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.

Name of the technology:*	Mepact / Mifamurtide / Liposomal muramyl tripeptide phosphatidyl-ethanolamine (L-MTP-PE)
Disease area for which the proposed patient access scheme applies:	MEPACT is indicated in children, adolescents and young adults for the treatment of high-grade resectable non-metastatic osteosarcoma after macroscopically complete surgical resection. It is used in combination with post-operative multi-agent chemotherapy. Safety and efficacy have been assessed in studies of patients 2 to 30 years of age at initial diagnosis.
*Please give all names that apply and include all trading names.	

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

Affordability is a key issue for the NHS and particularly within a budget constrained environment. Takeda UK has developed a Patient Access Scheme to make Mepact®, an ultra-orphan medicine more affordable to the NHS.
*Please keep this as concise as possible.

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

The proposed Patient Access Scheme is finance-based whereby an NHS Trust will be eligible for procurement of Mepact at [redacted] discount relative to the basic NHS list price.
*Please keep this as concise as possible.

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 proposed patient access scheme applies to the total population to which Mepact is licensed i.e. MEPACT is indicated in children, adolescents and young adults for the treatment of high-grade resectable non-metastatic osteosarcoma after macroscopically complete surgical resection. It is used in combination with post-operative multi-agent chemotherapy. Safety and efficacy have been assessed in studies of patients 2 to 30 years of age at initial diagnosis. There are no additional criteria for patient eligibility into the proposed patient access scheme.
*Please keep this as concise as possible.

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 patient access scheme applies to the total population to which Mepact is licensed i.e. MEPACT is indicated in children, adolescents and young adults for the treatment of high-grade resectable non-metastatic osteosarcoma after macroscopically complete surgical resection. It is used in combination with post-operative multi-agent chemotherapy. Safety and efficacy have been assessed in studies of patients 2 to 30 years of age at initial diagnosis. There are no additional criteria for patient eligibility into the proposed patient access scheme and will apply for the duration of the patient's treatment with Mepact.

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

The proposed patient access scheme applies to the total population to which Mepact is licensed i.e. MEPACT is indicated in children, adolescents and young adults for the treatment of high-grade resectable non-metastatic osteosarcoma after macroscopically complete surgical resection. It is used in combination with post-operative multi-agent chemotherapy. Safety and efficacy have been assessed in studies of patients 2 to 30 years of age at initial diagnosis. There are no additional criteria for patient eligibility into the proposed patient access scheme.

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

The proposed Patient Access Scheme is finance-based whereby an NHS Trust will be eligible for procurement of Mepact at [redacted] discount relative to the basic NHS list price. The discount will be applied to the original invoice sent to NHS Trusts from our distributer, Unidrug Distribution Group Ltd, Amber Park, Berristow Lane, South Normanton, Derbyshire.
*Please keep this as concise as possible.

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.

Takeda UK confirms no other documentation or administrative process is required to claim the discount via the patient access scheme. The discount will be applied to the original invoice sent to NHS Trusts from our distributer, Unidrug Distribution Group Ltd, Amber Park, Berristow Lane, South Normanton, Derbyshire.

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

The proposed Patient Access Scheme is finance-based whereby an NHS Trust will be eligible for procurement of Mepact at [redacted] discount relative to the basic NHS list price. The discount will be applied to the original invoice sent to NHS Trusts from our distributer, Unidrug Distribution Group Ltd, Amber Park, Berristow Lane, South Normanton, Derbyshire.
*Please keep this as concise as possible.

3.10 Please provide details of the duration of the scheme.

Takeda UK in consultation with the Department of Health may review the scheme offered to the NHS whilst the current NICE review is on-going. If the current patient access scheme is accepted, Takeda UK propose that this patient access scheme will be in place for 3 years in line with the NICE STA review timeframe after which the evidence and the scheme may be re-reviewed and reconsidered by Takeda UK in consultation with NICE & the Department of Health.
*Please keep this as concise as possible.

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?

Takeda UK does not consider there are any equity or equality issues relating to the Mepact Patient Access Scheme.
*Please keep this as concise as possible

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.

Takeda UK confirms no other documentation or administrative process is required to claim the discount via the patient access scheme. The discount will be applied to the original invoice sent to NHS Trusts from our distributer, Unidrug Distribution Group Ltd, Amber Park, Berristow Lane, South Normanton, Derbyshire.

