

# Pembrolizumab for neoadjuvant and adjuvant treatment of triple- negative early or locally advanced breast cancer

Technology appraisal guidance

Published: 14 December 2022

[www.nice.org.uk/guidance/ta851](https://www.nice.org.uk/guidance/ta851)

## Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should [assess and reduce the environmental impact of implementing NICE recommendations](#) wherever possible.

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# 1 Recommendations

1.1 Pembrolizumab is recommended, within its marketing authorisation, as an option with chemotherapy for neoadjuvant treatment and then continued alone as adjuvant treatment after surgery for adults with triple-negative:

- early breast cancer at high risk of recurrence or
- locally advanced breast cancer.

It is recommended only if the company provides pembrolizumab according to the [commercial arrangement](#).

## Why the committee made these recommendations

Treatment for triple-negative early or locally advanced breast cancer is usually chemotherapy then surgery.

Clinical trial evidence shows that adding pembrolizumab to chemotherapy before surgery (neoadjuvant), then continuing with pembrolizumab alone after surgery (adjuvant) increases the chance that the cancer will disappear. It also increases the time before any cancer recurs. It is not clear if pembrolizumab increases how long people live.

The cost-effectiveness estimates are likely to be within what NICE considers an acceptable use of NHS resources. So, pembrolizumab is recommended.

## 2 Information about pembrolizumab

### Marketing authorisation indication

- 2.1 Pembrolizumab (Keytruda, MSD) has a marketing authorisation 'in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, for the treatment of adults with locally advanced, or early-stage triple-negative breast cancer at high risk of recurrence'.

### Dosage in the marketing authorisation

- 2.2 The dosage schedule is available in the [summary of product characteristics for pembrolizumab](#).

### Price

- 2.3 The list price is £2,630 per 100 mg solution for infusion vial (excluding VAT; BNF online accessed September 2022).
- 2.4 The company has a [commercial arrangement](#). This makes pembrolizumab available to the NHS with a discount. 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 MSD, 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.

### Clinical need

#### **Adding pembrolizumab to standard care would be a welcome option for people with triple-negative breast cancer**

3.1 The patient expert explained that there are limited effective treatment options available for triple-negative early and locally advanced breast cancer, despite its particularly poor prognosis. They explained that many people who have pembrolizumab with chemotherapy feel lucky to have this treatment, which is seen as an additional lifeline. The patient expert also explained that people know that pembrolizumab may cause some adverse events (see [section 3.7](#)). But they consider that the potential benefits of treatment far outweigh any risks. This is particularly because triple-negative breast cancer is associated with younger people, who may have young families. Also, the disease has an increased risk of recurrence compared with other forms of breast cancer. The committee concluded that recently, there have been limited advances in treatment options for triple-negative early and locally advanced breast cancer. It further concluded that there is an unmet need for treatments for this disease and adding pembrolizumab to standard care would be welcomed.

### Treatment pathway

#### **Treatment for triple-negative early and locally advanced breast cancer varies, but adjuvant treatment is not standard care**

3.2 The clinical experts explained that standard care for triple-negative early

or locally advanced breast cancer is chemotherapy as neoadjuvant treatment then surgery. They explained that the most common chemotherapy regimen is an anthracycline taxane combination plus a platinum therapy. The clinical experts also noted that it varies whether adjuvant treatment is offered or whether disease is only monitored after surgery. They explained that capecitabine may be offered after surgery if there is no pathological complete response after neoadjuvant treatment. However, they explained that there is mixed evidence on the efficacy of adjuvant capecitabine, and that standard care does not include any adjuvant treatment. The clinical experts explained that if pembrolizumab was available for this indication, they would expect that practice would change to include neoadjuvant and adjuvant treatment. The committee concluded that standard care for triple-negative early or locally advanced breast cancer is chemotherapy as neoadjuvant treatment, then surgery with no adjuvant treatment, although practice varies.

## Clinical evidence

### **Pathological complete response is an important outcome for people with triple-negative breast cancer**

- 3.3 The patient and clinical experts emphasised that although other clinical outcomes are important, pathological complete response is a particularly important outcome for people with triple-negative breast cancer. Pathological complete response means that all the detectable cancer has disappeared after neoadjuvant treatment. The clinical experts explained that pathological complete response is an important outcome, and suggests improved longer-term outcomes. The patient experts explained that a pathological complete response has a great psychological benefit because people are aware that it makes better long-term outcomes more likely. It also offers the opportunity to use less invasive, breast-conserving surgery. Reducing mastectomies is beneficial because they have a longer recovery time, and sometimes people need reconstructive surgery and later revisions. The clinical experts explained that people have an improved quality of life with less invasive surgery, and that there are potential cost savings to the NHS if the number of mastectomies was reduced. The committee concluded that pathological complete response

is an important outcome for people with triple-negative breast cancer.

