

Pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy for untreated advanced oesophageal and gastro- oesophageal junction cancer

Technology appraisal guidance

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Your responsibility

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

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

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

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

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This guidance is partially replaced by TA997.

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 carcinoma of the oesophagus in adults whose tumours express PD-L1 with a combined positive score (CPS) of 10 or more. Pembrolizumab is only recommended if the company provides it according to the [commercial arrangement](#).

The recommendation for HER2-negative gastro-oesophageal junction adenocarcinoma has been updated and replaced by [NICE technology appraisal guidance on pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy for untreated advanced HER2-negative gastric or gastro-oesophageal junction adenocarcinoma](#).

Why the committee made these recommendations

Treatment for advanced oesophageal cancer or HER2-negative gastro-oesophageal junction adenocarcinoma includes platinum- and fluoropyrimidine-based chemotherapy. Clinical trial evidence shows that for people whose tumours express PD-L1 with a CPS of 10 or more, adding pembrolizumab increases how long they live. It also increases the time before their disease gets worse.

Pembrolizumab meets NICE's criteria to be considered a life-extending treatment at the end of life. The cost-effectiveness estimates are likely to be within what NICE considers an acceptable use of NHS resources. Therefore, it is recommended.

2 Information about pembrolizumab

Marketing authorisation indication

- 2.1 Pembrolizumab (Keytruda, MSD) has a marketing authorisation in the UK 'in combination with platinum- and fluoropyrimidine-based chemotherapy for the first-line treatment of patients with locally advanced unresectable or metastatic carcinoma of the oesophagus in adults whose tumours express PD-L1 with a CPS equal to or greater than 10'.

Dosage in the marketing authorisation

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

Price

- 2.3 The list price is £2,630 for a 100-mg vial (excluding VAT; BNF online accessed July 2021).
- 2.4 The company has a [commercial arrangement](#). This makes pembrolizumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The [appraisal committee](#) considered evidence submitted by MSD, a review of this submission by the evidence review group (ERG) and responses from stakeholders. See the [committee papers](#) for full details of the evidence.

The condition

Oesophageal and HER2-negative gastro-oesophageal junction cancer have a poor prognosis and a large impact on quality of life

3.1 The patient experts explained that advanced oesophageal cancer (squamous or adenocarcinoma) or HER2-negative gastro-oesophageal junction adenocarcinoma have a significant impact on quality of life. They explained that major symptoms include difficulty swallowing and malnutrition, which can lead to severe fatigue, weight loss and the need to use a feeding tube. These symptoms can be both painful and distressing, limiting people's ability to experience and participate in normal activities and social events. Around 40% of all new cases are in people aged 75 years and over, although the patient experts noted that increasing numbers of younger people are being diagnosed. The patient experts also explained that oesophageal and gastro-oesophageal junction cancer is more common in men than women but increasing numbers of women are being diagnosed. Diagnosis is often at an advanced stage. The committee concluded that oesophageal and HER2-negative gastro-oesophageal junction cancer have a poor prognosis and a large impact on quality of life.

Treatment pathway

People would welcome a new treatment option

3.2 The patient and clinical experts explained that people with advanced oesophageal and HER2-negative gastro-oesophageal junction cancer have a

poor prognosis and no curative treatment options. Palliative combination chemotherapy regimens are standard first-line treatment for people with a performance status of 0 to 2 and no significant comorbidities. The [NICE guideline on oesophago-gastric cancer: assessment and management in adults](#) recommends dual therapy with fluorouracil or capecitabine in combination with cisplatin or oxaliplatin, or triple therapy with the addition of epirubicin. The clinical experts stated that triple therapy is no longer standard of care as it does not provide additional efficacy and increases toxicity. The clinical experts explained that dual therapy regimens are preferred and that most people would have capecitabine and oxaliplatin (XELOX). This is because oxaliplatin is preferred to cisplatin as it is better tolerated and has a shorter infusion time; however, there is no evidence that any one dual therapy combination is more effective than others. They suggested that dual therapy would be the appropriate comparator in this appraisal (see [section 3.10](#)). Pembrolizumab is an immunotherapy that has a different mechanism of action to chemotherapy and would be given as an additional treatment alongside chemotherapy. Therefore, it would not significantly add to the treatment administration burden. The patient experts explained that most people with advanced oesophageal or HER2-negative gastro-oesophageal junction cancer would be willing to accept the additional side effects and treatment burden of pembrolizumab, because of its potential to improve quality of life and help people live longer. The committee concluded that there is an unmet clinical need in this population and people would welcome a new effective treatment option.

