NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy for untreated HER2-negative advanced gastric or gastro-oesophageal junction adenocarcinoma

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

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

The evaluation 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 age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

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Note that this document is not NICE's final guidance on pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy in the NHS in England.

For further details, see NICE's manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 26 March 2024
- Second evaluation committee meeting: 9 April 2024
- Details of the evaluation committee are given in section 4

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1 Recommendations

- 1.1 Pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy is not recommended, within its marketing authorisation, for untreated HER2-negative locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma in adults whose tumours express PD-L1 with a combined positive score (CPS) of 1 or more.
- 1.2 This recommendation is not intended to affect treatment with pembrolizumab with platinum- and fluoropyrimidine-based 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

Usual treatment for HER2-negative locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma that express PD-L1 with a CPS of 1 or more is platinum- and fluoropyrimidine-based chemotherapy (doublet chemotherapy). Treatment for advanced gastric or gastro-oesophageal junction adenocarcinoma that expresses PD-L1 with a CPS of 5 or more is nivolumab plus doublet chemotherapy.

Clinical trial evidence shows that pembrolizumab plus doublet chemotherapy increases how long people live and how long they have before their condition gets worse compared with placebo plus doublet chemotherapy, in people whose tumours express PD-L1 with a CPS of 1 or more.

Pembrolizumab plus doublet chemotherapy has not been directly compared in a clinical trial with nivolumab plus doublet chemotherapy. An indirect comparison suggests that it is likely to work as well as nivolumab for people whose tumours express PD-L1 with a CPS of 5 or more.

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Even when considering the condition's severity, and its effect on quality and length of life, the most likely cost-effectiveness estimates for pembrolizumab plus doublet chemotherapy compared with doublet chemotherapy alone are above the range that NICE considers an acceptable use of NHS resources. The cost-effectiveness estimates compared with nivolumab plus doublet chemotherapy are also above the range. So, pembrolizumab plus doublet chemotherapy is not recommended.

2 Information about pembrolizumab

Marketing authorisation indication

2.1 Pembrolizumab (Keytruda, Merck Sharp and Dohme) 'in combination with fluoropyrimidine and platinum-containing chemotherapy, is indicated for the first-line treatment of locally advanced unresectable or metastatic HER2-negative gastric or gastro-oesophageal junction adenocarcinoma in adults whose tumours express PD-L1 with a CPS ≥1'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the <u>summary of product</u> characteristics for pembrolizumab.

Price

- 2.3 The list price of pembrolizumab is £2,630 for a 100 mg per 4 ml concentrate for solution for infusion vial (excluding VAT; BNF online accessed February 2024)
- 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.

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3 Committee discussion

The <u>evaluation committee</u> considered evidence submitted by Merck Sharp and Dohme, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the <u>committee papers</u> for full details of the evidence.

The condition

Details of condition

3.1 The patient experts explained that the symptoms of gastric or gastrooesophageal junction (GOJ) cancer have a substantial impact on quality of life. Symptoms of the condition may include indigestion, poor appetite or early satiety, weight loss and abdominal pain. The patient expert noted that symptoms can cause eating and swallowing difficulties, which can lead to people needing a jejunostomy feeding tube as the condition advances. Side effects of current treatments, such as chemotherapies, can reduce the quality of life of those having treatment with them. The clinical and patient experts highlighted a particular unmet need in younger adults with gastric or GOJ cancer. Younger adults can have their nonspecific symptoms overlooked, which can lead to the condition being diagnosed at a later stage. A patient expert noted that younger adults with gastric or GOJ cancer may also particularly benefit from new technologies because they are more likely to be well enough to be able to cope with the treatment. If symptoms are present at the time of diagnosis, the cancer is often advanced and incurable, leading to poor survival prognosis. The committee concluded that the symptoms of gastric or GOJ cancer can have a considerable impact on quality of life and that life expectancy with the condition is poor. It noted that this may particularly be the case for younger adults who tend to be diagnosed when their cancer is more advanced.

