NICE National Institute for Health and Care Excellence

NICE guidance

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

Technology appraisal guidance
Published: 29 August 2024

www.nice.org.uk/guidance/ta997

Your responsibility

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

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

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

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

Contents

This guidance partially replaces TA737.

1 Recommendations

1.1 Pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy is recommended, within its marketing authorisation, as an option for untreated locally advanced unresectable or metastatic HER2-negative gastric or gastro-oesophageal junction adenocarcinoma in adults whose tumours express PD-L1 with a combined positive score (CPS) of 1 or more. Pembrolizumab is only recommended if the company provides it according to the commercial arrangement.

Why the committee made these recommendations

Usual treatment for locally advanced unresectable or metastatic HER2-negative gastric or gastro-oesophageal junction adenocarcinoma that expresses PD-L1 with a CPS of 1 to 4 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 have before their condition gets worse and how long they live 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.

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 within the range that NICE considers an acceptable use of NHS resources. Pembrolizumab plus doublet chemotherapy has similar costs to nivolumab plus doublet chemotherapy. So, pembrolizumab plus doublet chemotherapy is recommended.

2 Information about pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy

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 summary of product 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 June 2024).

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.

3 Committee discussion

The evaluation committee 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 committee papers for full details of the evidence.

The condition

Details of condition

3.1 Gastric and gastro-oesophageal junction (GOJ) adenocarcinomas are types of cancer. The patient experts explained that the symptoms of gastric or GOJ cancer have a substantial effect on quality of life. Symptoms may include indigestion, poor appetite or early satiety, weight loss and abdominal pain. A 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 non-specific symptoms that are not easily identified as cancer, which can lead to the condition being diagnosed at a later stage. A patient expert noted that younger adults may particularly benefit from new technologies because they are likely to be well enough to tolerate 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 effect 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.

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 a standard treatment in the NHS. This is 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 several factors. These include whether the treatment is oral or intravenous (because some people with gastric or GOJ cancer may have difficulty swallowing), the potential adverse effects and how often the doses are administered. Nivolumab plus platinum- and fluoropyrimidine-based chemotherapy (nivolumab plus doublet chemotherapy) is recommended for 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's technology appraisal guidance on nivolumab with platinum- and fluoropyrimidine-based chemotherapy for untreated HER2-negative advanced gastric, GOJ or oesophageal adenocarcinoma). 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 the subgroup of people whose tumours express PD-L1 with a CPS of 1 to 4. The committee also agreed that there was a particular unmet need for this group because there were no immunotherapy treatments recommended by NICE for people whose tumours express PD-L1 with a CPS of 1 to 4. 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 were 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 the KEYNOTE-859 trial. This was an international, phase 3, randomised, double-blind, placebo-controlled trial that included people with untreated, unresectable or metastatic HER2-negative gastric or GOJ adenocarcinoma. The relevant data came from the subgroup of people 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 October 2022) which had a median follow up of 11.9 months. For the CPS of 1 or more subgroup, pembrolizumab plus doublet chemotherapy statistically 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 whose cancer had a complete or partial response to treatment. In the pembrolizumab plus doublet chemotherapy arm 52.1% (95% CI 48.1 to 56.1) of people had cancer that reached this secondary outcome compared with 42.6% (95% CI 38.7 to 46.6) in the placebo plus doublet chemotherapy arm. As part of its response to draft guidance consultation, the company submitted results of the longer-term follow-up analysis (data cut August 2023). This analysis provided 10 months of data on progression-free survival and overall survival in addition to the interim analysis. The longer-term follow-up data also showed that for the CPS of 1 or more subgroup, pembrolizumab plus doublet chemotherapy statistically significantly improved both progression-free survival and overall survival, compared with placebo plus doublet chemotherapy. The committee concluded that pembrolizumab plus doublet chemotherapy was clinically effective compared with doublet chemotherapy alone. It concluded that it delayed the time to cancer progression, increased the proportion of people whose cancer responded to treatment and

improved overall survival.