## **KEYNOTE-522 is generalisable to people who would have pembrolizumab in the NHS**

3.4 KEYNOTE-522 is a randomised, double-blind, placebo-controlled trial (n=1,174). It was done in 21 countries worldwide and included 40 people from the UK. The trial compared 2 treatment arms: chemotherapy plus pembrolizumab and chemotherapy plus placebo. The chemotherapy plus pembrolizumab arm included:

- neoadjuvant treatment with:
  - carboplatin plus paclitaxel for cycles 1 to 4
  - doxorubicin or epirubicin plus cyclophosphamide for cycles 5 to 8
  - pembrolizumab for cycles 1 to 8
- surgery
- adjuvant treatment with pembrolizumab for 9 cycles.

The chemotherapy plus placebo arm included:

- neoadjuvant treatment with:
  - carboplatin plus paclitaxel for cycles 1 to 4
  - doxorubicin or epirubicin plus cyclophosphamide for cycles 5 to 8
  - placebo for cycles 1 to 8
- surgery
- adjuvant treatment with placebo for 9 cycles.

The clinical experts explained that the chemotherapy regimens used in the trial were broadly similar to the treatments used most often in the NHS (see [section 3.2](#)). However, they noted that doxorubicin, which is used as part of the chemotherapy regimen in both arms in the trial, is not often used in the UK. They also explained that the population in the trial was reflective of the



population in the marketing authorisation, which includes people with locally advanced or early-stage disease at high risk of recurrence. The clinical experts explained that although the study was done worldwide, most sites were in countries that have similar ethnicities to the UK, so the trial population was generalisable to UK clinical practice (see [section 3.6](#)). Overall, the clinical experts stated that based on the chemotherapy regimen and population included in the trial, they would expect the results from KEYNOTE-522 to be generalisable to NHS clinical practice. The committee concluded that KEYNOTE-522 is generalisable to people who would have pembrolizumab in the NHS.

## Clinical effectiveness

### **Pembrolizumab improves clinical outcomes compared with chemotherapy alone when considering the full trial population**

3.5 Median event-free survival and overall survival were not reached in either arm in KEYNOTE-522. The median duration of follow up was 37.8 months. The clinical outcomes for the full trial population included:

- The proportion of people with pathological complete response was 63.0% (95% confidence interval [CI] 59.5 to 66.4%) in the chemotherapy plus pembrolizumab arm and 55.6% (95% CI 50.6 to 60.6%) in the chemotherapy plus placebo arm.
- The difference in pathological complete response rate was 7.5% (95% CI 1.6 to 13.4%) favouring the chemotherapy plus pembrolizumab arm.
- Event-free survival rate at 42-month follow up was 83.5% (95% CI 80.5 to 86.0%) in the chemotherapy plus pembrolizumab arm and 74.9% (95% CI 69.8 to 79.2%) in the chemotherapy plus placebo arm.
- The difference in event-free survival rate at 42-month follow up was 8.6% (hazard ratio 0.63, 95% CI 0.48 to 0.82) favouring the chemotherapy plus pembrolizumab arm.
- Overall survival rate at 42-month follow up was 89.2% (95% CI 86.7 to 91.3%) in the chemotherapy plus pembrolizumab arm and 84.1% (95% CI 79.5 to 87.7%) in

the chemotherapy plus placebo arm.

- The difference in overall survival rate at 42-month follow up was 5.1% (hazard ratio 0.72, 95% CI 0.51 to 1.02) favouring the chemotherapy plus pembrolizumab arm.

The committee noted that no statistically significant difference in overall survival was shown with adding pembrolizumab to standard care. But there was a statistically significant difference seen for event-free survival. The clinical experts noted that the benefits seen for complete pathological response and event-free survival suggested that, with longer follow up, benefits for overall survival would also be seen. The ERG agreed that the lack of statistically significant benefit seen for overall survival may be because of immature data. The clinical experts also highlighted that the trial data does show a significant improvement in pathological complete response, which is an important outcome (see [section 3.3](#)). The committee concluded that in the full trial population, adding pembrolizumab to standard care improves the rate of pathological complete response and event-free survival.

