NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using osimertinib 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?

Issue date: July 2021

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 document.
- Subject to any appeal by consultees, the final appraisal document may be used as the basis for NICE's guidance on using osimertinib 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: 26 August 2021

Second appraisal committee meeting: TBC

Details of membership of the appraisal committee are given in section **Error! Reference source not found.**

1 Recommendations

1.1 The committee recognised that osimertinib is promising, but was not persuaded that there is sufficient evidence of clinical and cost effectiveness to recommend it for routine commissioning for the adjuvant treatment of stage 1b to 3a non-small-cell lung cancer (NSCLC) after complete tumour resection in adults whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.

1.2 The committee saw that osimertinib may be suitable for use in the Cancer Drugs Fund. Therefore, the company is invited to submit a proposal for including osimertinib in the Cancer Drugs Fund for this indication.

1.3 The Cancer Drugs Fund proposal should:

- detail any commercial access arrangements
- show plausible potential for cost effectiveness
- explain how data collection will address the main clinical uncertainties described in section 3
- state the likelihood that additional research will reduce uncertainty enough to support positive guidance in the future
- state how data will be collected and what data is currently available
- state when the results will be available.

  If appropriate data is already being collected, the proposal should summarise the study protocol.

Why the committee made these recommendations

There are currently no targeted adjuvant treatments (including those specific to EGFR mutations) available in England for NSCLC after complete tumour resection.

Current clinical trial evidence suggests that, compared with active monitoring, treatment with osimertinib increases how long people live. It may also lower the risk

of the disease coming back and the risk of death. However, this evidence is uncertain because information on what treatment patients were getting was revealed early.

Because of this, the cost-effectiveness estimates for osimertinib are also uncertain. It has the potential to be cost effective, but more evidence is needed to address these uncertainties before it can be recommended for routine use.

Osimertinib may be suitable for use in the Cancer Drugs Fund so that more data can be collected to address these uncertainties, So, the company is invited to submit a proposal for including osimertinib in the Cancer Drugs Fund for this indication.

2 Information about osimertinib

Marketing authorisation indication

2.1 Osimertinib (Tagrisso, AstraZeneca) is indicated for adjuvant treatment after complete tumour resection in adult patients with stage 1b to 3a non-small-cell lung cancer whose tumours have epidermal growth factor receptor exon 19 deletions or exon 21 (L858R) substitution mutations.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics.

Price

2.3 The list price for 30 x 80 mg tablets is £5,770 (BNF online, accessed July 2021).

2.4 The company has a commercial arrangement. This makes osimertinib available to the NHS with a discount and it would have also applied to this indication if the technology had been recommended. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee considered evidence submitted by AstraZeneca, a review of this submission by the evidence review group (ERG) and responses from stakeholders. See the committee papers for full details of the evidence.

The appraisal committee recognised that there were remaining areas of uncertainty associated with the analyses presented (see ERG post-FAC report, table 1, page 10), and took these into account in its decision making.

The appraisal committee was aware that none of the key issues identified was fully resolved during the technical engagement stage:

- uncertainty about whether better disease-free survival means better overall survival
- uncertainty about the company's cure assumptions and overall survival predictions
- uncertainty about later treatments with or without adjuvant osimertinib
- uncertainty about retreatment with osimertinib
- limitations in the available utility values for epidermal growth factor receptor epidermal growth factor receptor (EGFR) mutation-positive non-small-cell lung cancer (NSCLC)
- no subgroup analyses for patients with stage 1b NSCLC.