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

4 Cost effectiveness

4.1 If the population to whom the scheme applies (as described in sections 3.4 and 3.5) has not been presented in the main manufacturer/sponsor submission of evidence for the technology appraisal (for example, the population is different as there has been a change in clinical outcomes or a new continuation rule), please (re-)submit the relevant sections from the 'Specification for manufacturer/sponsor submission of evidence' (particularly sections 5.5, 6.7 and 6.9). You should complete those sections both with and without the patient access scheme. You must also complete the rest of this template.

Not Applicable. The population of patients is the same as the original manufacturer submission.

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.

Takeda UK confirms that the model has been updated to reflect the assumptions that the NICE Appraisal Committee considered to be most plausible, as follows:

- *Clinical data as per the pooled datasets of A/B versus A+/B+*
- *60 year time horizon.*
- *100% of the population starting in the Disease-free health state.*
- *Amputation and limb salvage costs included (changed as per ACD).*
- *Hearing loss adverse event not included (not changed as per ACD);*
- *Mortality risk reverting to general population after a given time period (changed as per ACD);*
- *Age related utility weights included (changed as per ACD);*
- *Discounting rates of 3.5% for both costs and outcomes applied;*

4.3 Please provide details of how the patient access scheme has been incorporated into the economic model. If applicable, please also provide details of any changes made to the model to reflect the assumptions that the Appraisal Committee considered most plausible.

The proposed Patient Access Scheme is finance-based whereby an NHS Trust will be eligible for procurement of Mepact at [redacted] discount relative to the basic NHS list price.

The PAS functionality in the model works on providing free vials and is not modifiable, hence this functionality has been turned off and the vial price has been directly modified to reflect a [redacted] discount on the basic NHS list price.

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

Not applicable. The patient access scheme is finance based and not outcome based. The primary source of data used in the economic model comes from the INT-0133 trial and results are as per the Takeda UK submission of evidence 8th February 2010.

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'

Table 1 Costs associated with the implementation and operation of the patient access scheme (PAS)

	Calculation of cost	Reference source
Stock management	N/A	
Administration of claim forms	N/A	
Staff training	N/A	
Other costs…	N/A	
…		
…		
Total implementation/ operation costs	N/A	

The proposed Patient Access Scheme is finance-based whereby an NHS Trust will be eligible for procurement of Mepact at [redacted] discount relative to the basic NHS list price.

Takeda UK confirms no other documentation or administrative process is required to claim the discount via the patient access scheme.

The discount will be applied to the original invoice sent to NHS Trusts from our distributer, Unidrug Distribution Group Ltd, Amber Park, Berristow Lane, South Normanton, Derbyshire.

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.

Table 2 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	N/A				
Monitoring tests	N/A				
Diagnostic tests	N/A				
Appointments	N/A				
Other costs…	N/A				
…					
…					
Total treatment-related costs	N/A				

Summary results

Base-case analysis

4.7 Please present in separate tables the cost-effectiveness results as follows.[1]

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

A suggested format is shown below (table 3).

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

Table 3: Base case using Appraisal Committee preferred parameters (without PAS)

	Mifamurtide + standard 3-4 agent maintenance therapy (A+/B+)	Standard 3-4 agent maintenance therapy alone (A/B)
Total costs £	167,626	72,095
Difference in total costs £	£95,530	
QALYs	16.49	15.36
QALYs difference	1.13	
Incremental cost per QALY gained £ - deterministic**	**£84,364**	
Incremental cost per QALY gained £ - probabilistic**	**£79,934**	

*Drug costs are adjusted to take account of actual doses administered from INT-0133 (mean of 38.4).
** Results are generated from the model so there are some rounding adjustments in the table.

Table 4: Base case using Appraisal Committee preferred parameters (with PAS)

	Mifamurtide + standard 3-4 agent maintenance therapy (A+/B+)	Standard 3-4 agent maintenance therapy alone (A/B)
Total costs £	140,269	72,095
Difference in total costs £	£68,174	
QALYs	16.49	15.36
QALYs difference	1.13	
Incremental cost per QALY gained £ - deterministic**	**£60,205**	
Incremental cost per QALY gained £ - probabilistic**	**£56,677**	

*Drug costs are adjusted to take account of actual doses administered from INT-0133 (mean of 38.4).
** Results are generated from the model so there are some rounding adjustments in the table.