It is preferable to give treatment with a PD-1 inhibitor early in the treatment pathway

- 3.3 The [NICE technology appraisal on nivolumab for previously treated unresectable advanced or recurrent oesophageal cancer](#) recommends nivolumab as treatment for oesophageal squamous cell carcinoma (but not adenocarcinoma) after chemotherapy. The clinical experts explained that because pembrolizumab and nivolumab are both PD-1 inhibitors, it would not be suitable to give nivolumab as second-line treatment after pembrolizumab with chemotherapy. They explained that it would be preferable to give pembrolizumab as first-line treatment rather than nivolumab as second-line treatment for people with squamous carcinoma. This is because approximately 60% of people are unable to have second-line

treatment and it is likely that immunotherapy is more effective when used earlier. The patient experts agreed that immunotherapy would be welcomed sooner in the treatment pathway. The committee concluded that pembrolizumab would potentially offer a first-line immunotherapy treatment option for people with advanced oesophageal cancer or HER2 gastro-oesophageal junction adenocarcinoma.

Marketing authorisation

The population included in the marketing authorisation is narrower than the population in the scope

- 3.4 The marketing authorisation specifies that pembrolizumab is indicated only for adults whose tumours express PD-L1 with a combined positive score (CPS) of 10 or more and is restricted to treatment of gastro-oesophageal junction adenocarcinoma for tumours that are HER2 negative (see [section 2.1](#)). This is narrower than the population included in the scope, which did not specify HER2 or CPS status. The committee agreed that the appropriate population to consider for decision making was adults with unresectable locally advanced or metastatic oesophageal cancer or HER2-negative gastro-oesophageal junction adenocarcinoma who had not had previous chemotherapy. The adults in the population should also have tumours that express PD-L1 with a CPS of 10 or more, in line with the marketing authorisation.

PD-L1 testing

PD-L1 testing is not routinely carried out in people with oesophageal cancer and HER2-negative gastro-oesophageal junction adenocarcinoma

- 3.5 Currently PD-L1 testing is not part of routine clinical practice in gastrointestinal cancers. However, it is routinely carried out for people with other types of cancer such as head and neck cancer. The clinical experts and the Cancer Drugs Fund

clinical lead explained that, ideally, PD-L1 testing should be done early and before chemotherapy is started, so as to prevent delays in accessing appropriate treatment. They explained that PD-L1 testing for people with oesophageal cancer and HER2-negative gastro-oesophageal junction adenocarcinoma should not be problematic, and that current diagnostic tests could be used. The committee concluded that PD-L1 testing is not currently routine for oesophageal and gastro-oesophageal junction cancers, but that this could be adopted easily in the NHS.

Clinical evidence

KEYNOTE-590 data for the subgroup of tumours with CPS of 10 or more is appropriate for decision making

3.6 KEYNOTE-590 is a randomised, double-blind, placebo-controlled trial (n=749). It compared cisplatin and fluorouracil, with or without pembrolizumab, as first-line treatment for locally advanced unresectable or metastatic oesophageal adenocarcinoma, squamous cell carcinoma or advanced gastro-oesophageal junction adenocarcinoma. It excluded people with known HER2 positive gastro-oesophageal junction cancer. The marketing authorisation restricts pembrolizumab to a subgroup whose tumours are PD-L1 positive with a CPS of 10 or more (see [section 3.4](#)). The proportion of people whose tumours had a CPS of 10 or more in the intention-to-treat population was similar in the pembrolizumab plus chemotherapy arm (49.9%) and the placebo plus chemotherapy arm (52.4%). The clinical experts explained that this proportion is comparable to UK clinical practice. The committee concluded that the data from the subgroup with a CPS of 10 or more is appropriate for decision making.

