

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

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.

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1 Recommendations

- 1.1 Nivolumab with platinum- and fluoropyrimidine-based chemotherapy is recommended, within its marketing authorisation, as an option for untreated HER2-negative, advanced or metastatic gastric, gastro-oesophageal junction or oesophageal adenocarcinoma in adults whose tumours express PD-L1 with a combined positive score (CPS) of 5 or more. Nivolumab is only recommended if the company provides it according to the [commercial arrangement](#).

Why the committee made these recommendations

There are no curative treatment options for HER2-negative, advanced or metastatic gastric, gastro-oesophageal junction or oesophageal adenocarcinoma that expresses PD-L1 with a CPS of 5 or more. The usual treatment is palliative chemotherapy. Most people have platinum- and fluoropyrimidine-based chemotherapy with capecitabine plus oxaliplatin (XELOX) or fluorouracil plus oxaliplatin with folinic acid (FOLFOX).

Clinical trial evidence shows that nivolumab plus XELOX or FOLFOX increases the length of time before gastric, gastro-oesophageal junction or oesophageal adenocarcinoma gets worse compared with XELOX or FOLFOX alone. Evidence also shows that people live longer if they have nivolumab plus XELOX or FOLFOX compared with XELOX or FOLFOX alone. But, it is uncertain how long people lived beyond the trial period and for how long nivolumab's benefit lasted.

People with these conditions on average have a short life expectancy, so nivolumab meets NICE's criteria to be considered a life-extending treatment at the end of life. The cost-effectiveness estimates for nivolumab are within what NICE considers an acceptable use of NHS resources. So, nivolumab with platinum- and fluoropyrimidine-based chemotherapy is recommended.

2 Information about nivolumab

Marketing authorisation indication

- 2.1 Nivolumab (Opdivo, Bristol Myers Squibb) is indicated for use 'in combination with fluoropyrimidine- and platinum-based combination chemotherapy for the first-line treatment of adult patients with HER2-negative advanced or metastatic gastric, gastro-oesophageal junction or oesophageal adenocarcinoma whose tumours express PD-L1 with a combined positive score (CPS) \geq 5'.

Dosage in the marketing authorisation

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

Price

- 2.3 The list price of nivolumab is £439 per 40 mg/4 ml concentrate for solution for infusion vial; £1,097 per 100 mg/10 ml concentrate for solution for infusion vial; and £2,633 per 240 mg/24 ml concentrate for solution for infusion vial (excluding VAT; BNF online, accessed July 2022).
- 2.4 The company has a [commercial arrangement](#). This makes nivolumab 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 from a number of sources. See the [committee papers](#) for full details of the evidence.

The condition

Gastric, gastro-oesophageal junction and oesophageal adenocarcinoma have a poor prognosis and a large impact on quality of life

- 3.1 The patient experts explained that gastric, gastro-oesophageal junction and oesophageal adenocarcinoma significantly impact 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 painful and distressing, limiting people's ability to live normally and participate in social events. Diagnosis is often at an advanced stage, and around 40% of all new cases are diagnosed in people aged 75 and over. Gastric, gastro-oesophageal junction and oesophageal adenocarcinoma are more common in men than women, although the patient experts report that increasing numbers of younger people and women are being diagnosed. The committee concluded that advanced gastric, gastro-oesophageal junction and oesophageal adenocarcinoma have a poor prognosis and a large impact on quality of life.

People would welcome a new treatment option

- 3.2 The patient and clinical experts explained that there are no curative treatment options for untreated HER2-negative advanced gastric, gastro-oesophageal junction or oesophageal adenocarcinoma. Standard first-line treatment for people with an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2 and no significant comorbidities is palliative chemotherapy. [NICE's guideline on oesophago-gastric cancer: assessment and management in adults](#) recommends dual

