NICE National Institute for Health and Care Excellence

NICE guidance

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

Technology appraisal guidance
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Contents

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1 Recommendations

1.1 Pembrolizumab plus chemotherapy (paclitaxel or nab-paclitaxel) is recommended as an option for treating triple-negative, locally recurrent unresectable or metastatic breast cancer in adults who have not had chemotherapy for metastatic disease. It is recommended only if:

- the tumours express PD-L1 with a combined positive score (CPS) of 10 or more and an immune cell staining (IC) of less than 1%, and
- the company provides pembrolizumab according to the commercial arrangement.

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

Treatment for untreated, triple-negative, locally recurrent unresectable or metastatic breast cancer includes chemotherapy such as docetaxel or paclitaxel, or atezolizumab plus nab-paclitaxel immunotherapy (from now, atezolizumab combination). There is an unmet need for alternative treatments for people who cannot have atezolizumab combination. Pembrolizumab plus paclitaxel or nab-paclitaxel (from now, pembrolizumab combination) is another immunotherapy that could be used. The company proposed pembrolizumab combination for people whose tumours express PD-L1 with a CPS of 10 or more and an IC of less than 1%. This is narrower than the marketing authorisation and makes pembrolizumab combination an alternative treatment for people who cannot have atezolizumab combination.

Clinical trial evidence shows that, compared with paclitaxel, pembrolizumab combination increases how long people have before their cancer gets worse and how long they live.

The cost-effectiveness estimates for pembrolizumab combination compared with both

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paclitaxel and docetaxel are within what NICE usually considers an acceptable use of NHS resources. Therefore, it is recommended.

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2 Information about pembrolizumab

Marketing authorisation indication

2.1 Pembrolizumab (Keytruda, Merck Sharp and 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 more than or equal to 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 for pembrolizumab.

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. 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.

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3 Committee discussion

The appraisal committee considered evidence submitted by Merck Sharp and 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 called 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 it can be very difficult to cope with the uncertainty of the outcome. People with locally recurrent unresectable and metastatic breast cancer must also organise their lives around hospital appointments, which restricts 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. The committee concluded that there is a high disease burden for people with triple-negative breast cancer (TNBC).

There is a need for first-line TNBC treatments, particularly for people who cannot have atezolizumab combination

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-

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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 guideline on advanced breast cancer: diagnosis and treatment). 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 not be able to have atezolizumab combination but 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. The PD-L1 expression for pembrolizumab combination 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). Both measurements use slightly different methods for 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 of the measurements would show PD-L1 positivity. The clinical expert and Cancer Drugs Fund clinical lead explained that the measurement used would vary between hospital trusts. They explained that trusts are likely to adopt one measurement in the first instance and only use the other if the first did not show PD-L1 positivity. The patient expert highlighted that, because of the differences in PD-L1 measurements, there is an unmet need for immunotherapy for people who cannot have atezolizumab combination. They explained that pembrolizumab combination could be a critical option for these people. The committee concluded that there is an unmet need for immunotherapy for untreated, triple-negative, locally recurrent unresectable or metastatic breast cancer, especially for people who cannot have atezolizumab combination.

Atezolizumab combination is not included as a comparator in the company's updated cost-effectiveness analyses, but additional testing costs need to be accounted for in the economic model

3.3 In its initial submission, the company included atezolizumab combination

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as a comparator. At the first committee meeting, the committee agreed atezolizumab combination was a relevant comparator for tumours that express PD-L1 with an IC more than 1% and CPS of 10 or more. In its response to consultation, the company did not include a comparison with atezolizumab combination. Instead, the company submitted updated cost-effectiveness results only for people whose tumours have an IC less than 1% and CPS of 10 or more. This is the group of people for whom atezolizumab combination is not indicated. The company explained that they chose to focus on this population because they recognised its high unmet need. It estimated this population would comprise approximately 17% of people with metastatic TNBC. The ERG highlighted that the removal of atezolizumab combination resulted in an underestimation of CPS and IC testing costs in the company model, because both tests would have to be done for some people. The Cancer Drugs Fund clinical lead explained that it will be difficult for pathology departments to do both tests and that the cost of both should be included in the economic model. The committee acknowledged the challenge for pathology departments with backlogs following the COVID-19 pandemic but noted that NHS implementation is beyond its remit. The ERG also cautioned that the company assumed the efficacy data from the trial using a CPS of 10 or more is generalisable to the more limited population. It explained that this added additional uncertainty. The Cancer Drugs Fund clinical lead explained that it is unknown if the trial data from the population with a CPS of 10 or more is generalisable to the proposed population. Therefore, they agreed with the ERG that it would have to be treated as an uncertainty. The committee agreed that the population the company had focused on had the greatest unmet need, but that increased testing costs would need to be accounted for in the economic model.