PD-L1 with a CPS of 1 to 4 subgroup

3.4 The committee noted that the data for pembrolizumab plus doublet chemotherapy compared with doublet chemotherapy alone came from a broader group of people than would currently have doublet chemotherapy alone in clinical practice. That is, the CPS of 1 or more subgroup included people whose tumours express PD-L1 with a CPS of 5 or more, who would have nivolumab plus doublet chemotherapy. A consultee commented that people whose tumours have a higher PD-L1 CPS potentially benefit more from immunotherapies such as pembrolizumab. So, the CPS of 1 or more subgroup may overestimate the clinical effectiveness of pembrolizumab plus doublet chemotherapy compared with doublet chemotherapy alone, if applied specifically to people whose tumours express PD-L1 with a CPS of 1 to 4. The company commented that KEYNOTE-859 was not powered to detect statistically significant differences in the PD-L1 CPS 1 to 4 subgroup. It also noted that the clinical trial's randomisation would need to be broken to be able to do analyses on this subgroup. The committee acknowledged that there was a risk that analyses using the CPS of 1 or more subgroup may overestimate the effectiveness of pembrolizumab plus doublet chemotherapy compared with doublet chemotherapy alone. But it also agreed that doing further subgroup analyses for people whose tumours express PD-L1 with a CPS of 1 to 4 would be less methodologically robust and be subject to bias. The committee concluded that it was appropriate to have applied the results from the CPS of 1 or more subgroup for people with a CPS of 1 to 4, for the comparison with doublet chemotherapy alone. The committee agreed it would take into account the uncertainty around potential overestimation of treatment effect in its decision making.

Network meta-analysis

3.5 There was no available direct comparison data between pembrolizumab plus doublet chemotherapy and nivolumab plus doublet chemotherapy. 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 placebo-controlled 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. The company presented results for people whose tumours express PD-L1 with a CPS of:

- 1 or more (the CPS of 1 or more subgroup)
- 5 or more (a post-hoc subgroup in KEYNOTE-859; the CPS of 5 or more subgroup)
- 10 or more (the CPS of 10 or more subgroup).

In its response to draft guidance consultation, the company's updated analyses used data from the CPS of 5 or more subgroup in its base case and used the longer-term follow-up data. The committee noted the EAG's concerns at the first committee meeting, that published data on baseline characteristics was not available for CHECKMATE-649 in each subgroup. 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 clinical expert also highlighted that comparing pembrolizumab with nivolumab across subgroups defined by CPS can be difficult because of different PD-L1 testing methods used in clinical practice. The test that is used to determine if a person can have pembrolizumab is different to the test used for nivolumab and CPS scores are not equivalent across tests. The company used time-varying hazard ratios instead of constant hazard ratios because the trial data for pembrolizumab plus doublet chemotherapy compared with placebo plus doublet chemotherapy showed that a proportional hazards assumption for overall survival was not met. The company selected a first-order fractional polynomial model for overall survival and a second-order fractional polynomial model for progression-free survival. The committee was satisfied that these model selections were appropriate. 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 5 or more subgroup. The company considers the exact results of the NMA to be confidential, so they could not be reported

here. 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 advanced HER2-negative gastric or GOJ adenocarcinoma in people whose tumours express PD-L1 with a CPS of 5 or more.

Adverse events

3.6 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 very similar for pembrolizumab and nivolumab and are manageable in clinical practice. The company also included a scenario that assumed that pembrolizumab's and nivolumab's adverse event profiles were equivalent, which had little effect on the incremental cost-effectiveness ratio (ICER). The committee concluded that pembrolizumab and nivolumab were similarly tolerated.

Economic model

Company's modelling approach

3.7 The company submitted a partitioned survival model to estimate the cost effectiveness 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). 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. That is, in the CPS of 1 or more population, a 3-knot odds spline model for overall survival and a 2-knot hazards spline for

progression-free survival were used in both treatment arms. In the CPS of 5 or more subgroup, fractional polynomial models were used (see section 3.5). For the CPS of 5 or more subgroup the company presented both cost-utility results and a cost-minimisation analysis. The committee acknowledged that the partitioned survival model is a standard approach used to estimate the cost effectiveness of cancer medicines and considered it to be appropriate for decision making.