New treatment option

Patients and their families would welcome new effective treatments that reduce the risk of recurrence

3.1 Surgical removal of tumours is the preferred treatment for many people with early-stage NSCLC because it is potentially a cure. But despite the curative intent of complete resection, the disease recurs within about 5 years of surgery in 45% of patients with stage 1b, 62% with stage 2, and 76% with stage 3 disease. In the UK, around 13% of people with stage 1b NSCLC up to about 50% of people with stage 3a NSCLC have adjuvant

chemotherapy after resection. Because it provides only a relatively small benefit in overall and disease-free survival compared with no chemotherapy over 5 years, many people decline adjuvant therapy. The patient experts explained that people with fully resected stage 1b to 3a EGFR mutation-positive NSCLC would welcome new effective adjuvant treatments that reduce the risk of recurrence. They highlighted that people with EGFR mutation-positive NSCLC tended to be younger than people with other types of NSCLC, so having a treatment option that delays or prevents recurrence is important. Being disease free allows people to spend more time working or with their families. The committee concluded that patients and their families would welcome new, effective treatments that reduce the risk of recurrence.

Treatment pathway

Osimertinib is an oral treatment in a new place in the pathway

3.2 The only treatment currently available in England as adjuvant therapy for NSCLC (including for EGFR mutations) after complete resection is adjuvant chemotherapy, which provides a small benefit in overall survival. Treatment options for people with resectable EGFR mutation-positive NSCLC are therefore only those that are generally available and are non-targeted. The clinical and patient experts explained that osimertinib is well tolerated with manageable side effects. The patient experts explained that having an oral option would be welcomed because it would not require a visit to hospital. The committee acknowledged that positioning osimertinib as an adjuvant treatment may address an unmet need for people who have resection and then have disease recurrence. It concluded that osimertinib is an oral treatment in a new place in the pathway.

Retreatment with osimertinib would be offered to some people whose disease has progressed

3.3 The company assumed that everyone who develops distant metastases within 5 years of starting adjuvant osimertinib treatment would have

pemetrexed plus cisplatin followed by docetaxel. It assumed that after this 5-year timepoint, 50% of people who develop distant metastases would be retreated with osimertinib as first-line therapy (see NICE's guidance on osimertinib for untreated EGFR mutation-positive NSCLC) followed by pemetrexed plus cisplatin, with the remaining 50% having pemetrexed plus cisplatin followed by docetaxel. The ERG explained that in its base case, it had included atezolizumab, bevacizumab, carboplatin and paclitaxel as a second-line treatment in both groups and that it had excluded retreatment with osimertinib in the adjuvant osimertinib group. The clinical experts suggested that people are likely to have chemotherapy or atezolizumab, bevacizumab, carboplatin and paclitaxel if their disease progresses during treatment with osimertinib, while osimertinib would be offered to people whose disease progresses after adjuvant treatment with osimertinib. The Cancer Drugs Fund clinical lead agreed that if disease relapsed after treatment with osimertinib stopped, then retreatment would be commissioned in the NHS. They explained that this would depend on the time since finishing osimertinib and the onset of metastatic disease. If this time gap was short then there may not be much benefit, but they noted that the time gap would not need to be as long as that assumed by the company (at least 2 years, depending on when how long adjuvant osimertinib is taken). The Cancer Drugs Fund clinical lead also said that atezolizumab, bevacizumab, carboplatin and paclitaxel would be offered first line if treatment with tyrosine kinase inhibitors is inappropriate. The committee was concerned that the 50% split used in the company model is arbitrary, while people may also have retreatment within 5 years of starting osimertinib. The committee concluded that retreatment with osimertinib would be offered to some people whose disease had progressed after having osimertinib as an adjuvant treatment.

Clinical evidence

The clinical evidence for osimertinib is from ADAURA, a phase 3, randomised, placebo-controlled trial

3.4 The clinical-effectiveness evidence for osimertinib is based on the ADAURA randomised controlled trial. This is a phase 3 randomised, double-blind, placebo-controlled, multicentre trial in adults with completely resected stage 1b to 3a NSCLC (stratified by EGFR mutation). ADAURA compared adjuvant osimertinib 80 mg (n=339) with placebo (n=343) over a follow-up period of 12 and 24 weeks. Some people in both arms of the trial also had adjuvant chemotherapy. The planned treatment duration was 3 years. However, the trial was unblinded 2 years early after determination of overwhelming efficacy with osimertinib. In the overall trial population, treatment with osimertinib resulted in significantly longer disease-free survival, with a lower risk of disease recurrence (hazard ratio: 0.20; 99.12% confidence intervals: 0.14, 0.30; $p<0.001$). However, the disease-free survival data is immature and there have been very few events from which to calculate overall survival.

