted for age | [redacted] | £47,287 |
| Scenario 4 – all 4 doses | [redacted] | £54,131 |
| Scenario 4 – +50% reinduction | [redacted] | £51,845 |
| Scenario 4 – -50% reinduction | [redacted] | £47,843 |
| Scenario 5 - One Curve Fit Both Arms – Best AIC | [redacted] | £101,955 |
| Scenario 5 - One Curve Fit Both Arms – Weibull | [redacted] | £142,704 |
| Scenario 5 - One Curve Fit BSC Arm – Best AIC | [redacted] | £46,394 |
| Scenario 5 - One Curve Fit BSC Arm – Weibull | [redacted] | £45,843 |
| Scenario 5 - Two Part Curve Fit – Best AIC without Melanoma Mortality (assumes cure after 5 years) | [redacted] | £40,861 |
| Scenario 5 - Two Part Curve Fit –Mortality Hazard one between arms | [redacted] | £54,003 |

| | | |
|---|---|---|
| Scenario 5 - Two Part Curve Fit – Mortality Hazard 0.5 between arms | [redacted] | £45,435 |
| Scenario 6 – Ipi Only | [redacted] | £43,162 |
| Scenario 6 – Ipi + GP100 | [redacted] | £65,091 |
| Scenario 7 – lifetime for all | [redacted] | £49,815 |
| Scenario 7 – 15 years | [redacted] | £61,592 |
| Scenario 7 – 20 years | [redacted] | £55,106 |
| Scenario 7 – 25 years | [redacted] | £52,026 |
| Scenario 7 – 30 years | [redacted] | £50,591 |
| Scenario 8 - MDX010-20 trial only | [redacted] | £51,584 |
| Scenario 8 - Compassionate use programme patients only | [redacted] | £49,487 |

PAS: patient access scheme.

# 4 Appendices

## *4.1 Appendix A: Additional documents*

4.1.1 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.

Response