The relevant comparators are paclitaxel and docetaxel

3.4 In its initial submission, the company used paclitaxel as its base-case comparator, docetaxel as a secondary comparator, 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 as a first-line treatment for metastatic disease. This is because it is difficult to

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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 and increasing number of people would be able to have it. In its response to consultation, the company explained that pembrolizumab combination is disadvantaged by using docetaxel as a comparator. This is because the company assumed docetaxel has the same efficacy as paclitaxel despite docetaxel having a worse safety profile and potentially a shorter treatment response. As an alternative, the company presented a blended comparator cost-effectiveness estimate where it assumed 70% of people are treated with paclitaxel and 30% of people are treated with docetaxel. This was estimated using clinical opinion and KEYNOTE-355 data. The Cancer Drugs Fund clinical lead explained that the ratio of paclitaxel to docetaxel use is continually changing because chemotherapy units are trying to minimise the number of visits people make. He estimated approximately 50% of people would be treated with paclitaxel and 50% of people would be treated with docetaxel. The ERG explained it preferred a fully incremental analysis where the 3 treatments were ranked individually rather than a blend of 2 comparators because it can improve the efficient allocation of resources. It also noted that it would have preferred the toxicity and potentially shorter treatment duration of docetaxel to have been included in the economic model, instead of a blend of 2 comparators assumed to be the same apart from cost. The committee acknowledged the blended comparator estimates but noted

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that a fully incremental analysis against paclitaxel and docetaxel was more methodologically robust. The committee concluded the blended comparator cost-effectiveness estimate was not appropriate. It also concluded that the relevant comparators are paclitaxel and docetaxel but that the cost-effectiveness estimates compared with docetaxel are potentially unfavourable to pembrolizumab combination. This was because of the company assumption that paclitaxel and docetaxel have the same efficacy.

Clinical evidence

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

3.5 The clinical evidence was based on KEYNOTE-355, a randomised double-blind placebo-controlled active-comparator trial in people with untreated, triple-negative, locally recurrent unresectable or metastatic breast cancer. The trial protocol was updated to only include TNBC with a CPS of 10 or more, which is 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. The committee recalled its conclusion that gemcitabine was not a relevant comparator (see section 3.4). 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 recalled that the company assumed the trial data for CPS of 10 or more was generalisable to the proposed population (see section 3.3). 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

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nab-paclitaxel

3.6 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 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 noted the long-term benefit of pembrolizumab combination was uncertain. In response to consultation, the company provided additional explanations and clinical opinion to demonstrate the long-term benefit of pembrolizumab combination. The company clinical experts estimated 20% survival at year 5 and 10% survival at year 10 for those having pembrolizumab combination. By contrast, they estimated survival of 10% at year 5 and 0% at year 10 for those having paclitaxel or docetaxel. The committee concluded that pembrolizumab combination is more effective than taxanes.

Indirect treatment comparison

The comparison with atezolizumab combination using a network meta-analysis is no longer needed for decision making

3.7 In the company's initial submission, atezolizumab combination was a secondary comparator. 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 company presented the results of the fixed-effect network meta-analysis because of the small number of studies in the network, which meant the between study heterogeneity could not be estimated. The point estimates favoured pembrolizumab combination but had wide credible intervals that crossed 1, meaning that the results were not statistically significant. The ERG considered that the network meta-analysis had limitations because of heterogeneity between trials and would have preferred a random-effects model. In response to consultation, the company removed atezolizumab combination as a comparator because it proposed that pembrolizumab should be used in a

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population for which atezolizumab was not indicated (IC less than 1% and CPS of 10 or more). The committee concluded the network meta-analysis results were no longer needed for decision making in this population.

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.

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

3.9 The company chose a log-normal model for pembrolizumab combination and a 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. It noted that the log-normal distribution showed a turning point within the first year, but 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. In response to consultation, the company further cautioned against over-interpreting smoothed hazard plots. The company explained that the lack of turning point could be because of the method used to

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generate the 'smoothed' hazard plot or the small sample size. It highlighted that NICE Decision Support Unit technical support document 14 states goodness-of-fit should not be measured by hazard plots but instead by using the survival curves. The ERG maintained its view that the exponential is the most appropriate extrapolation. It explained the constant hazard is in keeping with the observed hazards from KEYNOTE-355 and that the lack of observed turning point could be because there is no turning in the true distribution. The committee concluded that both extrapolations broadly fitted the data, but that the exponential distribution better fitted the smoothed hazard plot.

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

3.10 In KEYNOTE-355, treatment was stopped after about 2 years. A 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 depending 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

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treatment during the trial follow-up period. The ERG preferred a total 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. This increased the ICER of pembrolizumab combination compared with all comparators. The committee noted a 5-year treatment effect had been used in previous appraisals of immuno-oncology drugs when a stopping rule applied. In response to consultation, the company explained that an abrupt treatment-effect stop at a specific timepoint, as suggested by the ERG, was not clinically plausible. The company therefore presented an alternative scenario using the Surveillance, Epidemiology and End Results (SEER) program. This assumed a constant hazard rate for 4 years across both pembrolizumab combination and taxanes, which results in gradual treatment waning adjustments being made from 4 years onwards using the SEER data. The ERG explained that the SEER program is a US database that is unlikely to include a large proportion of patients treated with pembrolizumab combination. It also explained that this method of waning lacks face validity because the cost-effectiveness estimates decreased compared with no treatment waning. The committee concluded that there is a lack of clear evidence to predict a precise waning of effect. But a waning effect had been assumed in previous appraisals and was more plausible than a continuing effect long after treatment was stopped, even if the disease had progressed. It concluded that a 5-year treatment effect combined with the 2-year stopping rule was appropriate for pembrolizumab combination.