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Clinical management

Treatment pathway and comparators

3.2 People with an Eastern Cooperative Oncology Group performance status score of 0 to 2 and no significant comorbidities may be offered doublet chemotherapy comprising fluoropyrimidine-based chemotherapy (fluorouracil or capecitabine) with platinum-based chemotherapy (cisplatin or oxaliplatin). They can also be offered triplet chemotherapy comprising fluorouracil or capecitabine with cisplatin or oxaliplatin plus epirubicin (see NICE's guideline on oesophago-gastric cancer: assessment and management in adults). In previous technology appraisals for this condition, it has been noted by clinical experts that in practice, triplet chemotherapy is not standardly used in the NHS because it increases toxicity without increasing the clinical effectiveness of the chemotherapy. The committee heard from the clinical expert that each of the doublet chemotherapy combinations are considered clinically equivalent. The choice of chemotherapy may depend on whether it is an oral or intravenous treatment (because some people with gastric or GOJ cancer may have difficulty swallowing), the adverse effects and how often the doses are administered. Nivolumab plus platinum- and fluoropyrimidinebased chemotherapy (nivolumab plus doublet chemotherapy) is recommended for people with untreated HER2-negative, advanced or metastatic gastric, GOJ or oesophageal adenocarcinoma in adults whose tumours express PD-L1 with a combined positive score (CPS) of 5 or more (see NICE technology appraisal guidance on nivolumab with platinum- and fluoropyrimidine-based chemotherapy for untreated HER2negative advanced gastric, gastro-oesophageal junction or oesophageal adenocarcinoma). Pembrolizumab plus platinum- and fluoropyrimidinebased chemotherapy (pembrolizumab plus doublet chemotherapy) is indicated within its marketing authorisation for gastric or GOJ adenocarcinoma in people whose tumours express PD-L1 with a CPS of 1 or more. The committee noted that NICE's technology appraisal

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guidance on pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy for untreated advanced oesophageal and gastrooesophageal junction cancer recommends pembrolizumab plus doublet chemotherapy as an option for treating oesophageal or GOJ adenocarcinoma in people whose tumours express PD-L1 with a CPS of 10 or more, but that the indication in the marketing authorisation for GOJ adenocarcinoma has changed since that guidance was published. This means that this evaluation will replace that guidance for people with GOJ adenocarcinoma. The committee noted that current NICE guidance for immunotherapy treatment (nivolumab and pembrolizumab) for people with gastric and GOJ cancer does not apply to people whose tumours express PD-L1 with a CPS between 1 and 4. The committee agreed there is a particular unmet need for this group. In its submission, the company presented a comparison with doublet chemotherapy as the only comparator for people whose tumours express PD-L1 with a CPS of 1 or more. The committee agreed that this would be the relevant comparator for people whose tumours express PD-L1 with a CPS between 1 and 4, because in clinical practice these people do not currently have access to immunotherapy. Nivolumab plus doublet chemotherapy was the comparator for people whose tumours express PD-L1 with a CPS of 5 or more. The committee concluded that doublet chemotherapy and nivolumab plus doublet chemotherapy are appropriate comparators for this evaluation.

Clinical effectiveness

Clinical trial evidence

3.3 Clinical evidence for pembrolizumab plus doublet chemotherapy compared with placebo plus doublet chemotherapy is from KEYNOTE-859. This was an international, phase 3, randomised, double-blind, placebo-controlled trial, that included people with HER2-negative, previously untreated, unresectable or metastatic gastric or GOJ adenocarcinoma. The relevant data came from the subgroup of people