therapy with fluorouracil or capecitabine plus cisplatin or oxaliplatin, or triple therapy with epirubicin. 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 better tolerated than cisplatin and has a shorter infusion time. Some people may be offered fluorouracil with oxaliplatin and folinic acid (FOLFOX). People having FOLFOX treatment need more hospital visits (every 2 weeks) than people having XELOX (every 3 weeks). The patient and clinical experts agreed that there is unmet clinical need in this population. Nivolumab is an immunotherapy and has a different mechanism of action to chemotherapy. [NICE's technology appraisal guidance recommends pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy for untreated HER2-negative advanced oesophageal and gastro-oesophageal junction cancer in adults whose tumours express PD-L1 with a combined positive score \(CPS\) of 10 or more.](#) The committee noted that some people would be eligible for nivolumab plus chemotherapy but not pembrolizumab plus chemotherapy. As a result, there remains an unmet need in people with gastric cancer and a CPS of between 5 and 10 who cannot have pembrolizumab. The committee concluded that patients and clinicians would welcome a new treatment for untreated HER2-negative advanced gastric, gastro-oesophageal junction or oesophageal adenocarcinoma.

XELOX is the key comparator for this appraisal

- 3.3 The company suggested that XELOX and FOLFOX were the relevant comparators for this appraisal. The evidence review group (ERG) agreed with this approach and noted that most people would have XELOX because it is more convenient and cheaper than FOLFOX. Clinical experts also confirmed the company's approach and noted that dual chemotherapy regimens have similar efficacy. The committee concluded that XELOX was the key comparator for this appraisal.

Clinical evidence

Nivolumab plus chemotherapy improves progression-free survival and overall survival compared with chemotherapy alone

3.4 CheckMate 649 (n=1,581) was an open-label randomised multicentre trial (including 38 patients from 5 UK centres) that compared nivolumab plus XELOX or FOLFOX with XELOX or FOLFOX alone. It included people with untreated and unresectable, advanced or metastatic gastric, gastro-oesophageal junction or oesophageal adenocarcinoma who had an ECOG performance status of 0 to 1. People with known HER2-positive status and untreated central nervous system metastases were excluded from the study. The average age in the trial was 60.1 years. The primary outcomes were progression-free survival and overall survival in people whose tumours express PD-L1 with a CPS of 5 or more (n=955). Results from the latest data cut were based on a minimum follow-up of 24 months and showed that:

- nivolumab plus chemotherapy improved progression-free survival compared with chemotherapy alone (hazard ratio [HR] 0.70, 95% confidence interval [CI] 0.60 to 0.81)
- nivolumab plus chemotherapy improved overall survival compared with chemotherapy alone (HR 0.70, 95% CI 0.61 to 0.81).

The committee noted that this data was mature (meaning that more than half the trial population had disease progression or died during the follow-up period). The committee concluded that adding nivolumab to platinum- and fluoropyrimidine-based combination chemotherapy improved progression-free survival and overall survival compared with chemotherapy alone.

CheckMate 649 data is generalisable to NHS clinical practice

3.5 In the first committee meeting, the ERG heard clinical advice suggesting that the trial population, with a mean age of 60.1 years and ECOG performance status of 0 to 1 (see [section 3.4](#)), was younger and fitter than the population seen in NHS clinical practice. The ERG thought the best available estimates were that people seen in the NHS with

advanced or metastatic gastric, gastro-oesophageal junction or oesophageal adenocarcinoma had an average age between 64 and 66 (Cancer Research UK and Royal Marsden Hospital Trust data). The clinical experts explained that the average age of the trial population is expected to be younger than that of people seen in the NHS with these conditions. They agreed there is no evidence that treatment would be less effective in older people and stated that treatment should be based on patient fitness and comorbidities, regardless of age and performance status. The company noted that the trial age is aligned with UK data sources and that there is limited evidence to suggest outcomes differ between ECOG performance status scores. The committee concluded that CheckMate 649 data is generalisable to NHS clinical practice.

