The Department of Health has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using cobimetinib in combination with vemurafenib in the NHS in England. The appraisal committee has considered the evidence submitted by the company and the views of non-company consultees and commentators, clinical experts and patient experts.

This document has been prepared for consultation with the consultees. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the consultees and commentators for this appraisal and the public. This document should be read along with the evidence (see the committee papers).

The appraisal committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?
Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The appraisal committee will meet again to consider the evidence, this appraisal consultation document and comments from the consultees.
- At that meeting, the committee will also consider comments made by people who are not consultees.
- After considering these comments, the committee will prepare the final appraisal determination (FAD).
- Subject to any appeal by consultees, the FAD may be used as the basis for NICE’s guidance on using cobimetinib in combination with vemurafenib in the NHS in England.

For further details, see NICE’s guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 7 July 2016

Second appraisal committee meeting: 19 July 2016

Details of membership of the appraisal committee are given in section 6.
1 Recommendations

1.1 Cobimetinib in combination with vemurafenib is not recommended within its marketing authorisation for treating unresectable or metastatic melanoma in adults with a BRAF V600 mutation.

1.2 This guidance is not intended to affect the position of patients whose treatment with cobimetinib in combination with vemurafenib was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.

2 The technology

| Description of the technology | Cobimetinib (Cotellic, Roche) is an inhibitor of MEK 1 and MEK 2 kinases. Vemurafenib (Zelboraf, Roche) is an inhibitor of the BRAF protein. Both are taken as tablets. The BRAF protein and MEK 1 and 2 kinases are part of the same cell signalling pathway. Inhibiting these proteins stops proliferation and survival of melanoma cells. |
| Marketing authorisation | Cobimetinib in combination with vemurafenib is indicated for the treatment of unresectable or metastatic melanoma in adults with a BRAF V600 mutation. Vemurafenib has a marketing authorisation for use as monotherapy for this indication. Cobimetinib does not have a marketing authorisation for use as monotherapy. |
| Adverse reactions | The following common side effects affect more than 1 in 5 people: diarrhoea, rash, nausea, vomiting, fever, light sensitivity reaction, abnormal liver function tests and abnormal results for an enzyme related to muscle breakdown (creatine phosphokinase). Less common side effects include swelling of the retina (retinopathy) or effects on cardiac function (reduced left ventricular ejection fraction). It is advised that people taking cobimetinib plus vemurafenib are monitored for new and worsening visual disturbances, and for heart function. For full details of adverse reactions and contraindications, see the summary of product characteristics. |
### Recommended dose and schedule

- **Cobimetinib:** 3 tablets per day for 21 days followed by a 7-day break (days 22 to 28) before the next cycle is started.
- **Vemurafenib:** 960 mg (4 tablets of 240 mg) twice daily (equivalent to a total daily dose of 1,920 mg).

### Price

The company has stated that the cost of cobimetinib (excluding VAT) is £4,275.67 for a 63-tablet pack of 20 mg tablets.

The company has agreed a patient access scheme with the Department of Health for vemurafenib as monotherapy. It is provided to the NHS with a simple discount to the list price of vemurafenib, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme would not constitute an excessive administrative burden on the NHS.

If cobimetinib with vemurafenib had been recommended, the company would have provided vemurafenib for use in combination with cobimetinib with the same discount as that agreed for vemurafenib as monotherapy. Costs may vary in different settings because of negotiated procurement discounts.

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### 3 Evidence

The appraisal committee (section 6) considered evidence submitted by the company and a review of this submission by the evidence review group (ERG). See the [committee papers](#) for full details of the evidence.