It is not certain to what extent a benefit in disease-free survival translates into a benefit in overall survival

3.5 Because the ADAURA trial was unblinded 2 years early, disease-free survival data is immature. The company explained that even though overall survival data from ADAURA is very immature, adjuvant osimertinib is expected to have a long-term survival benefit. This is because of the size of the disease-free survival benefit, a significant reduction in central nervous system metastases, and a consistent overall survival benefit when it is used to treat metastatic disease. Both the ERG and clinical experts agreed that disease-free survival is a clinically relevant end point. The clinical experts also emphasised the important benefits of a reduction in central nervous system metastases. However, the ERG explained that because of the immaturity of the overall survival data from ADAURA, the

size of any potential overall survival benefit is uncertain. The committee acknowledged that uncertainty remains around the extent to which adjuvant osimertinib prevents disease recurrence compared with delaying disease recurrence. Very few patients had reached 3 years of treatment with osimertinib and data on recurrence after stopping treatment were not presented. Therefore, it is uncertain what will happen after stopping treatment. The committee was also aware of recent publications by Gyawali (2021) and Uprety (2021), which noted that other adjuvant tyrosine kinase inhibitors demonstrated disease-free survival benefits that have not translated to an overall survival benefit. The committee was concerned that the experience with earlier generation TKIs such as erlotinib suggested that disease often recurred after stopping treatment. However, a clinical expert cautioned against placing too much weight on this because erlotinib does not have the same brain penetration as osimertinib. The committee concluded that it was not certain to what extent a benefit in disease-free survival translates into a benefit in overall survival.

The company's economic model

The company's model structure is acceptable for decision making, but does not fully represent the expected treatment pathway

3.6 The company used a state transition, semi-Markov model with 5 health states: disease free, loco-regional recurrence, first-line treatment for distant metastases, second-line treatment for distant metastases, and dead. In the company's model, retreatment with osimertinib for distant metastases is assumed for 50% of people, with the remaining 50% having pemetrexed plus cisplatin. The committee recalled that chemotherapy or atezolizumab, bevacizumab, carboplatin and paclitaxel would be offered to people whose disease had progressed during treatment with osimertinib. Retreatment with osimertinib would be offered to people whose disease had progressed after adjuvant treatment with osimertinib (see section 3.3). In its model, the company had also assumed that 100%

of people in the active monitoring arm have osimertinib as their first treatment for metastatic disease (see section 3.10). The ERG explained that the company's model therefore did not reflect the expected treatment pathway. The company's model also included a structural cure assumption (see section 3.8). The ERG noted that the cure timepoint used in the company's model coincided with when retreatment is allowed, so the proportion of people relapsing in the model is also uncertain. The company explained that this proportion varied between its clinical experts. The committee concluded that the company's model structure is acceptable for decision making but may not fully represent the expected treatment pathway.

Including a 3-year stopping rule is acceptable but the impact of stopping treatment at 3 years is uncertain

3.7 The company included a 3-year treatment stopping rule in its model. This is based on the trial design of ADAURA, where the maximum possible treatment duration was 3 years. It is also stated in the summary of product characteristics that treatment for more than 3 years was not studied. The clinical experts said that adjuvant treatment could not be indefinite and that the 3-year time period is appropriate. However, the patient experts said they would prefer to continue treatment beyond 3 years if the disease had not progressed. They explained that some people would find stopping treatment difficult because they would fear the disease coming back. The committee noted that in ADAURA, 12% of patients in the intervention arm and 10% in the active monitoring arm had reached 3 years of treatment. The committee concluded that a 3-year treatment stopping rule, in line with the clinical and cost-effectiveness evidence, was acceptable but the impact of stopping treatment at 3 years is uncertain.