Long-term remission and cure

Some people may have long-term remission, but their life expectancy may be shorter than the general population

3.6 The company considered that evidence from CheckMate 649 suggested that the hazard of progression or death in people whose disease had not yet progressed decreases over time and plateaus at 30 months. The company proposed that people who had no disease progression 30 months or more after starting treatment were in 'long-term remission'. The company's estimates of the risk of dying in people with long-term remission were the same as the general population. The ERG noted that this meant the company assumed that people whose cancer had not progressed by 30 months after starting treatment were cured and had the same lifespan as the general population. The company considered that other evidence showing long-term survival in some people supports this assumption, for example, COUGAR-02, ATTRACTION-2, Chau 2009 and Royal Marsden Hospital Trust data. The ERG considered that none of the long-term evidence supported the cure assumption. The number of people in CheckMate 649 at 30 months was too low for conclusions about cure to be made. The clinical experts agreed that long-term data supporting a cure assumption does not exist. However, the clinical and patient experts explained that long-term survival is likely for some people because this has been seen with other immunotherapy treatments. The

clinical expert said that about 4% of people could be expected to achieve long-term remission with chemotherapy and that they expect nivolumab could double the number to 8%. The NHS clinical lead noted that disease in long-term remission can relapse, but this is uncommon. The clinical experts said that people in long-term remission have a low burden of disease and their quality of life is good. However, their fitness is unlikely to return to pre-treatment levels because of long-term toxicities with chemotherapy, such as irreversible neuropathy. They expected the mortality rate in people with long-term remission to be higher than that of the general population because they previously had advanced cancer and cytotoxic chemotherapy. The committee concluded that some people are likely to have long-term remission, but it was unclear if they were cured. The committee further concluded that people in whom disease did not recur would still be expected to have a shorter life expectancy than people who have not had this type of advanced cancer and chemotherapy.

The company's economic model

The company's updated model is suitable for decision making

3.7 In the first committee meeting, the company used a cohort-based semi-Markov model with 4 states: pre-progression, progressed disease, long-term remission, and death. All people in the pre-progression state at 30 months entered the long-term remission state and were assumed to have the same risk of dying as the general population and were assumed to be effectively cured (see [section 3.6](#)). The ERG explained that the company's model was unnecessarily complicated and differed from the 3-state partitioned survival models often used in NICE appraisals of cancer treatments. The model did not use overall survival data directly, even though this was as mature as the progression-free survival data used to derive overall survival estimates. The company modelled overall survival indirectly by using blinded independent central review progression-free survival data from CheckMate 649. The ERG explained that the company's model survival estimates were higher than the overall survival seen in the trial. Because the company's model did not correspond with the CheckMate 649 data, the ERG stated that the model

long-term survival estimates and cost-effectiveness results lack reliability. It suggested that a 3-state partitioned survival model could use the survival data from CheckMate 649 directly. The committee agreed with the ERG that 3-state partitioned survival models are suitable and noted that the inclusion of the long-term remission state in the company's original model made the model unsuitable for decision making. After consultation, the company presented a new partitioned survival model, which the committee concluded was appropriate for decision making.

Survival modelling

Progression-free survival is modelled appropriately

3.8 In the updated company base case, long-term survival with nivolumab was estimated using a semi-parametric approach. Kaplan–Meier estimates were directly used from CheckMate 649 for the first 6.44 months. This cut-off was chosen to reflect the fact that high-frequency assessments, which could influence the timing of progression-free survival measurements, had ended. After this point, each treatment arm was extrapolated using a log-normal distribution. The ERG agreed with the modelling approach and distribution choice, noting that there was no clinical evidence other than CheckMate 649 to choose between alternative parametric distributions. The committee concluded the method and distribution chosen for the projection of progression-free survival beyond the trial data was appropriate.

There are differences in the company's and ERG's approaches to modelling overall survival, but both are appropriate

3.9 The company and ERG suggested different approaches to extrapolate overall survival. In terms of similarities, both used a semi-parametric method which used CheckMate 649 Kaplan–Meier data for the first 6.44 months and then extrapolated the data using a parametric distribution. The company's base case used the Gompertz distribution whereas the ERG presented results using the Gompertz and generalised gamma distributions. In terms of differences, each used different

approaches to ensure that mortality hazards were never lower than those of the general population (see [section 3.6](#)). The company's approach added the excess mortality of the condition to the general population mortality. However, the ERG adjusted the extrapolation so that the mortality hazards were never below those of the general population. In a previous committee meeting, the ERG did not have enough information to assess the company's modelling approach and thought that the approach presented may have been implemented incorrectly. The ERG thought that the company may have double-counted deaths in its approach. Once the company fully explained how it had implemented its modelled overall survival, the ERG was satisfied and found it reasonable. The committee concluded that although the company and the ERG had different ways to model overall survival, both were reasonable.