### 4 Committee discussion

The appraisal committee reviewed the data available on the clinical and cost effectiveness of cobimetinib in combination with vemurafenib, having considered evidence on the nature of advanced (unresectable or metastatic) B RAF V600 mutation-positive melanoma and the value placed on the benefits of cobimetinib plus vemurafenib by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.
Clinical management of advanced melanoma

4.1 The committee discussed the clinical need of people with advanced BRAF V600 mutation-positive melanoma. It heard from the patient expert that the symptoms of advanced melanoma vary, partly depending on the sites of metastases, but they can be severe and wide ranging. Symptoms such as pain can have a major impact on quality of life. The patient expert explained that having a choice of effective treatments to switch to if there are side effects is of great value to patients. However, prolonging survival is of such importance to patients that many would be willing to accept considerable side effects if their chance of survival is improved. The committee concluded that the symptoms and impact on quality of life vary between patients with advanced melanoma, and that patients welcome having a choice of life-extending treatment options available to them.

4.2 The committee noted that people with BRAF V600 mutation-positive advanced melanoma could have an immunotherapy agent (ipilimumab, pembrolizumab or nivolumab) or a targeted BRAF inhibitor (vemurafenib or dabrafenib). The clinical expert stated that approximately 70% of patients with BRAF V600 mutation-positive disease have immunotherapy first line because of the long-term benefit that has been demonstrated in trials. BRAF inhibitors would usually be used first line only for people with rapidly progressing disease, high disease burden or elevated LDH (lactate dehydrogenase) levels, when a rapid onset of action is needed. BRAF inhibitors are considered to be equally effective whether given before or after immunotherapy. The committee concluded that most people with a BRAF V600 mutation-positive melanoma would receive a targeted therapy at some point in their treatment.
Comparators

4.3 The clinical expert stated that the 2 comparators listed in the scope, vemurafenib and dabrafenib, are considered to have similar clinical effectiveness but some people will experience side effects with either drug. The clinical expert noted that photosensitivity and rashes are more common with vemurafenib than dabrafenib, so dabrafenib tends to be prescribed more often. Because it is not possible to predict who will have side effects with either drug before starting treatment, it is valuable to have 2 BRAF inhibitors available for patients. The committee noted that NICE recently recommended another combination treatment (trametinib, a MEK inhibitor, in combination with dabrafenib) which has a similar mechanism of action to cobimetinib plus vemurafenib. However, it noted that the final guidance had not yet been issued and this treatment combination could not be considered established practice. The clinical expert stated that if the NHS routinely funded a combination of a BRAF inhibitor plus a MEK inhibitor this would be preferred over BRAF inhibitor monotherapy, because of the longer survival demonstrated in trials. The committee recognised that the treatment options for melanoma are likely to increase in the near future but concluded that, at present, the comparators in the scope issued by NICE were appropriate for its decision-making.

Clinical effectiveness

Evidence from the coBRIM trial

4.4 The committee discussed the generalisability of the clinical evidence from the coBRIM trial that compared cobimetinib plus vemurafenib with vemurafenib plus placebo. It noted that most patients in coBRIM had not previously had an immunotherapy agent, and in this regard the population in coBRIM was different to the population who would have cobimetinib plus vemurafenib in clinical practice in England. However, the committee took into account the comments from the clinical expert that the clinical
effectiveness of cobimetinib plus vemurafenib is not expected to differ if it is taken before or after an immunotherapy agent. It was therefore satisfied that the clinical-effectiveness evidence from coBRIM is generalisable to melanoma that has or has not been treated with immunotherapy.

4.5 The committee examined the results of coBRIM. It noted that, at the time of the latest data cut-off in the company’s submission, the combination of cobimetinib plus vemurafenib increased overall survival by 4.9 months compared with vemurafenib alone (median survival 22.3 months and 17.4 months respectively). The committee concluded that cobimetinib plus vemurafenib is clinically effective compared with vemurafenib alone.