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whose tumours express PD-L1 with a CPS of 1 or more (from now, the CPS of 1 or more subgroup) because this group reflects the population for whom pembrolizumab plus doublet chemotherapy is licensed. The company presented the results of the first interim analysis (data cut-off October 2022) which had a median follow up of 11.9 months. For the CPS of 1 or more subgroup, pembrolizumab plus doublet chemotherapy significantly improved both progression-free survival (hazard ratio [HR] 0.72, 95% confidence interval [CI] 0.63 to 0.82; p<0.0001) and overall survival (HR 0.74, 95% CI 0.65 to 0.84; p<0.0001), compared with placebo plus doublet chemotherapy. The clinical expert stated that response to treatment is a key outcome. They added that this affects not only symptomatic relief and increased survival but may enable people whose cancer responds to treatment to be able to have cytotoxic chemotherapy for a shorter time. Pembrolizumab plus doublet chemotherapy increased the proportion of people who had a complete or partial response to treatment. In the pembrolizumab plus doublet chemotherapy arm 52.1% (95% CI 48.1 to 56.1) reached this secondary outcome compared with 42.6% (95% CI 38.7 to 46.6) in the placebo plus doublet chemotherapy arm. The committee was aware that longer-term follow up of KEYNOTE-859 (data cut August 2023) had become available, but the data had not been critiqued by the EAG or presented to the committee. This was because it was not available at the time of the company submission, or at the clarification stage, and this evaluation had proceeded without an additional technical engagement step. The committee concluded that pembrolizumab plus doublet chemotherapy was clinically effective compared with doublet chemotherapy alone. It concluded that it delays the time to cancer progression, increases the proportion of people whose cancer responds to treatment and improves overall survival.

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Network meta-analysis

3.4 No direct comparison data between pembrolizumab plus doublet chemotherapy and nivolumab plus doublet chemotherapy was available. So the company did a network meta-analysis (NMA) using data from KEYNOTE-859 for pembrolizumab plus doublet chemotherapy and CHECKMATE-649 for nivolumab plus doublet chemotherapy. CHECKMATE-649 was an international, randomised open-label placebocontrolled trial, that compared nivolumab plus doublet chemotherapy with placebo plus doublet chemotherapy. The trial population was similar to KEYNOTE-859 but also included people with unknown HER2 status and oesophageal adenocarcinoma. At the time of the original company submission no subgroup data was available for people who had pembrolizumab plus doublet chemotherapy and whose tumours express PD-L1 with a CPS of 5 or more (from now, the CPS of 5 or more subgroup). This is the population for whom nivolumab plus chemotherapy is a treatment option. The company provided an indirect comparison in people whose tumours express PD-L1 with a CPS of 10 or more (from now, the CPS of 10 or more subgroup), making the case that it expected the treatment effect in this group to be the same as the CPS of 5 or more subgroup. At the clarification stage, the company provided a post-hoc analysis for the CPS of 5 or more subgroup. But it did not consider the results to be statistically valid because this was not a pre-specified subgroup in KEYNOTE-859. It explained that the trial was stratified by having a positive PD-L1 CPS score (the CPS of 1 or more subgroup) or a CPS score of less than 1. It added that the trial was powered to detect any statistically significant differences between treatment arms in the CPS of 10 or more subgroup, which was a pre-specified subgroup. The committee noted that the CPS of 5 or more subgroup included more people than the CPS of 10 or more subgroup. So, it would expect the CPS of 5 or more subgroup to also be powered to detect any statistically significant differences between trial arms. The committee noted the EAG's concerns that published data on baseline characteristics was not available