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

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

List the interventions and comparator(s) from least to most expensive. Present the incremental cost-effectiveness ratios (ICERs) in comparison with baseline (usually standard care), and the incremental analysis ranking technologies in terms of dominance and extended dominance. A suggested format is presented in table 4.

All relevant information as requested for question 4.8 is presented in the response to question 4.7. Osteosarcoma is a rare condition and mifamurtide was granted orphan status by the EMA, hence treatment comparators are limited.

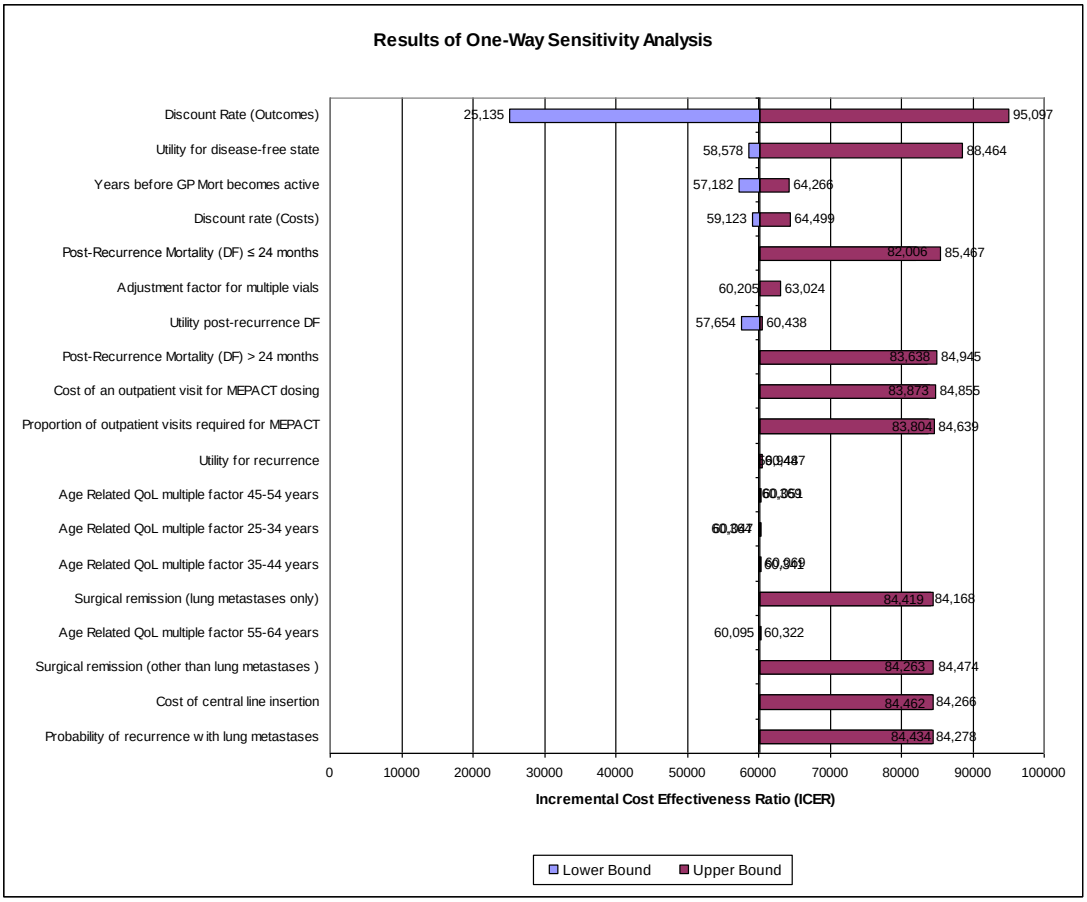
Sensitivity analyses

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.

One way sensitivity analyses are presented below in Figure 4.9. These results include the new proposed PAS.

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

Figure 4.9: One Way Sensitivity Results



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

The results of the probabilistic sensitivity analysis are shown in Figure 4.10 and Figure 4.101. Both analyses have assumed a willingness to pay (WTP) threshold of £50,000 and also reflect the affect of having the treatment cost primarily in the early years (mainly year 1) by the flatness of the cost-effectiveness scatter plot.