Treatment-effect waning

3.8 The company's economic model included a 35-cycle maximum treatment duration for pembrolizumab based on KEYNOTE-859. 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 EAG commented that it was not reasonable to assume a lifetime treatment effect after pembrolizumab plus doublet chemotherapy has stopped. 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 term or not. They added that, for the 10% to 15% of people whose cancer has a complete response, treatment-effect waning would not be expected. But for people whose cancer has not had a response within 3 to 6 months, treatment-effect waning would be expected because they would have moved on to less clinically effective follow-on treatments. For the CPS of 1 or more subgroup, the company assumed a gradual treatment-effect waning beginning 7 years after starting treatment that reduced to the same as the comparator arm over the next 2 years. This assumption was only applied to the proportion of people whose cancer did not have a complete response to pembrolizumab plus doublet chemotherapy in KEYNOTE-859. The company considers the exact percentage of people whose cancer did not have a complete response to be confidential, so it could not be reported here. The EAG was satisfied with this approach. It also noted that the impact of applying a treatment-effect waning assumption to all people (irrespective of response to treatment) had a minimal effect on the cost-effectiveness results. The company also provided scenario analyses in which treatment-effect waning began 6 years and 5 years after starting treatment. The company's chosen timepoints for when treatment-effect waning began 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 HER2-negative advanced gastric, GOJ or oesophageal adenocarcinoma. In that appraisal, the company preferred treatment-effect waning to start 6.5 years after starting treatment with nivolumab plus doublet chemotherapy. But the EAG preferred treatment-effect waning to start 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 concluded that it was appropriate to apply treatment-effect waning for pembrolizumab for the CPS of 1 or more subgroup. It agreed that scenarios in which waning starts at either 5 years, 6 years or 7 years after starting treatment and reduces to the same as the comparator after 2 years, were all plausible. For the CPS of 5 or more subgroup, the company assumed there was no treatment-effect waning for pembrolizumab plus doublet chemotherapy in its base-case analysis. The committee noted that if waning assumptions were applied to the pembrolizumab plus doublet chemotherapy arm and nivolumab plus doublet chemotherapy arm, they would likely cancel each other out. So, the committee concluded that treatment-effect waning did not need to be applied to the CPS of 5 or more subgroup.

Chemotherapy time on treatment

3.9 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 for more 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 doublet chemotherapy 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. The clinical expert 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 after 6 cycles is modest. So, healthcare professionals will aim to prescribe doublet chemotherapy for the shortest course possible to give a response without toxicity. The clinical expert 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 cost-effectiveness results. The committee concluded that applying a cap of 6 cycles on the costs of doublet chemotherapy in the model was appropriate. So the company's method for modelling survival estimates reflected what would be expected in NHS practice.

Utility values

3.10 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 the non-progressed and progressed condition. The company explained that there were a limited number of utility assessments for people with progressed cancer in KEYNOTE-859. So, 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 could not be reported here. The EAG agreed that the time-to-death approach may have been 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-to-death or health-state approach had a minimal effect on both the cost-effectiveness 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.

Cost-minimisation analysis

3.11 At the first committee meeting the committee concluded that pembrolizumab plus doublet chemotherapy is likely to have similar clinical effectiveness and tolerability to nivolumab plus doublet chemotherapy. So, it agreed that it may be relevant to include a cost-minimisation analysis for the CPS of 5 or more

subgroup. As part of its response to draft guidance consultation, the company submitted a cost-minimisation analysis for the CPS of 5 or more subgroup. The analysis used the longer-term follow-up data from KEYNOTE-859. Quality-adjusted life years (QALYs) were made equal in the pembrolizumab plus doublet chemotherapy arm and the nivolumab plus doublet chemotherapy arm. This reflected that the overall survival, progression-free survival and adverse events were all assumed to be equal in each of the treatment arms. Time on treatment was based on Kaplan–Meier data from KEYNOTE-859 and was also assumed to be the same in both treatment arms. Treatment costs in the pembrolizumab plus doublet chemotherapy arm were the same or lower than the treatment costs in the nivolumab plus doublet chemotherapy arm. Costs for managing the condition, adverse events, progression, subsequent treatments and end of life care were equivalent in both treatment arms. Before the second committee meeting, the company submitted a correction of a programming error in its cost-minimisation model that had underestimated the administration costs for nivolumab. The EAG confirmed that the correction was appropriate. The company also noted that the treatment administration costs for the pembrolizumab and doublet chemotherapy arm could be reduced by using a 6-weekly administration regimen. The committee concluded that the cost-minimisation analysis submitted by the company was appropriate.

