

**NATIONAL INSTITUTE FOR HEALTH AND CARE
EXCELLENCE**

Appraisal consultation document

**Pembrolizumab plus chemotherapy for
untreated, triple-negative, locally recurrent
unresectable or metastatic breast cancer**

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using pembrolizumab 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, sex, 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 document.
- Subject to any appeal by consultees, the final appraisal document may be used as the basis for NICE's guidance on using pembrolizumab 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: 29 March 2022

Second appraisal committee meeting: 12 April 2022

Details of membership of the appraisal committee are given in section 5.

1 Recommendations

- 1.1 Pembrolizumab plus chemotherapy (paclitaxel or nab-paclitaxel) is not recommended, within its marketing authorisation, for treating triple-negative, locally recurrent unresectable or metastatic breast cancer in adults whose tumours express PD-L1 with a combined positive score of 10 or more and who have not had chemotherapy for metastatic disease.
- 1.2 This recommendation is not intended to affect treatment with pembrolizumab plus chemotherapy that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Current treatment for untreated, triple-negative, locally recurrent unresectable or metastatic breast cancer includes chemotherapy such as docetaxel, paclitaxel, or the immunotherapy atezolizumab plus nab-paclitaxel (from now, atezolizumab combination). Pembrolizumab plus paclitaxel or nab-paclitaxel (from now, pembrolizumab combination) is another immunotherapy that could be used.

Clinical trial evidence shows that pembrolizumab combination increases how long people have before their cancer gets worse and how long they live compared with paclitaxel. However, the long-term benefit is uncertain. Pembrolizumab combination and atezolizumab combination have only been compared indirectly, so how their effectiveness compares is uncertain.

The company did not make a robust case for applying end of life criteria. This means the cost-effectiveness estimates are higher than what NICE usually considers an acceptable use of NHS resources. Therefore, it is not recommended.

2 Information about pembrolizumab

Marketing authorisation indication

- 2.1 Pembrolizumab (KEYTRUDA, Merck Sharp & Dohme) has a marketing authorisation for use in combination with chemotherapy ‘for the treatment of locally recurrent unresectable or metastatic triple-negative breast cancer in adults whose tumours express PD-L1 with a CPS \geq 10 and who have not received prior chemotherapy for metastatic disease’.

Dosage in the marketing authorisation

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

Price

- 2.3 The company’s list price is £2,630 per 100 mg solution for infusion vial (excluding VAT, BNF online accessed January 2022).
- 2.4 The company has a commercial arrangement. This makes pembrolizumab 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 Merck Sharp & Dohme, 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 and treatment pathway

Triple-negative breast cancer has a high disease burden

3.1 Some breast cancers test negative for oestrogen and progesterone receptors (hormone receptor-negative) and human epidermal growth factor receptor 2 (HER2-negative). They are known as triple-negative and account for about 15% of all breast cancers. The patient expert explained that being diagnosed with locally recurrent unresectable or metastatic breast cancer is extremely difficult for people, and their family and friends. It can cause considerable anxiety and fear, and the uncertainty of the outcome can be very difficult. Also, people with locally recurrent unresectable and metastatic breast cancer must organise their lives around hospital appointments, which restrict their everyday activities. There is no cure for metastatic breast cancer. Treatment aims to stop progression of the disease, extend life, and maintain or improve quality of life for as long as possible. Treatment is continued for as long as it works. The committee concluded that there is a high disease burden for people with triple-negative breast cancer.