The summary cost per QALY derived from the PSA is £56,677.

Figure 4.10: PSA Cost-effectiveness Plot

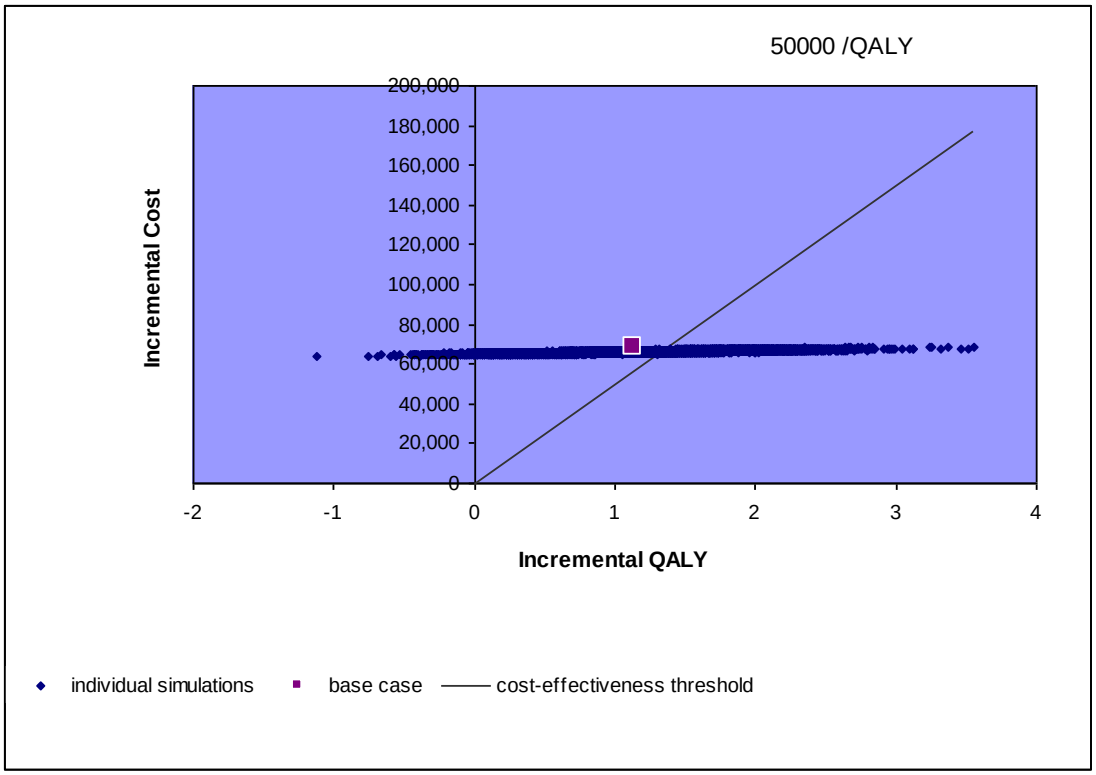
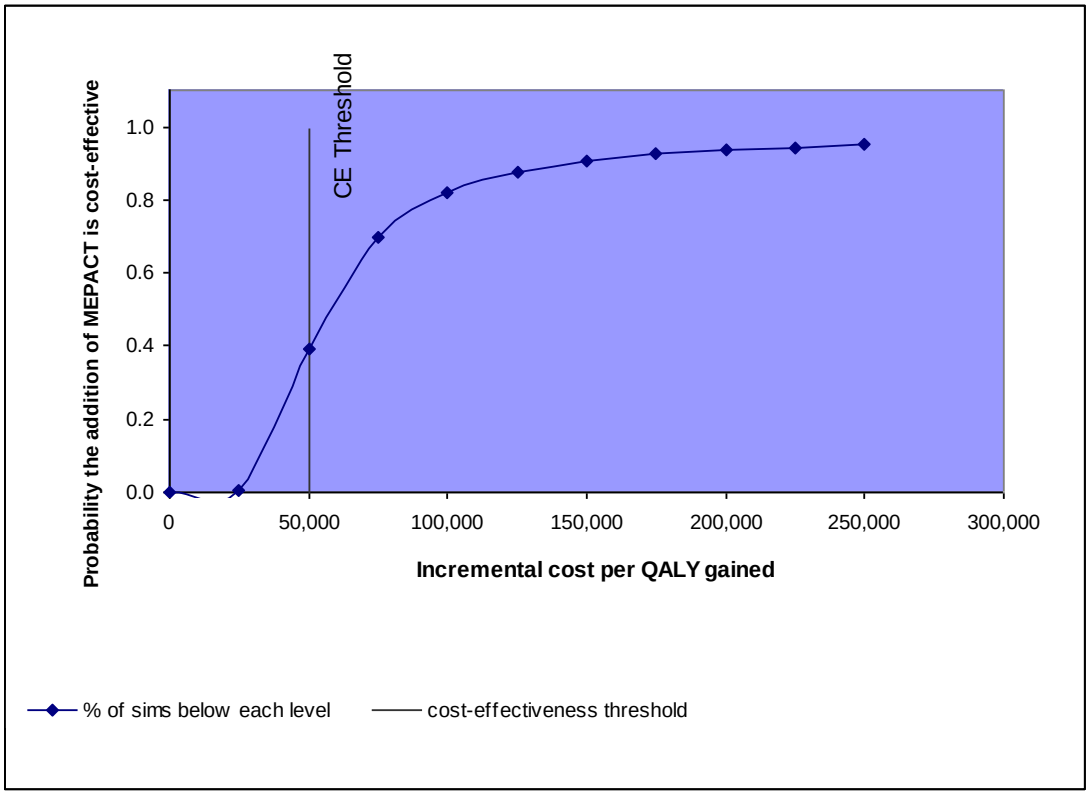