Company’s network meta-analyses

4.6 The committee considered the company’s indirect comparison of cobimetinib plus vemurafenib with dabrafenib alone, noting that there were no direct head-to-head clinical trials comparing cobimetinib plus vemurafenib with dabrafenib. It agreed with the evidence review group (ERG) that the rationale and methods for the indirect comparison were appropriate, but the potential heterogeneity of the trials in the network had not been fully explored in the company’s submission. The committee noted that the trials comparing dabrafenib with dacarbazine (BREAK-3) and vemurafenib with dacarbazine (BRIM-3), which were included in the meta-analysis, included similar populations to coBRIM but there were differences in the trial designs. For example, BREAK-3 and BRIM-3 allowed crossover from the dacarbazine arm to the dabrafenib or vemurafenib arm, but coBRIM did not allow crossover between treatment arms. The committee noted, and the company confirmed, that crossover had not been adjusted for in the network meta-analysis. The committee agreed with the ERG that the clinical effectiveness of dabrafenib and vemurafenib as monotherapies may have been underestimated in the network. The committee also noted that there was only 1 trial for each comparator in the network, which increased its uncertainty in the results. It
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concluded that taking into account the unexplored potential heterogeneity between the trials, and the limited number of trials in the network, the indirect comparison of cobimetinib plus vemurafenib with dabrafenib was associated with considerable uncertainty.

4.7 Given the uncertainty surrounding the indirect comparison, the committee discussed whether it would be more appropriate to assume that the results of coBRIM are generalisable to a comparison with dabrafenib monotherapy. The committee was inclined towards this approach because it had heard that vemurafenib and dabrafenib monotherapies are considered to be of similar clinical effectiveness (see section 4.3) and because there was less uncertainty surrounding the clinical trial results. The committee agreed that the most important comparison for its decision-making was the clinical and cost effectiveness of cobimetinib plus vemurafenib compared with a BRAF inhibitor taken as monotherapy, and that vemurafenib and dabrafenib may be interchangeable in this regard. The committee concluded that the most robust comparative data were from the coBRIM trial of cobimetinib plus vemurafenib compared with vemurafenib alone. These data should therefore be used for its decision-making.

Cost effectiveness

The company’s model

4.8 The committee noted that the 3-state partitioned model used by the company was similar to the structure of models used in previous appraisals of technologies for treating melanoma, and met the NICE reference case. The committee also considered that the time horizon of 30 years was appropriate. The committee concluded that the model was in line with accepted NICE methods and appropriate for its decision-making.
Utility values

4.9 The company used 2 approaches to convert EQ-5D-5L data from coBRIM into utility values for the progression free survival health state. The committee accepted the company’s rationale for choosing between these 2 approaches: that is, the company used the method that produced lower utility values, which were more plausible than the alternative approach which produced utility values above those for people without melanoma. The committee accepted that because the company had not been able to collect EQ-5D-5L data from many people after their melanoma had progressed the utility values derived from the trial may not reflect quality of life for people with progressed disease. The committee noted that the company’s preferred alternative came from a study (Beusterien et al. 2009) which did not meet the NICE reference case and reported quality of life would be much worse in the first 5 years of progressed disease (0.590) than if a person survived for more than 5 years with progressed disease (0.770). The committee considered that this may be plausible but noted that the difference between the 2 values was large. The committee was aware that several approaches to the calculation of utility values had been used in previous melanoma appraisals, without uniform agreement on the most appropriate method. The ERG’s alternative utility value for the progressed disease state (0.73) was the same as that used in NICE’s technology appraisal guidance on nivolumab for treating advanced (unresectable or metastatic) melanoma. The committee considered that there was uncertainty surrounding the most appropriate utility value, especially for people with progressed disease, because of data limitations. It noted that the patient expert had highlighted that there may be variation in the extent to which melanoma affects quality of life (see section 4.1). The committee concluded that there was uncertainty surrounding utility values and it was appropriate to take into account the impact of a range of utility values, provided by sensitivity analyses, in its decision-making.
Assumptions

4.10 The company used different model inputs when comparing cobimetinib plus vemurafenib with vemurafenib alone, than it did for cobimetinib plus vemurafenib compared with dabrafenib. The committee noted the following differences:

- Cobimetinib plus vemurafenib compared with vemurafenib alone
  - extrapolating progression-free survival and overall survival data from coBRIM data. The same extrapolation distribution was used for each treatment arm
  - extrapolating time on treatment from coBRIM data. Different extrapolation distributions were used to extrapolate the trial data over the long term for each treatment arm
  - estimating the drug dosages using data from coBRIM, in which people could have dose reductions.
- Cobimetinib plus vemurafenib compared with dabrafenib
  - extrapolating progression-free survival and overall survival data from coBRIM for cobimetinib plus vemurafenib, but from the network meta-analysis for dabrafenib monotherapy. The same extrapolation distribution was used for each treatment arm
  - assuming that time on treatment was the same as progression-free survival for cobimetinib plus vemurafenib and for dabrafenib. The same extrapolation distribution was used to extrapolate progression-free survival data for each treatment arm
  - estimating the drug dosages using data from coBRIM for cobimetinib plus vemurafenib, and using the licensed dose for dabrafenib (with no adjustments for drug dose reductions).

The company’s rationale for using different assumptions for each comparison was that they did not have access to the patient-level data needed to model time on treatment and dose modifications for dabrafenib. The committee accepted this but noted that the costs for dabrafenib may
have been overestimated, because the company did not account for dose modifications of dabrafenib. The committee considered that using progression-free survival as a proxy measure for time on treatment would overestimate time on treatment and consequently drug costs, because people may stop treatment before disease progression. The committee noted that the total costs for cobimetinib plus vemurafenib in the company’s base case were higher using assumptions from the comparison of cobimetinib plus vemurafenib against dabrafenib, than using those for the comparison with vemurafenib. This appeared to be due to using progression-free survival as a surrogate for time on treatment in the comparison with dabrafenib. The committee concluded that the differences in modelling assumptions had a substantial impact on costs, but only a marginal impact on the quality-adjusted life year (QALY) estimates.

4.11 The committee noted that the ERG had presented results using the same assumptions for each modelled treatment arm and a different utility value for the progressed disease health state. The committee agreed with the ERG that where possible modelling assumptions should be consistent between treatment arms, however the committee noted that in order to do this the ERG had had to use data from the network meta-analysis and make further adjustments for potential dose modifications with dabrafenib. As such, the committee considered the ERG’s modelling was based on less robust data than the company’s comparison of cobimetinib plus vemurafenib with vemurafenib. The committee concluded that it preferred:

- using data for cobimetinib plus vemurafenib compared with vemurafenib alone to inform its decision-making, given the lack of patient-level data available for dabrafenib and the uncertainties in the network meta-analysis for the indirect comparison of cobimetinib plus vemurafenib with dabrafenib alone
• adjusting the drug costs for dose modifications using data on doses received in clinical trials
• using time on treatment observed in clinical trials to estimate duration of drug treatment in clinical practice
• considering sensitivity analyses to reflect the range of utility values that have been presented for other melanoma treatments appraised by NICE, and the potential variation in quality of life experienced by people with advanced melanoma in its decision making.

Estimates of cost-effectiveness

4.12 The cost-effectiveness estimates provided by the company and the ERG used the list prices for both drugs or used the patient access scheme prices for vemurafenib and dabrafenib. These produced incremental cost-effectiveness ratios (ICERs) that were over £100,000 per QALY gained. This is substantially above the range usually considered to be a cost-effective use of NHS resources. The company already provides vemurafenib to the NHS at a discounted price as part of a patient access scheme, but no patient access scheme for cobimetinib in combination with vemurafenib had been agreed with the Department of Health for the current appraisal.