KEYNOTE-590 data is generalisable to people in NHS clinical practice

3.7 KEYNOTE-590 recruited people from 26 countries including the UK. 54.8% of the CPS of 10 or more subgroup were from Asia. The ERG suggested that KEYNOTE-590 may not be generalisable if disease prognosis or treatment pathways used in Asia differ from clinical practice in the NHS. However, the

clinical experts explained that treatment regimens used in Asia and the NHS are similar, and common international guidelines are used. They also explained that there is no reason, based on molecular biology, that the effect of pembrolizumab on oesophageal cancer or gastro-oesophageal junction adenocarcinoma would differ between the trial population and the population treated in the NHS. The ERG also suggested that the proportion of people with squamous cell carcinoma and adenocarcinoma in KEYNOTE-590 is different to the distribution seen in UK clinical practice. The clinical experts explained that PD-L1 status and CPS was a more important biomarker than carcinoma type for predicting treatment effect. They explained that it is possible that people with squamous cell carcinoma (who appear to be more sensitive to immunotherapies) would benefit more from pembrolizumab than people with adenocarcinoma. However, the magnitude of benefit is smaller between the 2 cancer types when CPS is 10 or more. The clinical experts explained that although there is a difference in the proportion of people with squamous cell carcinoma and adenocarcinoma in KEYNOTE-590 and UK clinical practice, the results are generalisable to people with oesophageal cancer or HER2 gastro-oesophageal junction adenocarcinoma with a CPS of 10 or more. The committee concluded that although this is an area of uncertainty, for the subgroup of interest, KEYNOTE-590 is generalisable to clinical practice in the NHS.

Clinical effectiveness

Pembrolizumab improves progression-free survival and overall survival compared with chemotherapy alone

- 3.8 Median progression-free survival in KEYNOTE-590 for people with a tumour with a CPS of 10 or more was 7.5 months in the pembrolizumab plus chemotherapy arm and 5.5 months in the placebo plus chemotherapy arm. The difference in median progression-free survival was 2 months (hazard ratio 0.51, 95% confidence interval [CI] 0.41 to 0.65; $p < 0.001$). The corresponding median overall survival for the pembrolizumab plus chemotherapy arm was 13.5 months and 9.4 months in the placebo plus chemotherapy arm. The difference in median overall survival was 4.1 months (hazard ratio 0.62, 95% CI 0.49 to 0.78; $p < 0.001$). The committee concluded that adding pembrolizumab to chemotherapy improves

both progression-free survival and overall survival for people with locally advanced unresectable or metastatic oesophageal cancer or HER2-negative gastro-oesophageal junction adenocarcinoma whose tumours express PD-L1 with a CPS of 10 or more.

Company's economic model

The company's economic model is appropriate for decision making

- 3.9 The company presented a 3-state partitioned survival model to estimate the cost effectiveness of pembrolizumab plus chemotherapy compared with chemotherapy alone. The 3 health states were progression-free, progressive disease and death. The ERG agreed that the company's model structure captured all relevant health states and partitioned survival models are widely used in cancer modelling. The committee concluded that the company's model structure was acceptable for decision making.

Assumptions in the economic model

A dual chemotherapy regimen is the most appropriate comparator

- 3.10 The scope included dual and triple chemotherapy regimens. The company assumed equivalent efficacy between dual and triple regimens and used a dual therapy regimen in its economic model. The ERG stated that all relevant scope comparators, including triple therapy, should be considered. The clinical experts reiterated that dual chemotherapy regimens are more commonly used in UK clinical practice (see [section 3.2](#)). The Cancer Drugs Fund clinical lead also confirmed that the use of triple regimens is rapidly diminishing. The committee concluded that a dual chemotherapy regimen would be the appropriate comparator for this appraisal.