Severity

3.12 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 greater weight to QALYs (a severity modifier) 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 weight of 1.2 should be applied to the QALYs. 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 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

3.13 The cost-effectiveness estimates used by the committee for decision making took into account all of the available confidential discounts, including those for the comparators and follow-up treatments. The company considers the exact estimates to be confidential so they could not be reported here. For the population with a CPS of 1 or more, the committee noted that the company's and EAG's base cases used the same assumptions. Also, both ICERs were within the range NICE usually considers a cost-effective use of NHS resources (between £20,000 and £30,000 per QALY gained). The committee noted that the company had updated its base case after the first meeting, to use longer follow-up data to inform its modelling and to adhere to the committee's preferred assumptions. The committee also noted that it was helpful to see all the treatment-effect waning scenarios presented by the company and EAG. The company's and EAG's cost-effectiveness estimates for different treatment-effect waning scenarios (see section 3.8) were all between £20,000 and £30,000 per QALY gained. The exact ICERs could not be reported here because they are considered confidential by the company. For the population with a CPS of 5 or more, the committee was satisfied that pembrolizumab plus doublet chemotherapy and nivolumab plus doublet chemotherapy were similarly effective (see section 3.5) and tolerated (see section 3.6). At the first committee meeting, the committee agreed that this meant it was reasonable to consider that the QALYs were the same for the 2 treatments and to compare only the costs for the modelling. As part of its response to draft guidance consultation, the company submitted a cost-minimisation analysis for the CPS of 5 or more subgroup (see section 3.11). The total costs of pembrolizumab plus doublet chemotherapy were the same or lower than nivolumab plus doublet chemotherapy over 2-year and 30-year time horizons. The exact costs could not be reported here because they are considered confidential by the company and included confidential comparator discounts.

Acceptable ICER

3.14 NICE's manual on health technology evaluations notes that, above a most plausible ICER of £20,000 per 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. But it will also take into account other aspects including uncaptured health benefits. The committee noted that there are no immunotherapy treatments recommend by NICE for people whose tumours express PD-L1 with a CPS of 1 to 4 (see section 3.2). So, it concluded that there is a particular unmet need for this group. The committee noted that a severity weight of 1.2 was applied to the QALYs for the CPS of 1 or more subgroup and took this into account. It also acknowledged that no severity weighting was applied to the QALYs for the CPS of 5 or more subgroup (see section 3.12). The committee noted there was uncertainty around potential overestimation of treatment effect for people whose tumours express PD-L1 with a CPS of 1 to 4 (see section 3.4). So, an acceptable ICER would be sufficiently below £30,000 to take into account the uncertainty around the exact treatment effect in the subgroup of people whose tumours express PD-L1 with a CPS of 1 to 4. For the CPS of 1 or more subgroup, the committee concluded that an acceptable ICER would be towards the upper end of the range NICE considers a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained). For the subgroup of people whose tumours express PD-L1 with a CPS of 5 or more, in a cost-minimisation analysis pembrolizumab would have to have the same or lower costs than nivolumab to be considered a cost-effective use of NHS resources.

Other factors

Equality

3.15 No equality issues were raised by the company, EAG or stakeholders. The committee did not identify any equality issues.

Conclusion

Recommendation

3.16 The committee was aware that for the CPS of 1 or more subgroup, the company's and EAG's cost-effectiveness estimates for pembrolizumab with doublet chemotherapy compared with doublet chemotherapy alone were within the range that NICE considers an acceptable use of NHS resources. The committee noted that the company's and EAG's cost-effectiveness estimates for pembrolizumab plus doublet chemotherapy compared with nivolumab plus doublet chemotherapy in the CPS of 5 or more subgroup were cost effective. This was because pembrolizumab plus doublet chemotherapy had the same or lower costs than nivolumab plus doublet chemotherapy in the cost-minimisation analysis. So, the committee concluded that pembrolizumab plus doublet chemotherapy is recommended for untreated locally advanced unresectable or metastatic HER2-negative gastric or GOJ adenocarcinoma in adults whose tumours express PD-L1 with a CPS of 1 or more.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation 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 cost comparison evaluation), at which point funding will switch to routine commissioning budgets. The NHS England 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 guidance 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 draft guidance.

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 locally advanced unresectable or metastatic HER2-negative gastric or gastro-oesophageal junction adenocarcinoma and the healthcare professional responsible for their care thinks that pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy is the right treatment, it should be available for use, in line with NICE's recommendations.

5 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 committee A.

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

Chair

Radha Todd and James Fotheringham
Chairs, 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

Janet Robertson
Associate director

ISBN: 978-1-4731-6451-2