## **There is no clear reason why there would be differences in effect due to ECOG score or geographical region**

- 3.6 Several subgroup analyses were pre-specified in the KEYNOTE-522 study protocol. Most subgroups showed no difference in outcomes compared with the full trial population. However, for the subgroup of people with an Eastern Cooperative Oncology Group score of 1 (ECOG 1), the ERG noted that the hazard ratio point estimate for event-free survival was higher than for the full trial population (see [section 3.5](#)) and that the confidence intervals for this subgroup cross 1 (n=155; hazard ratio 0.81, 95% CI 0.41 to 1.62). The ERG also noted that there was a difference in the hazard ratio for the subgroup of people having treatment in Europe (referred to from now as the Europe subgroup) compared with the full trial population. This information is academic in confidence and cannot be reported here. The clinical experts explained that there is no clear reason why there would be less benefit in event-free survival for people with an ECOG score of 1. They suggested this result may be because of the small sample size in this subgroup. They suggested that a possible reason for the different hazard ratio for event-free survival rate in the

Europe subgroup was because of differences in clinical practice in different countries and would be unlikely to be because of physiological differences. However, the company explained that the KEYNOTE-522 protocol restricted the use of different treatment approaches. The clinical experts also explained that there is no evidence for differences in clinical outcomes for the different surgical approaches used worldwide. So the clinical experts could not identify a clear reason why event-free survival rate would be influenced by geographical region. The company highlighted that no explanation of the different results seen across regions could be identified by looking at the baseline characteristics of each population. It also explained that KEYNOTE-522 was not powered to detect differences in subgroups by region so the results should be interpreted with caution. The Cancer Drugs Fund clinical lead highlighted that because the trial was not stratified by geographical region, it is possible that some imbalances between the treatment arms contributed to the different hazard ratios seen in different subgroups. They also highlighted that the hazard ratio for event-free survival for the subgroup including Europe, Israel, North America and Australia was close to the hazard ratio for the full trial population. The committee concluded that although the hazard ratios for event-free survival for the ECOG 1 and Europe subgroups were different to the hazard ratio for the full trial population, there was no underlying reason to explain why these differences were observed.

## **There are additional adverse events associated with adding pembrolizumab to standard care**

3.7 KEYNOTE-522 results showed that there were more serious adverse events in the chemotherapy plus pembrolizumab arm (43.6%) compared with the chemotherapy plus placebo arm (28.5%). The clinical experts explained that this result is expected with adding another treatment to standard care. They also noted that data on drug-related adverse events leading to death needs to be assessed as the data matures, but that there is not enough evidence at this stage to say that pembrolizumab increases the number of treatment-related deaths. The patient experts explained that the additional adverse events with adding pembrolizumab are manageable, and the potential benefits of treatment outweigh the potential adverse events. The clinical experts explained that the risk of

adverse events would be considered by individuals. They would expect most people to accept these risks and tolerate the adverse events, given the potential benefits of adding pembrolizumab to chemotherapy. The committee concluded that additional adverse events are associated with adding pembrolizumab to standard care, and these should be taken into account by patients and clinicians when considering treatment options.

## Economic model

### **The company's economic model is acceptable for decision making**

3.8 The company presented a 4-state Markov model to estimate the cost effectiveness of chemotherapy plus pembrolizumab compared with chemotherapy plus placebo. The 4 health states were event-free, locoregional recurrence, distant metastasis and death. The ERG highlighted that the distant metastasis state does not differentiate between pre-progressed and post-progressed disease. The company explained that evidence is limited for triple-negative breast cancer. So including distinct states for pre- and post-progression in the distant metastasis health state would need unnecessary assumptions and add complexity and uncertainty. The ERG also highlighted that for people who had first-line metastatic treatment in the distant metastasis state, the company's model included the costs for second and subsequent line metastatic treatments as a lump sum. Because these treatment costs make up around a third of all costs in the chemotherapy arm, the ERG raised concerns around the lack of precision using this approach. The committee understood that the model structure was limited by the evidence available for triple-negative breast cancer. It concluded that although there were limitations with the model, these could not be addressed without increasing the model's complexity and uncertainty. So it concluded that the company's model is acceptable for decision making.