The dual chemotherapy regimen used by the company in its model is acceptable for decision making

3.11 The company base case included the dual regimen of cisplatin and fluorouracil as used in KEYNOTE-590, both in the comparator arm and in combination with pembrolizumab in the intervention arm. The clinical experts explained that dual therapy is the standard of care. However, they explained that several combinations are available, and oxaliplatin is more commonly used than cisplatin in the NHS (see [section 3.2](#)). The ERG provided a scenario analysis exploring an alternative dual regimen of oxaliplatin and capecitabine in both the pembrolizumab and comparator arms. This scenario included differences in costs but assumed equal efficacy to cisplatin and fluorouracil used in the company's model. The company also presented a scenario analysis using a blended comparator arm, which applied the costs of chemotherapy based on UK market share data. The company stated that they agreed with the ERG's approach to exploring an additional scenario but that both the ERG's and the company's scenarios have a negligible effect on the cost-effectiveness estimate. The committee agreed that the ERG's scenario using oxaliplatin and capecitabine was most reflective of current clinical practice, and that it was likely that this regimen would also be used in combination with pembrolizumab. However, it noted that there was comparable efficacy between the different dual regimens and that which combination the model used had little effect on the cost-effectiveness estimate. It therefore concluded that, although it was not reflective of clinical practice, it was appropriate to use the dual regimen included in the company's model for decision making.

Multiple models for estimating overall survival are plausible

3.12 The company modelled overall survival in both treatment arms using Kaplan–Meier data from KEYNOTE-590, with a log-logistic extrapolation from 40 weeks. The ERG considered this approach to be broadly acceptable but focused on 3 alternative scenarios to explore uncertainty associated with overall survival extrapolation: a log-logistic piecewise model plus treatment waning (presented by the company as a scenario analysis); a generalised gamma piecewise model; and a log-logistic fully parametric model. The ERG stated that, according to clinical expert opinion, all the scenarios, including the company's

base case, are plausible. The ERG's preferred scenario was the log-logistic piecewise model plus treatment waning, which is the same as the company's preferred model for overall survival but also includes a treatment waning effect between 5 and 7 years. The ERG preferred this scenario as it results in survival estimates in the middle of the range of the 4 plausible scenarios and addressed the uncertainty around pembrolizumab having a lifetime treatment effect. The company suggested that the generalised gamma piecewise model had a poor statistical fit, and the log-logistic fully parametric model did not have as good a visual fit to the observed overall survival data as the piecewise model. The company also commented that clinical evidence indicates a sustained treatment benefit with pembrolizumab and therefore including a treatment waning effect was conservative. The clinical experts agreed that a small proportion of people receiving pembrolizumab could be cured or enter long-term remission. The Cancer Drugs Fund clinical lead also stated that it is very likely there will be long-term survivors but there will also be people who relapse after 2 years, and stated that, although it is unclear if there is a treatment waning effect, it is a reasonable assumption. The committee acknowledged the long-term uncertainty in overall survival and concluded that all 4 scenarios presented provided plausible estimates of overall survival and resulted in a range of cost-effectiveness estimates. However, the scenarios preferred by the company and ERG were not widely different.

Progression-based utilities are preferred for use in the model because the values are more plausible

- 3.13 Utility values were calculated using EQ-5D data from KEYNOTE-590. The company used a time-to-death approach to calculate utility values in its base case, which produced utility values using groupings of utility observations based on how close the values were reported to the patient's overall survival time. The ERG explained that the time-to-death approach was a reasonable method but that it produced utility values that were higher than expected when compared with the general population, especially for the group who were more than 1 year from death. The company responded to this at technical engagement by capping the utility values for the group who were more than 1 year from death to the general population utility values. The ERG suggested that it was not plausible that the quality of life for a person with advanced oesophageal or HER2 gastro-