Figure 4.101: Cost Effectiveness Acceptability Curve



The result of the cost effectiveness acceptability curve shows that the probability of mifamurtide being a cost effective use of NHS resources at a willingness to pay of £50,000 is approximately 40%.

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

Not applicable. The most appropriate scenario for consideration has already been defined by the appraisal committee.

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.

All relevant information as requested for question 4.13 is presented in the response to question 4.7. Osteosarcoma is a rare condition and mifamurtide was granted orphan status by the EMA, hence treatment comparators are limited.

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.

Not Applicable.

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.

Not Applicable.

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.

Not Applicable.

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.

Not Applicable.

5.2.4 For outcome-based schemes, as defined in the PPRS, please provide the full details of the new information (evidence) planned to be collected, who will collect it and who will carry the cost associated with this planned data collection. Details of the new information (evidence) may include:

- design of the new study
- patient population of the new study
- outcomes of the new study
- expected duration of data collection
- planned statistical analysis, definition of study groups and reporting (including uncertainty)
- expected results of the new study
- planned evidence synthesis/pooling of data (if applicable)
- expected results of the evidence synthesis/pooling of data (if applicable).

Not Applicable.

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

Not Applicable.

5.2.6 Please provide the clinical effectiveness data resulting from the evidence synthesis and used in the economic modelling of the patient access scheme at the different time points when the additional evidence is to be considered.

Not Applicable.

5.2.7 Please provide the other data used in the economic modelling of the patient access scheme at the different time points when the additional evidence is to be considered. These data could include cost/resource use, health-related quality of life and utilities.

Not Applicable.

5.2.8 Please present the cost-effectiveness results as follows.

- For proven value: price increase schemes, please summarise in separate tables:
  - the results based on current evidence and current price
  - the anticipated results based on the expected new evidence and the proposed higher price.
- For expected value: rebate schemes, please summarise in separate tables:
  - the results based on the expected new evidence and the current price (which will be supported by the additional evidence collection)
  - the results based on the current evidence and the lower price (if the new evidence is not forthcoming).
- For risk-sharing schemes, please summarise in separate tables:
  - the results based on current evidence and current price
  - the results based on the expected new evidence and the current price (which will be supported by the additional evidence collection)
  - the results based on the current evidence and the lower price (if the new evidence is not forthcoming)
  - the anticipated results based on the expected new evidence and the proposed higher price.

A suggested format is shown in table 3, section 4.7.

5.2.9 Please present in separate tables the incremental results for the different scenarios as described above in section 5.2.8 for the type of outcome-based scheme being submitted.

List the interventions and comparator(s) from least to most expensive. Present the incremental cost-effectiveness ratios (ICERs) in comparison with baseline (usually standard care), and the incremental analysis ranking technologies in terms of dominance and extended dominance. A suggested format is presented in table 4, section 4.8.