There is a need for first-line triple-negative breast cancer treatments

3.2 Until recently, there were limited first-line treatment options for people with triple-negative, locally recurrent unresectable or metastatic breast cancer, especially compared with other types of breast cancer. Atezolizumab plus nab-paclitaxel (from now, atezolizumab combination) is the only immunotherapy recommended by NICE for this condition (see [NICE's technology appraisal guidance on atezolizumab with nab-paclitaxel for untreated PD-L1-positive, locally advanced or metastatic, triple-negative breast cancer](#)). Other first-line treatment options for triple-negative, locally recurrent unresectable or metastatic breast cancer are paclitaxel, docetaxel, nab-paclitaxel, anthracycline-based chemotherapy, or gemcitabine with or without carboplatin (see [NICE's clinical guideline on breast cancer: diagnosis and management](#)). The clinical expert explained that atezolizumab combination is an option for some people whose

tumours express PD-L1. However, they explained that some people would be ineligible for atezolizumab combination that could have pembrolizumab plus paclitaxel or nab-paclitaxel (from now, pembrolizumab combination). This is because the marketing authorisation for each treatment option includes a different measurement of PD-L1 expression. Pembrolizumab PD-L1 expression is measured using combined positive score (CPS). However, in [NICE's technology appraisal guidance on atezolizumab with nab-paclitaxel](#), it is based on immune cell staining (IC). The 2 measurements use slightly different methods of measuring and calculating PD-L1 expression. The company estimated that the overall percentage agreement between the 2 measures is 75%. However, it also stated that there are some instances in which only 1 measurement would show PD-L1 positivity, and when the results of both measures would not overlap. The clinical expert and Cancer Drugs Fund clinical lead agreed that there is an overlap between the 2 measurements. However, they explained that the population with a CPS of 10 or more would be larger than the population with a IC of 1% or more. They also explained that the measurement used would vary between hospital trusts and that this would drive the treatment offered. Currently, hospital trusts are set up to test for IC because of atezolizumab use. However, CPS measurement is used in other tumour sites. The clinical expert and Cancer Drugs Fund clinical lead highlighted that it is unlikely hospital trusts would test for both CPS and IC because of the cost. They explained that it is likely trusts would adopt 1 measurement and only use the other measurement if the original measurement did not show PD-L1 positivity (for example, if IC score was not 1% or more, the CPS score would be measured). The committee concluded that there is an unmet need for immunotherapy for untreated, triple-negative, locally recurrent unresectable metastatic breast cancer, especially for people who cannot have atezolizumab combination.

The relevant comparators are paclitaxel, docetaxel and atezolizumab combination

3.3 The company used paclitaxel as its base-case comparator, docetaxel and atezolizumab combination as secondary comparators, and did not include gemcitabine with or without carboplatin or nab-paclitaxel. The clinical expert agreed that gemcitabine with or without carboplatin and nab-paclitaxel were not relevant comparators. Gemcitabine with or without carboplatin is not widely used in the NHS, especially first line in metastatic disease. This is because it is difficult to administer and has a high toxicity. The clinical expert and Cancer Drugs Fund clinical lead also explained that nab-paclitaxel is rarely used in the NHS because of its cost. However, there is currently some use of nab-paclitaxel because access has been given during COVID-19. Also, because of recent resource pressures in the NHS, docetaxel is being used more often. This is because docetaxel and nab-paclitaxel are given at 3-weekly intervals, compared with paclitaxel, which is usually given weekly. The company explained that docetaxel is not relevant as a primary comparator because it is used at earlier stages of breast cancer and has a less favourable safety profile than paclitaxel. The committee recalled that docetaxel was not considered a relevant comparator in [NICE's technology appraisal guidance on atezolizumab with nab-paclitaxel](#). However, the Cancer Drugs Fund clinical lead explained the recent resource pressures that have resulted in the move to docetaxel use are likely to remain in chemotherapy units post-COVID-19 pressures. The clinical expert also noted that docetaxel would not be used if someone had had it before, but that a substantial number of people would be able to have it, and that its use was increasing. The company explained that atezolizumab combination was not used as a primary comparator because of the limited population overlap between the clinical trials. The clinical expert explained that atezolizumab combination would be used for people who are PD-L1 positive based on the IC PD-L1 measurement. The committee concluded

that the relevant comparators are paclitaxel, docetaxel and atezolizumab combination.