oesophageal junction adenocarcinoma would be equal to or similar to the general population. It preferred to use a progression-based approach to calculate utility values, as the values from this approach appeared more plausible. The company suggested that the time-to-death approach was more appropriate as it captures more health states than the progression-based approach. It stated that this was more important for a condition that has a short life expectancy, as quality of life decreases rapidly as people approach the end of life. The company also explained that EQ-5D scores were collected once from people who had progressed disease, which may not have fully captured quality of life for the progressed health state. At technical engagement, the company also presented an interaction utility model that combined progression status and time-to-death categories, to aim to address the ERG's concerns around the plausibility of the values produced. The ERG commented that this approach could not be fully evaluated based on the information provided, and that the same issue persisted: the utility values for the group furthest from death were higher than the general population. The committee discussed that any of the time-to-death, progression-based and interaction approaches could be appropriate for capturing quality of life as direct trial data was used for them all. However, it noted that progression-based utilities are more common in cancer appraisals and the values were more plausible. It also noted that the ERG had not been able to fully critique the interaction approach. The committee concluded that it preferred the progression-based utilities for decision making because the values were more plausible.

It is appropriate to include the cost of subsequent treatment with nivolumab in the model

3.14 The [NICE technology appraisal on nivolumab for previously treated unresectable advanced or recurrent oesophageal cancer](#) was published before technical engagement. It recommends nivolumab for treating unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma in adults after fluoropyrimidine and platinum-based therapy (see [section 3.3](#)). At technical engagement, the company updated its base case to include costs associated with nivolumab. The updated model included costs for nivolumab based on the number of people in the KEYNOTE-590 CPS of 10 or more subgroup who received an anti-PD-1 or anti-PD-L1 treatment after pembrolizumab with chemotherapy or placebo with chemotherapy. The ERG agreed that the

company's approach is the most suitable method to include nivolumab within the treatment pathway without having to make assumptions about efficacy, because this is captured in the outcomes of people in KEYNOTE-590 who received a subsequent anti-PD-1 or anti-PD-L1 treatment. However, the ERG noted that in KEYNOTE-590 some people received an anti-PD-1 or anti-PD-L1 treatment after pembrolizumab with chemotherapy, which is not what would happen in UK clinical practice (see section 3.3). The ERG also noted that the proportion of people in KEYNOTE-590 who received an anti-PD-1 or anti-PD-L1 treatment was likely to be lower than the number of people who receive nivolumab after first-line chemotherapy without pembrolizumab in UK clinical practice. To address this, it provided a scenario to reflect how nivolumab is likely to be used in clinical practice that estimated the costs and efficacy of nivolumab. This scenario assumed that all participants who had received a subsequent treatment in the placebo with chemotherapy arm in the KEYNOTE-590 CPS of 10 or more subgroup, received nivolumab as second-line treatment. However, the ERG explained that there were several limitations to this scenario analysis, including uncertainty around the impact nivolumab would have on overall survival, and unconventional adjustments being made to the survival curves as needed by the partitioned survival model framework. Therefore, it did not include this analysis in its base case. The committee was aware that both the company's and the ERG's approaches had limitations but concluded that it was appropriate to include the costs of nivolumab as a subsequent treatment in the model.

The company and the ERG have appropriately incorporated PD-L1 testing into the model

3.15 PD-L1 testing is currently not routinely funded for oesophageal or gastro-oesophageal junction cancer (see [section 3.5](#)). The company and the ERG included the costs of PD-L1 testing in their models, as this is an additional cost to current care for oesophageal and gastro-oesophageal junction cancer. The committee concluded that introducing PD-L1 testing for oesophageal and gastro-oesophageal junction cancer would be unlikely to add a significant burden to the NHS and that it was appropriate to include the costs of testing in the model.

End of life

Pembrolizumab meets the end of life criteria

3.16 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](#). Data from KEYNOTE-590 showed that, for the subgroup of people whose tumours express PD-L1 with a CPS of 10 or more, median overall survival was 9.4 months for people receiving placebo with chemotherapy (see [section 3.8](#)). The clinical and patient experts also agreed that the average life expectancy of people with advanced oesophageal cancer or HER2-negative gastro-oesophageal junction adenocarcinoma was less than 2 years. In the subgroup of interest (people whose tumours express PD-L1 with a CPS of 10 or more), KEYNOTE-590 showed an increase in median overall survival with the addition of pembrolizumab to chemotherapy of 4.1 months (see [section 3.8](#)). The company's model also indicated that pembrolizumab increased mean overall survival by 13.9 months. The ERG agreed that, in the subgroup of people whose tumours express PD-L1 with a CPS of 10 or more, there is an improvement in overall survival of at least 3 months with pembrolizumab. The committee concluded that pembrolizumab meets the end of life criteria for this population.