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for CHECKMATE-649. So it was not possible to determine whether there were any differences in the baseline characteristics of people in each subgroup between the 2 clinical trials, which may have biased the results. The expert also highlighted that comparing pembrolizumab with nivolumab across CPS subgroups can be difficult because of different PD-L1 testing methods used in clinical practice. The test used to determine if a person can be treated with pembrolizumab is different to the test used for nivolumab and CPS scores are not equivalent across tests. The company used constant hazard ratios for the indirect comparison which assumes the proportional hazards assumption is met. The EAG commented that this approach was inconsistent with the company's proportional hazards test for the CPS of 1 or more subgroup and CPS of 5 or more subgroup. The company agreed with the EAG that using time-varying hazard ratios would have been more appropriate. The committee agreed that using time-varying hazard ratios would be its preferred method but that it was possible to reach a conclusion on the analyses using the company's approach. There were no statistically significant differences in overall survival or progression-free survival between pembrolizumab plus doublet chemotherapy and nivolumab plus doublet chemotherapy for the CPS of 1 or more subgroup or the CPS of 5 or more subgroup. There was no statistically significant difference in overall survival for the CPS of 10 or more subgroup. Progression-free survival was not reported for the CPS of 10 or more subgroup in CHECKMATE-649, so no comparison could be made. The company considers the exact results of the NMA to be confidential, so they cannot be reported here. Overall, the committee agreed with the company and EAG that the results were consistent across the subgroups. Taking into account any potential differences between the trials, the committee concluded that pembrolizumab plus doublet chemotherapy and nivolumab plus doublet chemotherapy are similarly effective at treating HER2-negative advanced gastric or GOJ adenocarcinoma in people whose tumours express PD-L1 with a CPS of 5 or more.

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Adverse events

3.5 The company suggested that any observed differences in the adverse event profiles for pembrolizumab and nivolumab from the trials are explained by the difference in their concomitant doublet chemotherapy. The clinical expert confirmed this assumption, noting that adverse events related to immunotherapy are the same between pembrolizumab and nivolumab and are manageable in clinical practice. The company also included a scenario that assumed that pembrolizumab and nivolumab adverse event profiles were equivalent, which had little impact on the incremental cost-effectiveness ratio (ICER). The committee concluded that pembrolizumab and nivolumab were similarly tolerable.

Economic model

Company's modelling approach

3.6 The company submitted a partitioned survival model to estimate the costeffectiveness of pembrolizumab plus doublet chemotherapy compared
with doublet chemotherapy alone (for the CPS of 1 or more subgroup) and
nivolumab plus doublet chemotherapy (for the CPS of 5 or more
subgroup). Data from the CPS of 10 or more subgroup was used as a
proxy to inform the CPS of 5 or more subgroup. It had 3 health states:
progression-free, progressed disease and death. The model included
survival curves for progression-free survival and overall survival which
were extrapolated beyond the trial period. The company and EAG used
the same methods for extrapolating beyond the trial period in their base
case and exploratory base case respectively. The committee
acknowledged that the partitioned survival model is a standard approach
to estimate the cost effectiveness of cancer medicines and considered it
to be appropriate for decision-making.

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Treatment effect waning

3.7 The company's economic model included a 35-cycle maximum treatment duration for pembrolizumab based on KEYNOTE-859. The company assumed that there was no treatment effect waning for pembrolizumab plus doublet chemotherapy in its base-case analysis. That is, that the treatment effect of pembrolizumab plus doublet chemotherapy would be maintained after stopping treatment rather than reducing over time (waning). The company noted that there was no clear evidence of treatment effect waning based on the independent estimation of survival curves for the intervention and comparator arms of the clinical trials. The company provided a scenario that applied gradual treatment effect waning 7 years after starting pembrolizumab plus doublet chemotherapy, that reduced to the same as the comparator arm over the next 2 years. The EAG commented that it was not reasonable to assume a lifetime treatment effect after pembrolizumab plus doublet chemotherapy has stopped. The EAG preferred to apply gradual treatment effect waning 5 years after starting treatment that reduced to the same as the comparator arm over the next 2 years. The company's and EAG's chosen timepoints for when treatment effect waning begins were influenced by treatment effect waning assumptions from previous technology appraisals. This included NICE's technology appraisal guidance on nivolumab with platinum- and fluoropyrimidine-based chemotherapy for untreated HER2negative advanced gastric, gastro-oesophageal junction or oesophageal adenocarcinoma. In the previous appraisal, the company preferred a treatment waning effect starting 6.5 years after starting treatment with nivolumab plus doublet chemotherapy, whereas the EAG preferred a treatment waning effect starting 5 years after starting treatment. For both assumptions, the hazard of dying became the same as the comparator arm at the point of treatment waning. The committee heard from the clinical expert that the available follow-up data is for less than 5 years. So there is no data to demonstrate whether the treatment effect of