End-of-life considerations

4.13 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE’s final Cancer Drugs Fund technology appraisal process and methods. The committee noted that the median survival of people having vemurafenib monotherapy in coBRIM was around 17 months. The committee noted that in its recent appraisal of trametinib plus dabrafenib it had agreed that life expectancy in people with advanced BRAF V600 mutation-positive melanoma was likely to be under 24 months. There was no evidence to suggest that life expectancy has changed since that decision because the recommendations from that appraisal have not yet become established practice. However, the
treatment pathway for advanced melanoma is changing as new treatments become available so life expectancy of this patient population is expected to improve. The committee accepted that results from coBRIM demonstrated that cobimetinib plus vemurafenib extended life by more than 3 months compared with vemurafenib monotherapy. The committee concluded that cobimetinib plus vemurafenib met the end of life criteria and that this should be taken into account in its decision making.

4.14 The committee noted that even taking into account end of life the cost effectiveness estimates for cobimetinib plus vemurafenib compared with vemurafenib were above the range considered to be a cost effective use of NHS resources. The committee considered the company’s statement that even if it provided cobimetinib free of charge, the ICER would remain above this range so there was no price at which it could offer cobimetinib that would allow it to be recommended. The committee noted that this assertion was made using the list prices for both products, but there was already a patient access scheme for vemurafenib. The company had itself presented a scenario showing that a price of zero for cobimetinib would not be required for the combination to result in an ICER within a similar range to previous melanoma appraisals, in which those technologies had been recommended. The committee was not convinced that there was no price for cobimetinib, taken in combination with vemurafenib, which had the potential to be considered a cost-effective combination. Cobimetinib is not licensed for use as a monotherapy and must be taken with vemurafenib. Therefore the committee stated that the combined drug costs for both cobimetinib and vemurafenib compared with BRAF inhibitor monotherapy were relevant for its cost-effectiveness analysis. The committee was disappointed that the company had not submitted a patient access scheme for cobimetinib in combination with vemurafenib, but accepted that this was a commercial decision for the company. It concluded that it could not recommend cobimetinib in combination with vemurafenib as a cost-effective use of NHS resources.
Pharmaceutical Price Regulation Scheme (PPRS) 2014

4.15 The committee was aware of NICE’s position statement on the Pharmaceutical Price Regulation Scheme (PPRS) 2014, and in particular the PPRS payment mechanism. It accepted the conclusion ‘that the 2014 PPRS payment mechanism should not, as a matter of course, be regarded as a relevant consideration in its assessment of the cost effectiveness of branded medicines’. The committee heard nothing to suggest that there is any basis for taking a different view about the relevance of the PPRS to this appraisal. It therefore concluded that the PPRS payment mechanism was not relevant in considering the cost effectiveness of the technology in this appraisal.

Summary of appraisal committee’s key conclusions

<table>
<thead>
<tr>
<th>TAXXX</th>
<th>Appraisal title:</th>
<th>Section</th>
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</thead>
<tbody>
<tr>
<td><strong>Key conclusion</strong></td>
<td>Cobimetinib in combination with vemurafenib is not recommended within its marketing authorisation for treating unresectable or metastatic melanoma in adults with a BRAF V600 mutation.</td>
<td>1.1, 4.12</td>
</tr>
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In all of the analyses presented to the appraisal committee the incremental cost effectiveness ratios were over £100,000 per QALY gained. This is substantially over the range usually considered a cost effective use of NHS resources

Current practice
Clinical need of patients, including the availability of alternative treatments | There are numerous treatment options available and more treatments that improve survival are either becoming available or are anticipated to be available to patients in the near future. Patients value life-extending treatment options but also value having various options available, because some people will experience side effects which means that they need to switch treatment. | 4.1 to 4.3

The technology

Proposed benefits of the technology | The combination of cobimetinib plus vemurafenib improves survival compared to a BRAF inhibitor (vemurafenib or dabrafenib) taken alone.
Cobimetinib plus vemurafenib is the second MEK inhibitor taken in combination with a BRAF inhibitor to be licensed for use in England. Trametinib plus dabrafenib has been licensed for the same patient population. | 4.5, 4.3, 4.7

How innovative is the technology in its potential to make a significant and substantial impact on health-related benefits?