Cost-effectiveness estimate

Pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy is likely to be cost effective

3.17 The company's base case included the following assumptions:

- Using the dual chemotherapy regimen from KEYNOTE-590 in the model, both alone as the comparator and in combination with pembrolizumab as the intervention (see [section 3.11](#)).
- Using a log-logistic extrapolation for modelling overall survival (see [section 3.12](#)).

- Using utilities obtained using time-to-death methodology (see [section 3.13](#)).
- Adding the costs of nivolumab as a subsequent treatment into the model (see [section 3.14](#)).
- Adding the costs of PD-L1 testing to the model (see [section 3.15](#)).

The ERG's base case included the same assumptions as the company in its model on the choice of dual chemotherapy (see section 3.11), the costs of nivolumab (see section 3.14), and the costs of PD-L1 testing (see section 3.15). It included different assumptions to the company on overall survival modelling (using a log-logistic extrapolation plus a treatment waning effect between 5 and 7 years [see section 3.12]) and used the committee's preferred assumption of progression-based utilities (see section 3.13). The incremental cost-effectiveness ratios (ICERs) cannot be reported here because of confidential commercial arrangements for pembrolizumab and subsequent treatments. Although including the ERG's assumptions increased the ICER compared with the company's base case, both the company's and the ERG's cost-effectiveness estimates are below £50,000 per quality-adjusted life year gained. As end of life criteria have been met (see [section 3.16](#)) the committee concluded that it was likely that pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy is likely to be a cost-effective use of NHS resources.

Conclusion

Pembrolizumab in combination with platinum- and fluoropyrimidine-based chemotherapy is recommended

- 3.18 The committee noted that both the company's and the ERG's base cases show that pembrolizumab with platinum-based chemotherapy is likely to be cost effective compared with chemotherapy alone, when considering a life-extending treatment for people with short life expectancy (see section 3.17). The committee was aware of continuing uncertainty related to the generalisability of the population in KEYNOTE-590 to clinical practice in the NHS (see [section 3.7](#)) and

the most appropriate method to extrapolate overall survival (see [section 3.12](#)). However, despite the remaining areas of uncertainty, it was agreed that the cost-effectiveness estimates are likely to be within the range usually considered a cost-effective use of NHS resources for a life-extending treatment for people with short life expectancy. Therefore, pembrolizumab in combination with platinum- and fluoropyrimidine-based chemotherapy is recommended for use in the NHS as an option for treating locally advanced unresectable or metastatic carcinoma of the oesophagus or HER2-negative gastro-oesophageal junction adenocarcinoma in adults whose tumours express PD-L1 with a CPS of 10 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 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 locally advanced unresectable or metastatic carcinoma of the oesophagus and their tumours express PD-L1 with a CPS of 10 or more, and the doctor responsible for their care thinks that pembrolizumab in combination with platinum and fluoropyrimidine is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee A](#).

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

The [minutes of each appraisal committee meeting](#), which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

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

Albany Meikle

Technical lead

Joanna Richardson

Technical adviser

Thomas Feist

Project manager

Update information

August 2024: Recommendation 1.1 was updated and partially replaced by [NICE technology appraisal guidance on pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy for untreated advanced HER2-negative gastric or gastro-oesophageal junction adenocarcinoma \(TA997\)](#). This is because the marketing authorisation for pembrolizumab has been updated since this guidance was published, and it now has a marketing authorisation for 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. Because HER2-negative locally advanced unresectable or metastatic gastro-oesophageal junction adenocarcinoma is now covered by the new recommendation in TA997, this indication has been removed from the recommendation in this guidance.

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