Clinical evidence

KEYNOTE-355 trial data excluding gemcitabine is appropriate for decision making

3.4 The clinical evidence was based on KEYNOTE-355, a randomised double-blind placebo-controlled active-comparator trial for people with untreated, triple-negative, locally recurrent unresectable or metastatic breast cancer. The trial protocol was updated to only include triple-negative breast cancer with a CPS of 10 or more, in line with the marketing authorisation. Chemotherapies included in the trial, either with pembrolizumab or placebo, were nab-paclitaxel, paclitaxel or gemcitabine plus carboplatin. Most (57%) people had gemcitabine plus carboplatin in KEYNOTE-355, but the company excluded this clinical trial data in the clinical and economic analysis. It only included the population who had a taxane (that is, paclitaxel or nab-paclitaxel). The company excluded the gemcitabine plus carboplatin data because this treatment would not be expected to be used in the UK setting. The committee recalled its conclusion that gemcitabine was not a relevant comparator (see section 3.3). The ERG noted that the baseline characteristics were stratified by chemotherapy combinations, so randomisation was not broken when the gemcitabine data was removed for the economic analysis. The committee concluded the trial data, excluding gemcitabine with or without carboplatin, was appropriate for decision making.

Pembrolizumab combination is more effective than paclitaxel or nab-paclitaxel but the long-term benefit is uncertain

3.5 KEYNOTE-355 compared pembrolizumab plus nab-paclitaxel, paclitaxel or gemcitabine and carboplatin compared with placebo plus nab-paclitaxel, paclitaxel or gemcitabine and carboplatin. However, only the clinical trial evidence for the taxane population was presented (the

evidence for gemcitabine and carboplatin was not included in the analysis; see section 3.4). The trial results showed a consistent clinically meaningful and statistically significant benefit for pembrolizumab combination compared with taxanes alone for both progression-free survival (exact progression-free survival results are considered confidential by the company and cannot not be reported here) and overall survival. The hazard ratio for overall survival was 0.54 (95% confidence interval, 0.36 to 0.82). The committee concluded that pembrolizumab combination is more effective than taxanes.

Indirect treatment comparison

The network meta-analysis results should be interpreted with caution

3.6 There is no head-to-head evidence comparing pembrolizumab combination with atezolizumab combination. Therefore, the company did a network meta-analysis to allow for an indirect treatment comparison. The network included 2 clinical trials, KEYNOTE-355 and IMpassion130. IMpassion130 was a double-blind randomised clinical trial comparing atezolizumab plus nab-paclitaxel with placebo plus nab-paclitaxel in people with triple-negative advanced breast cancer who had not had previous treatment for metastatic disease. The company noted there were systematic differences between the patient populations in the trials and that each connection in the network was only described by a single trial. The 2 trials also used different PD-L1 measurements based on the treatment being administered (see section 3.2). The ERG agreed that the network meta-analysis had limitations because of heterogeneity between trials. The committee concluded that the network meta-analysis was suitable for decision making given there was no other available data, but that the results should be interpreted with caution.

It is unclear whether pembrolizumab combination is more effective than atezolizumab combination

3.7 The company presented the results of the fixed-effect network meta-analysis because of the low number of studies in the network which meant the between study heterogeneity could not be estimated. This was because of the low number of studies in the network meta-analysis. The point estimates favoured pembrolizumab combination but had wide credible intervals that crossed 1, meaning that the results were not statistically significant. The exact results are considered confidential by the company so cannot be reported here. The ERG explained that it preferred a random-effects model because of the heterogeneity in the studies. The company did not provide random-effects network meta-analysis results after technical engagement, so the ERG could not include random effects in their preferred analysis. It noted that the choice of fixed effects compared with random effects was unlikely to influence the point estimates but would increase the credible intervals. As a scenario analysis, the ERG set the efficacy of pembrolizumab combination and atezolizumab combination to equal. The company explained that it thought this was overly simplistic and created the inappropriate assumption of transferability between the KEYNOTE-355 and IMpassion130 trial populations. The committee concluded that the relative efficacy of pembrolizumab combination compared with atezolizumab combination was uncertain.