## Assumptions in the economic model

### **It is appropriate to consider the full trial population in the**

## economic model

3.9 The ERG highlighted the different hazard ratios for event-free survival from KEYNOTE-522 for people having treatment in Europe and in the full trial population (see [section 3.6](#)). The ERG suggested that the Europe subgroup is more likely to be generalisable to the UK than the full trial population. So it preferred to use the hazard ratio from the Europe subgroup to represent pembrolizumab's efficacy in the model. The company used pembrolizumab's efficacy from the full trial population in its model. The committee agreed that it is appropriate to consider evidence within the cost-effectiveness model that reflects the population in the NHS. However, it agreed it is also important to assess the reliability of the subgroup results and discussed that KEYNOTE-522 was not powered to show a difference across regions. The committee considered the clinical experts' view that there is no clear reason why event-free survival would be influenced by geographical region and that the full trial population is generalisable to UK clinical practice (see [section 3.4](#) and [section 3.6](#)). Given this, the committee agreed that it was not appropriate to use results from the Europe subgroup which is not powered to show a difference in effect, when results from the full trial population, which is appropriately powered, are available. Therefore, the committee concluded that it was appropriate to use the results from the full trial population in the economic model.

## The comparator treatment in KEYNOTE-522 is appropriate for use in the economic model

3.10 The comparator included in the company's model was aligned with the comparator used in KEYNOTE-522 (see [section 3.4](#)). The ERG stated that this might not reflect NHS clinical practice. It highlighted that more people had doxorubicin than epirubicin as neoadjuvant chemotherapy in KEYNOTE-522 and this may not reflect how frequently these chemotherapy agents are used in practice. The ERG highlighted that a subgroup analysis in KEYNOTE-522 showed better efficacy for doxorubicin than epirubicin. The clinical experts explained that doxorubicin is not often used in clinical practice (see [section 3.4](#)) but it is still a reasonable comparator. The ERG also questioned if placebo monotherapy as adjuvant treatment was appropriate because some

people may have capecitabine. The clinical experts explained that standard care does not typically include adjuvant treatment so placebo after surgery is an appropriate comparator (see [section 3.2](#)). The committee concluded that the comparator in KEYNOTE-522 was appropriate for use in the economic model.

## **The ERG's approach to event-free survival extrapolation is methodologically appropriate, although it may be conservative**

3.11 Extrapolation of event-free survival Kaplan–Meier data from KEYNOTE-522 was used to model transitions from the event-free health state to each of the other health states. The probability of the first event in each treatment arm being locoregional recurrence, distant metastasis or death was determined from KEYNOTE-522. It was applied to the extrapolated event-free survival data to estimate the transition probabilities into each health state. The company used a log-normal curve for the chemotherapy plus placebo arm and a generalised gamma curve for the chemotherapy plus pembrolizumab arm. The ERG stated that, unless there are very strong arguments to not do so, survival extrapolation should use the same extrapolation curve in both treatment arms, as per [NICE's Decision Support Unit technical support document 14](#). So it preferred to use a log-normal extrapolation of event-free survival in both arms because it did not consider that sufficient justification was provided for using different extrapolations for each treatment arm. The ERG was also concerned that in the company's model, the event-free survival rate accelerated within the extrapolated period, meaning the event-free survival gains are mostly from the unobserved extrapolated data. The company argued that it was appropriate to use different curves for each arm because chemotherapy and pembrolizumab have different mechanisms of action. It also stated that the log-normal curve for the chemotherapy plus pembrolizumab arm was inappropriate. This was because it did not show a plateau associated with a decrease in the number of progression events over time so would underestimate the pembrolizumab treatment effect. The clinical experts explained that most relapses of triple-negative breast cancer happen within the first 3 years of diagnosis. There is increased certainty of longer-term survival for people whose disease has not relapsed by this time. So it is reasonable that the extrapolated curves for

event-free survival should plateau after 3 years. The committee concluded that the ERG's method of using the same extrapolation curve for each treatment arm was methodologically appropriate but this was likely to provide a conservative estimate of event-free survival.

## **Both data sources for estimating overall survival in the distant metastasis state are uncertain**

3.12 In the model, the company used data on overall survival from KEYNOTE-355 to estimate the transition probabilities from the distant metastasis state to death for people who had treatment for metastatic disease. KEYNOTE-355 (n=882) is a randomised placebo-controlled trial in people with recurrent triple-negative inoperable or metastatic breast cancer. It compared chemotherapy plus pembrolizumab with chemotherapy plus placebo. The company used KEYNOTE-355 data to estimate overall survival in the distant metastasis state because the data in KEYNOTE-522 is immature. The ERG noted that there are differences in the observed survival between KEYNOTE-522 and KEYNOTE-355 so the populations in the studies may not be comparable. It preferred to use direct trial data from KEYNOTE-522 to estimate transition probabilities in the distant metastasis state. The committee noted that KEYNOTE-522 overall survival data for people whose disease has metastasised is immature, so is uncertain. However, it also noted the potential bias that could be introduced into the model by using data sourced from a different population. The committee concluded that there is uncertainty with both data sources for estimating overall survival in the distant metastasis state.