Modelling survival and cure assumptions

Other approaches to modelling overall survival may be plausible

3.8 The predicted overall survival gain is a function of all transitions included in the model (see section 3.6), most of which are informed by external data and the company's structural cure assumption (a reduction in risk by 95% for people without disease recurrence at 5 years in both arms). The company's choice of survival models was based on a visual inspection of the combined disease-free survival and overall survival curves, with input from its clinical experts. In line with advice in the NICE Decision Support Unit Technical Support Document 14, the company applied the same parametric curves across both treatment arms. For the transition from disease free to loco-regional recurrence, the company applied log-normal curves, whereas generalised gamma curves were applied for the transition from disease free to distant metastatic NSCLC. The committee was concerned that the company's choice of extrapolations was driven by the company's cure assumption rather than the goodness of fit. The committee was aware that disease-free survival was a key driver of the company's economic model. It was concerned that most of the disease-free and overall survival benefits were gained during the extrapolated period, so the choice of extrapolation has a significant effect on the results. The ERG explained that none of the parametric modelling curves fits with the cure assumption. It highlighted that the evidence was uncertain because the data is immature and noted that there had been very few death events to inform overall survival. Clinical expert advice to the ERG suggested that the company's survival predictions may be optimistic. The ERG did additional sensitivity analyses in which it applied alternative parametric survival models to represent the transition from disease free to distant metastatic NSCLC. These used a log-normal distribution in:

- both arms of the model (the log-normal has the best statistical fit to the observed data)

- the treatment arm of the model only.

The committee considered that the log-normal distribution was as plausible as the generalised gamma. Usually it is appropriate to use the same distribution for both arms. However, given the cure assumption and stopping of treatment with osimertinib, the committee considered that it was possible that there might be a different profile of hazards between the 2 arms. The committee concluded that other approaches to modelling overall survival may be plausible and it would consider these in its decision making.

There is uncertainty about the company's cure assumptions

3.9 The company originally applied a 5-year cure timepoint in its modelling based on information from its clinical experts. Clinical expert advice to the ERG was that, for the active monitoring arm of the model, a 5-year cure timepoint may be appropriate, but a potential cure timepoint for the intervention arm is uncertain. The ERG did exploratory analyses to assess the effect of changing the timepoint at which the cure assumption is applied in the company's economic model. The ERG's optimistic analysis retained the company's original approach, whereas the pessimistic analysis applied a later timepoint for cure in the adjuvant osimertinib group of 8 years (5-year cure timepoint in the active monitoring group plus the 3-year osimertinib treatment period). The company explained that it considered the ERG's pessimistic analysis was overly pessimistic and clinically implausible because of the suggested change in survival probabilities being equal at the relative cure points. In response to technical engagement, the company proposed a 6-year cure timepoint, which was supported by its clinical experts. The committee was aware that the maximum follow-up period in ADAURA was 4 years, so the company's cure assumption was uncertain. Very few patients reached 3 years of treatment with osimertinib so it is also uncertain what will happen after stopping treatment. The committee recognised that osimertinib may delay rather than prevent recurrence. The committee

concluded that there was significant uncertainty about the company's cure assumptions. Taking into account that there was no data on people who have stopped osimertinib treatment, and the evidence from other tyrosine kinase inhibitors used as adjuvant treatment (see section 3.5), the committee concluded that the ERG's pessimistic analysis may be plausible.