pembrolizumab plus doublet chemotherapy is maintained in the longer
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term or not. They added that, for the 10 to 15% of people who have a complete response, treatment effect waning would not be expected. But, for people who have not had a response within 3 to 6 months, treatment effect waning would be expected as they would have moved on to less clinically effective follow-on treatments. The committee concluded that it was appropriate to apply treatment effect waning for pembrolizumab. It agreed that treatment effect waning starting either 5 years or 7 years after starting treatment and reducing to the same as the comparator after 2 years, were both plausible.

Chemotherapy time on treatment

3.8 In the company model, the costs for people having doublet chemotherapy were capped at 6 cycles in line with what the company reported as NHS clinical practice. In KEYNOTE-859, some people had doublet chemotherapy treatments for longer than 6 cycles. The EAG noted that capping doublet chemotherapy costs at 6 cycles does not account for the fact that overall survival and progression-free survival in both treatment arms were based on some people having some doublet chemotherapies for more than 6 cycles. The EAG noted that overall survival and progression-free survival in KEYNOTE-859 may have been higher than what would be observed in clinical practice. Clinical experts explained that there isn't a cap on doublet chemotherapy in clinical practice although treatment beyond 6 cycles would be rare. This is because the treatment effect of doublet chemotherapy past 6 cycles is modest. So clinicians will aim to prescribe doublet chemotherapy for the shortest course possible to give a response without toxicity. The clinical experts also noted that the number of cycles could be influenced by the adverse event profiles of different doublet chemotherapy combinations and the use of concomitant immunotherapies. The company stated that a scenario in which the cap on chemotherapy cycles was not applied had a minimal effect on the costeffectiveness results. The committee concluded that applying a cap of 6 cycles on the costs of doublet chemotherapy in the model was

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appropriate. So the company's method for modelling survival estimates reflected what would be expected in NHS practice.

Utility values

3.9 Utility values were estimated using EQ-5D data from the KEYNOTE-859 trial using 2 different approaches. In its base case the company used a time-to-death approach and presented a health state approach in scenario analyses. The time-to-death approach estimates utilities using time intervals that describe life expectancy rather than utility values associated with non-progressed and progressed disease. The company explained that because of the limited collection of assessments with cancer progression in KEYNOTE-859, health state utilities from the trial data may only reflect quality of life close to the time of cancer progression rather than the entirety of living with progressed cancer. The company considers the exact estimated utility values to be confidential, so they cannot be reported here. The EAG agreed that the time-to-death approach may be more appropriate to capture the quality of life for people with progressed cancer in this evaluation. The EAG also noted that using either a time-todeath or health state approach had a minimal effect on both the costeffectiveness results and the company's preferred base case. The committee concluded that using a time-to-death approach to estimate utilities based on KEYNOTE-859 was appropriate for decision making.

Severity

3.10 The committee considered the severity of the condition (the future health lost by people living with the condition and having standard care in the NHS). The committee may apply a severity modifier (a greater weight to quality-adjusted life years [QALYs]) if technologies are indicated for conditions with a high degree of severity. The company provided absolute and proportional QALY shortfall estimates in line with NICE's health technology evaluations manual. For the CPS of 1 or more subgroup, both the company's and EAG's shortfall analyses suggested that a severity

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weight of 1.2 should be applied to the QALYs. So the EAG applied a severity weight of 1.2 to the QALYs in its base-case analysis. But the company commented that the current evaluation would have met the endof-life criteria used in NICE's previous health technology evaluation methods. It added that at the time those methods were applicable, they would have allowed for up to a 1.7 severity weight to be applied to the QALYs. So the company applied a severity weight of 1.7 to the QALYs in its base-case analysis, despite its shortfall analysis suggesting a severity weight of 1.2. The committee was aware that the methods for assessing end-of-life criteria had been replaced with the methods for applying a severity modifier. This was to better reflect society's preferences on the value of treatments for severe conditions. For the CPS of 5 or more subgroup, both the company's and EAG's shortfall analyses suggested a severity weight was not applicable. The committee agreed that current NICE methods for health technology evaluation should be followed. So, the committee concluded that, for the CPS of 1 or more subgroup, a severity weight of 1.2 should be applied to the QALYs. The committee also concluded that, for the CPS of 5 or more subgroup, no severity weight should be applied to the QALYs.