Cost-effectiveness evidence

The company's economic model uses a standard approach

3.8 The company submitted a partitioned survival model to estimate the cost effectiveness of pembrolizumab combination compared with paclitaxel, docetaxel and atezolizumab combination. It had 3 health states: progression-free survival, post-progression survival and death. The committee considered that the partitioned survival model is a standard approach to estimate the cost effectiveness of cancer drugs.

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Exponential distribution for extrapolating overall survival better fitted the smoothed hazard plot

3.9 The company chose a log-normal model for pembrolizumab combination and log-logistic model for paclitaxel to extrapolate overall survival. It chose these curves based on goodness of fit statistics, clinical plausibility of long-term extrapolations and validity of long-term projections. The ERG agreed with the company's choice of log-logistic extrapolation for paclitaxel but preferred an exponential model for pembrolizumab combination. It explained that the goodness of fit statistics between the exponential and log-normal models both corresponded with the observed data. However, it noted that the log-normal distribution showed a turning point within the first year whereas the smoothed hazard plot of the observed data did not show a turning point in the underlying hazard. The exponential distribution did not have a turning point. Using the exponential distribution resulted in a substantial increase in the incremental cost-effectiveness ratio (ICER). The company disagreed with the choice of an exponential distribution. It stated that this was overly simple and assumed a constant hazard that was not seen in the trial. The committee concluded that both extrapolations broadly fitted the data, but that the exponential distribution better fitted the smoothed hazard plot.

Assuming that the time to treatment discontinuation (TTD) is the same for pembrolizumab and atezolizumab is over simplistic

3.10 An indirect treatment comparison was done because there was no direct head-to-head evidence comparing pembrolizumab combination with atezolizumab combination (see section 3.6). The company explained there was a lack of specific data for the CPS of 10 or more group in IMpassion130. Therefore, data from the indirect treatment comparison was not appropriate to estimate the TTD for atezolizumab combination. Instead, it assumed that the TTD for atezolizumab combination was equal to the TTD for pembrolizumab combination. The ERG explained that it preferred to apply the progression-free survival hazard ratio between

atezolizumab combination and pembrolizumab combination to the pembrolizumab combination TTD. It explained that it thought this was more appropriate than arbitrarily assuming the 2 TTDs were equal. This had the effect of increasing the ICER of pembrolizumab combination compared with atezolizumab combination. The committee concluded that assuming that the TTD was the same for pembrolizumab combination and atezolizumab combination was an over simplistic assumption. It thought that the TTD for atezolizumab combination was better estimated by applying the progression-free survival hazard ratio between atezolizumab combination and pembrolizumab combination to pembrolizumab combination TTD.

The duration of benefit for pembrolizumab combination should include an assumption that the treatment effect wanes after stopping treatment

3.11 In KEYNOTE-355, treatment was stopped after about 2 years. The stopping rule was not included in the marketing authorisation, but the company assumed a stopping rule would apply in line with the trial. The company assumed that, despite stopping treatment after a maximum of 2 years, the treatment benefit would be maintained for a lifetime horizon. It explained that this was because the unique mode of action of pembrolizumab results in an extended period of benefit after treatment has stopped. Also, KEYNOTE-355 showed no evidence of treatment benefit decreasing over the median follow-up duration (the exact follow-up period is considered confidential by the company and cannot be reported here). The company highlighted that, in [NICE's technology appraisal guidance on atezolizumab with nab-paclitaxel](#), a treatment waning effect was considered inappropriate. The committee recalled that, in this appraisal, there was no stopping rule and people could continue to have atezolizumab combination beyond 2 years. The ERG explained a lifetime treatment benefit created the possibility that 2 people alive at year 7 on third-line treatment would have different chances of death dependent on their first course of treatment. The committee considered that this was implausible and noted that, in some people who had pembrolizumab