What is the position of the treatment in the pathway of care for the condition? | For most people with BRAF V600 mutation-positive melanoma, the combination of cobimetinib plus vemurafenib will be taken after an immunotherapy agent and as an alternative treatment option to a BRAF inhibitor (vemurafenib or dabrafenib) | 4.2, 4.3
### Adverse reactions

The summary of product characteristics notes that people taking a combination of cobimetinib plus vemurafenib should be monitored for visual disturbances and cardiac function. Adverse reactions can be managed with dose reductions, treatment breaks or stopping treatment.

<table>
<thead>
<tr>
<th>Evidence for clinical effectiveness</th>
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<tbody>
<tr>
<td><strong>Availability, nature and quality of evidence</strong></td>
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</tbody>
</table>

| **Relevance to general clinical practice in the NHS** | Clinical evidence from coBRIM was generalisable to clinical practice in England. |

<p>| 2 |
| 4.4, 4.6, 4.7 |</p>
<table>
<thead>
<tr>
<th>Uncertainties generated by the evidence</th>
<th>The relative clinical effectiveness of cobimetinib plus vemurafenib compared with dabrafenib was uncertain because no trials had directly compared these treatment options. However, it was expected to be similar to the clinical effectiveness of cobimetinib plus vemurafenib compared with dabrafenib because the 2 BRAF inhibitors are thought to be similarly clinically effective.</th>
<th>4.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are there any clinically relevant subgroups for which there is evidence of differential effectiveness?</td>
<td>No.</td>
<td></td>
</tr>
<tr>
<td>Estimate of the size of the clinical effectiveness including strength of supporting evidence</td>
<td>Cobimetinib plus vemurafenib extends survival by an average (median) of 4.9 months compared with vemurafenib.</td>
<td>4.5</td>
</tr>
</tbody>
</table>

### Evidence for cost effectiveness

<p>| Availability and nature of evidence | The company used a model with a consistent structure to that used in previous melanoma technology appraisals. | 4.8 |</p>
<table>
<thead>
<tr>
<th>Uncertainties around and plausibility of assumptions and inputs in the economic model</th>
<th>The company used different assumptions when comparing cobimetinib plus vemurafenib with vemurafenib than when comparing cobimetinib plus vemurafenib with dabrafenib because of the availability [to the company] of some trial data for dabrafenib. The committee preferred the assumptions for cobimetinib plus vemurafenib compared with vemurafenib, and thought that the clinical data used to inform these assumptions in the modelling was robust.</th>
<th>4.10, 4.11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorporation of health-related quality-of-life benefits and utility values</td>
<td>Utility values for people whose disease had not progressed were derived from coBRIM trial data. There were less trial data available on the quality of life of people with progressed disease and the company and ERG presented different estimates for the utility of these people. The committee thought it was appropriate that a range of utility values should be considered in its decision-making because it had heard from the clinical expert that quality of life may vary from person to person with advanced melanoma.</td>
<td>4.9</td>
</tr>
</tbody>
</table>
Are there specific groups of people for whom the technology is particularly cost effective? | No.
---|---
What are the key drivers of cost effectiveness? | The cost of cobimetinib and vemurafenib and the cost of its comparators. The duration of treatment and associated drug costs.
Most likely cost-effectiveness estimate (given as an ICER) | Over £100,000 per QALY gained.

### Additional factors taken into account

| Patient access schemes (PPRS) | Vemurafenib and dabrafenib have patient access schemes agreed with the Department of Health. These are simple discounts to the list price for vemurafenib and dabrafenib. The level of these discounts are confidential. | 2 |
| End-of-life considerations | Cobimetinib plus vemurafenib met end-of-life criteria and the committee took this into account in its decision-making. | 4.13 |
| Equalities considerations and social value judgements | No equality issues were raised. | |
5 Proposed date for review of guidance

5.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Jane Adam
Chair, appraisal committee
May 2016

6 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee A.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.
Mary Hughes  
Technical Lead

Joanna Richardson  
Technical Adviser

Liv Gualda  
Project Manager

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