It is not appropriate to assume 100% of people in the active monitoring arm have osimertinib as their first treatment for metastatic disease

3.10 NICE recently recommended osimertinib for untreated EGFR mutation-positive NSCLC for metastatic disease. The company base case assumes that 100% of people in the active monitoring arm will have osimertinib as their first treatment for metastatic disease. However, the most recent data shows that around two thirds of people currently have osimertinib. The committee recognised that people in the ADAURA trial are being actively monitored and disease may be identified at an earlier stage of progression than in current practice. Therefore, more people could be fit enough to have treatment, so outcomes in advanced disease could be better than seen in the FLAURA trial data. The ERG presented a scenario analysis using a different mix of tyrosine kinase inhibitors. This was based on the latest tyrosine kinase inhibitor prescribing data as presented by the company. The committee considered that the proportion of people having osimertinib is likely to increase over time but may not reach 100%. It concluded that it was appropriate to base its decision making on the latest available prescribing data.

Health-related quality of life

The company's utility values are acceptable for decision making

3.11 The company included utility values based on EQ-5D-3L estimates from ADAURA, EQ-5D-3L estimates from FLAURA (a randomised double-blind, phase 3 controlled trial comparing osimertinib with erlotinib or gefitinib for the first-line treatment of EGFR mutation-positive advanced

NSCLC), and published EQ-5D-3L estimates from the literature (Labbé et al. 2017). Disutilities associated with adverse events were based on published literature (Nafees et al. 2008, standard gamble) and on a previous appraisal of osimertinib used second line for metastatic disease (see NICE's guidance on osimertinib for EGFR T790M mutation-positive advanced NSCLC). The ERG was concerned that the utility values applied in the disease free, loco-regional recurrence and distant metastatic NSCLC health states may be implausibly high compared with the general population. The ERG was also concerned that the model does not include health-related quality of life decrements for late effects of adjuvant treatment or downstream adverse events. However, it suggested that although the utility values may have been overestimated, they did not necessarily favour osimertinib. The ERG explained that it did an additional sensitivity analysis using utility values from a study by Andreas et al. (2018). This had a limited effect on the cost-effectiveness estimates. The committee concluded that the company's utility values were acceptable for decision making.

Cost-effectiveness estimate

The most plausible incremental cost-effectiveness ratios (ICERs) for osimertinib are highly uncertain

3.12 Because of confidential discounts for subsequent therapies, the cost-effectiveness results are commercial in confidence and cannot be reported here. However, the company's base case including all discounts was less than £20,000 per quality-adjusted life year (QALY) gained. The ERG made several changes to the company's base case and presented 2 analyses. The first was based on a 5-year cure point in both arms and produced a similar ICER to the company's base case. The second was based on an 8-year cure point in the osimertinib arm and produced an ICER greater than £20,000 per QALY gained. The committee considered several modelling assumptions plausible:

- The ERG's base case, which included a cure point at 8 years for the osimertinib group and 5 years for the active monitoring group.
- Including a mix of tyrosine kinase inhibitors as first-line treatments for people in the active monitoring group.
- Alternative plausible modelling assumptions for the transition from the disease free to distant metastatic NSCLC health states using a log-normal distribution in
  - both arms of the model
  - in the treatment arm of the model only.
- Including retreatment with osimertinib after recurrence in the intervention arm of the model.

Combining any of these assumptions increased the ICER to above £30,000 per QALY gained. Combining the first 2 with the log-normal extrapolation for the transition from the disease free to distant metastatic in the treatment arm only increased the ICER substantially above £30,000 per QALY gained. Using these preferred assumptions, the committee considered that the most plausible ICER range for osimertinib was higher than £30,000 per QALY gained.

The committee concluded that the cost-effectiveness estimates for osimertinib may be higher than what NICE normally considers a cost-effective use of NHS resources.

Osimertinib is not recommended for routine use in the NHS

3.13 Because ADAURA was unblinded 2 years early, the disease-free survival and overall survival data for osimertinib is immature. After considering the uncertainty with the clinical evidence along with its preferred assumptions, the committee decided that the upper end of the most plausible ICER range may not be within the range usually considered a cost-effective use of resources. The committee concluded it could not recommend osimertinib for the adjuvant treatment of stage 1b to 3a NSCLC after complete resection in adults whose tumours have EGFR exon 19

deletions or exon 21 (L858R) substitution mutations for routine use in the NHS.