combination in the trial, their cancer still progressed after 2 years. The ERG also noted that subsequent treatment use from KEYNOTE-355 showed that many people moved on to second-line treatment. Also, some people moved on to third- and fourth-line treatment during the trial follow-up period. The ERG preferred a treatment benefit duration of 5 years (3 years after treatment is stopped). It explained that KEYNOTE-355 did not provide long-term data to support a lifetime treatment benefit. The committee noted that, in the ERGs application of a 5-year treatment benefit, it assumed that all treatments under consideration (including atezolizumab combination) stopped working at 5 years. Because atezolizumab does not have a stopping rule, this may have underestimated the health outcomes of atezolizumab combination. However, this assumption was needed for the model structure because the atezolizumab combination overall survival is dependent on the pembrolizumab combination overall survival. This increased the ICER of pembrolizumab combination compared with all comparators. The committee noted a 5-year treatment effect had been used in previous technology appraisals for immuno-oncology drugs when a stopping rule applied. The committee concluded that a 5-year treatment effect with a 2-year stopping rule was appropriate for pembrolizumab combination.

Vial sharing should be included in the analysis

3.12 The company included vial sharing for intravenous drugs but not pembrolizumab and atezolizumab in its base case. It understood that vial sharing would be routine practice to minimise drug wastage. The ERG did not include vial sharing in its model, which had a small upward effect on the ICER. The clinical expert and Cancer Drugs Fund clinical lead explained that vial sharing does happen in clinical practice, and is particularly encouraged for expensive chemotherapies. The committee concluded that vial sharing should have been included in the analysis but noted that not doing this did not have a major effect on the cost-effectiveness estimates.

Using the time-to-death approach to estimate utilities is appropriate

3.13 The company used 2 methods to estimate utility in the economic model: the time-to-death approach and the health-state approach. The time-to-death approach categorises utility based on the length of time before death. The health-state approach categorises utilities based on the health states in the model (progression-free survival, post-progression, death). The company's base case used the time-to-death approach but the company stated that it did not have a preference for which approach should be used. It explained that it chose the time-to-death approach because it is most appropriate based on the aggressiveness of triple-negative breast cancer and had been accepted in NICE appraisals in other disease areas. The ERG noted both methods have their limitations. It explained that neither approach overcomes the main limitation that the data collected has been heavily censored, either at the point of progression, or at treatment discontinuation. The ERG also stated that it had no preference for which approach was used. However, it noted that the health-state approach consistently had slightly higher ICERs than the time-to-death approach. The committee concluded that both approaches were acceptable, but that it would consider the time-to-death approach in its decision making based on the aggressiveness of triple-negative breast cancer.

End of life

The extension-to-life criterion is likely to be met for taxanes, but is uncertain for atezolizumab combination

3.14 The committee considered the advice about life-extending treatments for people with a short life expectancy in [NICE's guide to the methods of technology appraisal](#). The ERG agreed with the company that the extension-to-life criterion was met for taxanes. However, it noted that the atezolizumab combination life-expectancy estimates were based on the network meta-analysis, which was uncertain (see section 3.6). The ERG also noted that atezolizumab combination improved life expectancy. The

committee concluded that the extension-to-life criterion was met for pembrolizumab combination compared with taxanes, and may be met compared with atezolizumab combination based on point estimates. However, it recalled its conclusion that it was unclear whether pembrolizumab combination is more effective than atezolizumab combination because of uncertainty in the indirect comparison.