## **The utility values used in the model have a limited impact on the incremental cost-effectiveness ratio**

3.13 The company's economic model used utility values sourced from EQ-5D-5L data from KEYNOTE-522, mapped to EQ-5D-3L. The utility values were pooled across the chemotherapy plus pembrolizumab and the chemotherapy plus placebo arms for each health state. Event-free survival utilities were separated into values for being on and off treatment. The ERG highlighted that the utility values for the distant metastasis health state were relatively low compared with other studies,

such as KEYNOTE-355. However, it noted that this may be because of the small number of EQ-5D-5L questionnaires completed by people in KEYNOTE-522 with disease that had metastasised. The ERG and the company did scenario analyses using utility data from other sources, which showed that the utility values had a very limited impact on the incremental cost-effectiveness ratio (ICER). The committee concluded that although there was some uncertainty around the validity of the utility values used in the model, it has a limited impact on the cost-effectiveness results.

## Cost-effectiveness estimate

### **Adding pembrolizumab to standard care for early and locally advanced triple-negative breast cancer is likely to be cost effective**

3.14 The company's model included the following assumptions:

- Estimating pembrolizumab efficacy from the full trial population (see [section 3.9](#)).
- Using chemotherapy regimens as used in KEYNOTE-522 in the treatment and comparator arm (see [section 3.10](#)).
- Using a log-normal extrapolation of Kaplan-Meier data in the chemotherapy plus placebo arm (see [section 3.11](#)).
- Using a generalised gamma extrapolation of Kaplan-Meier data in the chemotherapy plus pembrolizumab arm (see [section 3.11](#)).
- Estimating overall survival in the distant metastasis state using data from KEYNOTE-355 (see [section 3.12](#)).
- Estimating utility values from EQ-5D-5L data from KEYNOTE-522 (see [section 3.13](#)).

The ERG's base case included some of the same assumptions, but included different assumptions on:



- Estimating pembrolizumab efficacy, for which it preferred to use the hazard ratio from the Europe subgroup (see section 3.9).
- The choice of curve for extrapolation of Kaplan-Meier data in the chemotherapy plus pembrolizumab arm, for which it preferred to use a log-normal extrapolation (see section 3.11).
- The source of overall survival data in the distant metastasis state, for which it preferred to use KEYNOTE-522 data (see section 3.12).

The committee considered that the full trial population results for event-free survival should be used in the model because it was uncertain why there were differences in effect seen in the Europe subgroup (see section 3.9). However, it agreed that other assumptions included in the ERG's base case were reasonable. It noted that the ERG presented an alternative base case using the full trial population. The committee concluded that its preferred assumptions were those in the ERG's alternative base case, using the hazard ratio for event-free survival from the full trial population. The ICERs cannot be reported here because of confidential commercial arrangements for subsequent treatments in the pathway. However, the ERG's alternative base case is below the range normally considered a cost-effective use of NHS resources. The committee discussed the unmet need for treatment options for triple-negative early or locally advanced breast cancer (see [section 3.1](#)). It also discussed that there could be potential cost savings to the NHS, which had not been included in the model, if the number of invasive breast surgery procedures was reduced (see [section 3.3](#)). Considering all these factors, pembrolizumab with chemotherapy is likely to be a cost-effective use of NHS resources.

## Conclusion

### **Pembrolizumab is recommended**

- 3.15 The committee noted that based on its preferred assumptions, pembrolizumab with chemotherapy is likely to be cost effective compared with chemotherapy alone (see [section 3.14](#)). There was some uncertainty, particularly about the long-term outcome benefits of adding pembrolizumab to standard care. However, because the committee preferred conservative assumptions for event-free and overall survival, it

considered that pembrolizumab is likely to be at the lower end of the range normally considered a cost-effective use of NHS resources. So pembrolizumab with chemotherapy as neoadjuvant treatment, and then continued alone as adjuvant treatment, is recommended for use in the NHS as an option for adults with triple-negative:

- early breast cancer at high risk of recurrence or
- locally advanced breast cancer.

## 4 Implementation

- 4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication
- 4.2 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for routine commissioning, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Interim funding will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early Access to Medicines Scheme designation or fast track appraisal), at which point funding will switch to routine commissioning budgets. The NHS England and NHS Improvement Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.
- 4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.
- 4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has triple-negative locally advanced or early breast cancer at high risk of recurrence and the doctor responsible for their care thinks that pembrolizumab is the right treatment, it should be available for use, in line with NICE's recommendations.

## 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 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.

**Albany Chandler**

Technical lead

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ISBN: 978-1-4731-4878-9