Osimertinib may be suitable for use in the Cancer Drugs Fund

3.14 Having concluded that osimertinib could not be recommended for routine use, the committee then considered if it could be recommended for treating stage 1b to 3a NSCLC within the Cancer Drugs Fund. The committee discussed the arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting NICE's Cancer Drugs Fund methods guide (addendum). The committee acknowledged that the disease-free survival and overall survival data from ADAURA was not mature and that further data collection may help address uncertainty. However, the company said that the disease-free survival and the predicted overall survival data are strong enough to support a recommendation for routine commissioning. It highlighted that ADAURA is currently ongoing. The company did not consider the Cancer Drugs Fund to be a suitable approach because it did not feel that the uncertainty about the overall survival data would be addressed within the Cancer Drugs Fund timeframe. The committee was aware that, although a period of time in the Cancer Drugs Fund may not produce enough mature overall survival data for a partitioned survival model, there would still be benefits:

- the disease-free survival data will be more mature
- there will be a better understanding of the impact of the 3-year stopping rule
- more data will be available to estimate the extent of the cure proportion.

The committee acknowledged that osimertinib has plausible potential to be cost effective. It understood that there is uncertainty around both the 8-year cure time point and whether the log-normal or generalised gamma distribution should be used to extrapolate overall survival. If the cure time point was earlier than 8 years then osimertinib may represent a cost-effective use of NHS resources. The Cancer Drugs Fund clinical

lead indicated that they would welcome collecting data on osimertinib through the Cancer Drugs Fund because osimertinib is not recommended for routine commissioning.

Innovation

Osimertinib is recognised as an innovative therapy in the adjuvant setting

3.15 The company said that osimertinib is innovative because there has been little innovation in adjuvant treatment for stage 1b to 3a EGFR mutation-positive NSCLC, aside from adjuvant chemotherapy, in 20 years. Osimertinib has been reviewed as part of Project Orbis because it is considered an innovative adjuvant treatment. The committee agreed with these points but concluded that it did not consider there were any additional benefits associated with osimertinib that had not been captured in the economic analysis.

Equality

EGFR mutation-positive NSCLC is more common in women and people with a Chinese family background

3.16 The clinical experts explained that EGFR mutation-positive NSCLC tends to be more common in women and people with a Chinese family background. The committee noted that the issue of different disease prevalence cannot be addressed in a technology appraisal.

Other factors

Less common EGFR mutations were not considered

3.17 The only EGFR mutations considered within the scope of this appraisal are EGFR exon 19 deletions or exon 21 (L858R) substitution mutations. This is in line with osimertinib's current marketing authorisation. The Cancer Drugs Fund clinical lead explained that if NICE recommends osimertinib for these mutations, NHS England would consider

commissioning adjuvant osimertinib treatment for other less common EGFR mutations. The committee noted that NICE can only appraise a medicine within its marketing authorisation and welcomed the comments from the Cancer Drugs Fund clinical lead.

The end of life criteria are not met

3.18 The company did not make a case for osimertinib meeting NICE's end of life criteria. NICE's advice about life-extending treatments for people with a short life expectancy did not apply.

Conclusion

3.19 The committee recognises that osimertinib is a promising new treatment option for the adjuvant treatment of stage 1b to 3a NSCLC after complete tumour resection, in adults whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations. However, there is not enough clinical and cost-effectiveness evidence to recommend it for routine use in the NHS. The company is invited to submit a proposal for osimertinib in the Cancer Drugs Fund.

4 Proposed date for review of guidance

4.1 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 comments 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.

Gary McVeigh
Chair, appraisal committee
July, 2021

5 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 D.

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.

Laura Coote and Samuel Harper
Technical leads

Caron Jones
Technical adviser

Louise Jafferally
Project manager

ISBN: [to be added at publication]