Vial sharing should be included in the analysis

3.11 The company included vial sharing for intravenous drugs but not pembrolizumab in its base case. Pembrolizumab is given in fixed doses, so vial sharing does not apply. It understood that vial sharing would be routine practice to minimise drug wastage of intravenous drugs. 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 be included in the analysis.

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

3.12 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 and 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 TNBC and had been used in other NICE appraisals. 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 TNBC.

The economic model is suitable for decision making

3.13 When considering the end of life criteria, the committee recalled that the life expectancy in NICE's technology appraisal guidance on atezolizumab with nab-paclitaxel was around half that projected in the pembrolizumab model for a similar population (see section 3.14). The committee therefore questioned the validity of the company's pembrolizumab model results and whether they were suitable for decision making. In its response to consultation, the company explained that these differences could be due to differences in trial design, population characteristics and alternative survival extrapolation assumptions. The company also used published studies and clinical opinion to validate survival predictions in the economic model. Median overall survival in the published studies ranged from 14.3 months to 21.3 months. The percentage of survivors at 2 years in the real-world evidence ranged from 12.1% to 36.58%. Overall

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survival and percentage survivorship from KEYNOTE-355 and the economic model are considered confidential by the company so cannot be reported here. It concluded that the model accurately predicts short- to medium-term taxane overall-survival projections and longer-term overall survival based on a 12-year study. The committee concluded that the economic model was suitable for decision making.

End of life

Pembrolizumab combination meets end of life criteria

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 pembrolizumab combination compared with taxanes. The ERG disagreed with the company that the short life-expectancy criterion was met. The company's base-case model estimated that the mean 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 considered confidential by the company 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

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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 pembrolizumab model for a similar population. In response to consultation, the company explored the mean, median and 2-year survivorship in this submission and NICE's technology appraisal guidance on atezolizumab with nab-paclitaxel. It explained that median survival demonstrated a high level of consistency in modelled short-term predictions. The exact numbers are considered academic in confidence by the company and cannot be reported here. The company explained that the end of life estimate for taxanes produced by the model should be considered an upper estimate of the mean survival for this very aggressive type of cancer. The ERG cautioned that the longer life expectancy shown in KEYNOTE-355 may be due to the study recruiting healthier patients. The committee considered that as the trial population is mainly younger people this could skew the estimates because they would have fewer co-morbidities, and possibly therefore live longer with their cancer. The committee considered the appeal outcome of NICE's technology appraisal guidance on avelumab, which stated that 'normally less than 24 months' allowed a committee discretion to apply end of life criteria even if it felt some measures of life expectancy may be over 24 months. Based on the percentage survival at 24 months in KEYNOTE-355, the real-world evidence and the observed and modelled medians, the committee concluded that survival is normally less than 24 months for the population treated with taxanes. Therefore, the committee accepted that the end of life criteria had been met.

Cost-effectiveness results

Pembrolizumab combination is a cost-effective use of NHS resources

3.15 As there are confidential commercial arrangements for pembrolizumab, nab-paclitaxel and post-progression therapies, the ICERs are confidential and cannot be reported here. The company addressed several of the committee's concerns in its response to consultation, including model validation and survival estimates. However, the committee noted the

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company's updated base case was not fully aligned with its preferences and instead considered the following ERG scenarios in its decision making:

- overall-survival extrapolations based on the exponential function (see section 3.9)
- a 5-year treatment benefit duration for pembrolizumab combination (see section 3.10)
- the inclusion of vial sharing (see section 3.11)
- utilities based on the time-to-death approach (see section 3.12).

Taking into account all confidential discounts, the committee concluded that the cost-effectiveness estimates for pembrolizumab combination compared with paclitaxel and docetaxel were within the range NICE considers a cost-effective use of NHS resources.

Innovation

Pembrolizumab combination improves the treatment options for TNBC

3.16 Until recently, there have been limited treatment options for TNBC compared with other types of breast cancer. Pembrolizumab combination provides benefit for people with TNBC whose tumours express PD-L1 with an IC of less than 1% and a CPS of 10 or more. The committee concluded that pembrolizumab combination has potential benefits for people with TNBC who cannot have atezolizumab combination, and that the health-related quality-of-life gains had been captured in the quality-adjusted life year calculations.

Conclusion

3.17 Having concluded that pembrolizumab combination is a cost-effective use of NHS resources for tumours that express PD-L1 with a CPS of 10 or more and an IC less than 1%, the committee recommended it for routine

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use in the NHS.

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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 clinical commissioning groups, 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 untreated, triple-negative, locally recurrent unresectable or metastatic breast cancer and the doctor responsible for their care thinks that pembrolizumab plus paclitaxel or nab-paclitaxel is the right treatment, it should be available for use, in line with NICE's

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recommendations.

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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

Rufaro Kausi
Technical adviser

Thomas Feist
Project manager

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