The company does not make a robust case for the short life-expectancy criterion

3.15 The ERG disagreed with the company that the short life-expectancy criterion was met. The company's base-case model estimated that the average life expectancy was longer than 24.0 months for taxanes at 27.7 months, atezolizumab combination at 30.4 months and pembrolizumab combination at 54.5 months. The committee also considered overall survival at 24.0 months in KEYNOTE-355 to assess whether the short life-expectancy criterion was met. It appreciated that a large proportion of people in the placebo arm had an overall survival of less than 24.0 months. The exact overall survival numbers are confidential and cannot be reported here. The clinical expert explained that, in some people, there is a prolonged response to standard therapies. The committee appreciated that, when the whole population was modelled over a lifetime horizon (not just over the trial follow up), having people who survived a long time would make the mean estimates higher than the median in the trial. The committee noted that this effect would apply to all survival estimates, including the treatment arm. This meant that the mean modelled overall survival in the treatment arm would also be longer than might be predicted based on the Kaplan–Meier curves, in this case 54.5 months. The committee was aware that all sources of evidence should be considered. It also recalled that the short life-expectancy criterion was met in [NICE's technology appraisal guidance on atezolizumab with nab-paclitaxel](#). The life-expectancy estimates in the modelling in that appraisal were 13.8 months for paclitaxel and 14.3 months for docetaxel. This was around half that projected in the

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pembrolizumab model for a virtually identical population. Because of this difference, the committee questioned the validity of the company's pembrolizumab model results and whether they were suitable for decision making. The committee noted that the most logical approach would be to accept the company's economic model outputs as accurate, and the same evidence source for both end of life criteria. But noted that doing this would mean the short life-expectancy criterion was not met. It agreed that the company should further explore the validity of the economic model outputs, particularly the life-expectancy estimates. After considering the data presented to it, the committee concluded that a robust case for the end of life criteria and had not been made.

Cost-effectiveness results

The cost-effectiveness estimates are higher than what NICE considers a cost-effective use of NHS resources

3.16 [NICE's guide to the methods of technology appraisal](#) notes that above a most plausible ICER of £20,000 per quality-adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. Because of confidential commercial arrangements for pembrolizumab, atezolizumab, nab-paclitaxel and post-progression therapies, the ICERs are confidential and cannot be reported here. The committee noted that neither the company's nor ERG's base cases fully met the committee preferences of:

- overall survival extrapolations based on the exponential function (see section 3.9)
- estimating TTD for atezolizumab combination by applying the progression-free survival hazard ratio between atezolizumab

combination and pembrolizumab combination to pembrolizumab combination TTD (see section 3.10)

- a 5-year treatment benefit duration for pembrolizumab combination (see section 3.11)
- including vial sharing (see section 3.12)
- utilities based on the time-to-death approach (see section 3.13).

There was also a significant uncertainty about the relative effectiveness of pembrolizumab and atezolizumab combinations. The committee stated they would also like to see:

- additional model validity analysis (see section 3.14)
- exploration of how the short life-expectancy end of life criterion could be met, including a clear justification of why the company's model estimates of 27.7 months and 30.4 months should not be used to define eligibility for the 24.0-month end of life criterion, when the cost-effectiveness results are based on these model outputs (see section 3.14).

Taking into account all confidential discounts, the committee noted that the company's base-case ICER compared with taxanes was above £30,000 per QALY gained, and compared with atezolizumab combination was above £20,000 per QALY gained. If all the suggested adjustments were incorporated, the ICERs would be much higher. The committee concluded that the cost-effectiveness estimates for pembrolizumab combination compared with taxanes and atezolizumab combination were higher than what NICE considers a cost-effective use of NHS resources. Therefore, the committee did not recommend pembrolizumab combination for use in the NHS.

Innovation

Pembrolizumab combination improves the treatment options for triple-negative breast cancer

- 3.17 Until recently, there have been limited treatment options for triple-negative breast cancer compared with other types of breast cancer.
- Pembrolizumab combination provides benefit for triple-negative breast cancer in people whose tumours express PD-L1 with a CPS of 10 or more. The committee concluded that pembrolizumab combination has potential benefits for people with triple-negative breast cancer, and that the health-related quality of life gains had been captured in the QALY calculations.

4 Proposed date for review of guidance

- 4.1 NICE proposes that the guidance on this technology is considered for review 3 years after publication of the guidance. NICE welcomes comment on this proposed date. NICE 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

March 2022

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.

Sarah Wilkes

Technical lead

Alexandra Filby

Technical adviser

Thomas Feist

Project manager

ISBN: [to be added at publication]