Cost-effectiveness estimates

The committee's preferences and cost-effectiveness estimates

3.11 The cost-effectiveness estimates used by the committee for decision making took into account all of the available confidential discounts, including those for comparators and follow-up treatments. The exact estimates are confidential and cannot be reported here. In the population with CPS of 1 or more, the committee noted that the company's and EAG's base cases differed on which severity modifier was applied and the assumption of treatment effect waning. The committee preferred the model to include:

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- Gradual treatment effect waning that reduces to the same as the comparator arm over 2 years, applied to pembrolizumab plus doublet chemotherapy. In the absence of data to demonstrate otherwise, the committee agreed it was plausible that this may start 5 or 7 years after starting treatment (see section 3.7).
- A 1.2 QALY modifier for severity (<u>see section 3.10</u>).

For the population with a CPS of 1 or more, the company also calculated a cost-effectiveness estimate using a scenario analysis with a 1.2 QALY modifier for severity. Both this, and the EAG's base case were above £30,000 per QALY gained. For the population with a CPS of 5 or more the company's and EAG's base cases differed only in the application of a treatment waning assumption (for both arms). Both the company's and EAG's base cases were substantially above £30,000 per QALY gained. This reflected higher total costs of pembrolizumab plus doublet chemotherapy with relatively small modelled QALY gains compared with nivolumab plus doublet chemotherapy. The committee was satisfied that pembrolizumab plus doublet chemotherapy and nivolumab plus doublet chemotherapy were similarly effective (see section 3.4) and tolerated (see section 3.5). For the modelling, the committee stated that this meant that it was reasonable to consider that the QALYs were the same for the 2 treatments and to compare only the costs. So the committee stated that its preference would be for the company to present a cost-minimisation analysis for this subgroup.

Other factors

Equality

3.12 No equality issues were raised by the company, EAG or stakeholders.

The committee did not identify any equality issues.

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Conclusion

Recommendation

- 3.13 The committee was aware that the following company and EAG costeffectiveness estimates for pembrolizumab with doublet chemotherapy
 were above the range that NICE considers an effective use of NHS
 resources:
 - compared with doublet chemotherapy for the CPS of 1 or more subgroup, with a severity weight of 1.2 applied to the QALYs
 - compared with nivolumab plus doublet chemotherapy, for the CPS of 5 or more subgroup.

The committee recognised that there was an unmet need in those whose tumours express PD-L1 with a CPS between 1 and 4 (see section 3.2). Because pembrolizumab plus doublet chemotherapy was not cost effective in the CPS of 1 or more subgroup compared with doublet chemotherapy, the committee could not recommend it for people whose tumours express PD-L1 with a CPS between 1 and 4. It could also not recommend pembrolizumab plus doublet chemotherapy for people whose tumours express PD-L1 with a CPS of 5 or more because it was not cost effective in the CPS of 5 or more subgroup compared with nivolumab plus doublet chemotherapy. So, pembrolizumab plus doublet chemotherapy is not recommended for untreated HER2-negative advanced gastric or GOJ adenocarcinoma in adults whose tumours express PD-L1 with a CPS of 1 or more.

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4 Evaluation committee members and NICE project team

Evaluation committee members

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

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

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

Chair

James Fotheringham

Chair, technology appraisal committee A

NICE project team

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

Giacomo De Guisa

Technical lead

Mary Hughes

Technical adviser

Thomas Feist

Project manager

ISBN: [to be added at publication]

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