After stopping treatment, nivolumab's treatment effect may not last for a person's lifetime

- 3.10 People in CheckMate 649 could continue to have nivolumab for a maximum of 24 months, even if their cancer had not progressed at this time. The marketing authorisation for nivolumab has this 24-month stopping rule. The model had an assumption that people would continue to experience treatment effect benefit after stopping treatment. The clinical experts and company suggested some persistence of benefit is plausible after stopping nivolumab because nivolumab enhances the immune system to mediate an anti-tumour response against cancer cells, resulting in tumour destruction. The company stated that the trial had a 49.5-month follow up. During this time, there was no evidence of a treatment waning effect; that is a reduction in the treatment effect for nivolumab plus XELOX compared with XELOX alone after 24 months. The company also suggested that trials of nivolumab for treating melanoma or non-small-cell lung cancer suggested a long-term benefit of nivolumab in those cancers. The committee noted that it did not have enough comparator data from these trials to confirm no treatment waning. This is because the trials may have had different rules on stopping nivolumab to CheckMate 649 and it was unclear whether any persistence of effect after stopping nivolumab would be consistent across different tumour types. The committee agreed that it was unproven that the benefit of a 24-month course of nivolumab would last

indefinitely after it was stopped. It agreed it was more likely that the effect would wear off at some stage. The committee noted that both the company and ERG had provided treatment waning scenarios. In these scenarios the risk of death in the nivolumab plus XELOX arm became the same as the XELOX arm at 6.5 years in the company's scenario and 5 years in the ERG's model. The committee commented that this suggested that the treatment benefit of nivolumab ceased abruptly at these times. It commented that this contrasted with ways of modelling treatment waning seen in some other appraisals. That is, in which the treatment benefit is modelled to start decreasing at the point people stop treatment and gradually decreases over a period of time until there is no treatment benefit over the comparator. The committee noted that:

- The company's 6.5-year cut-off was based on the longest available follow-up data from CheckMate 067. This trial compared nivolumab plus ipilimumab or nivolumab alone with ipilimumab in people with advanced melanoma.
- The company thought the ERG's cut-off was too pessimistic given that the company's observed trial data at 4 years did not show a sustained increase in the risk of dying as shown in the ERG's scenario.
- The ERG considered its own 5-year cut-off to be arbitrary and non-evidence-based, but reflective of assumptions in previous appraisals which assumed a 3-year persistence of benefit after stopping nivolumab.
- NICE's technology appraisal guidance on pembrolizumab with chemotherapy for oesophageal and gastro-oesophageal cancer had applied a treatment waning effect between 5 and 7 years. However, this did not imply that the company's choice of 6.5 years was valid for this appraisal, which included a population with predominantly gastric cancer, and a different treatment.

The committee recognised that there was no evidence underpinning either the 5- or 6.5-year treatment waning assumption or a lifetime treatment effect. The committee concluded that nivolumab's treatment effect may not last for a person's lifetime after treatment is stopped. Although treatment waning is uncertain, it would take both the company's and ERG's scenarios on treatment waning into account in its decision making.

The company's and ERG's approaches give plausible results at

20 years, but these are uncertain

3.11 The committee recalled that the company's preferred parametric distribution for extrapolating overall survival was the Gompertz distribution, and the ERG considered both generalised gamma and Gompertz distributions (see [section 3.9](#)). The committee noted that the choice of parametric distribution and the treatment waning assumption had a particularly large effect on the modelled long-term overall survival after 5 years in the nivolumab plus XELOX arm. This also had a large effect on the cost-effectiveness estimates for nivolumab plus XELOX compared with XELOX alone. The committee noted:

- The ERG's approach using Gompertz distribution predicted that after 20 years, 5.9% of people who had nivolumab plus XELOX would be alive, compared with 0.5% predicted by the ERG's preferred generalised gamma distribution. In the XELOX-only arm, the ERG's approach using Gompertz distribution predicted that 0.9% of people would be alive after 20 years, compared with 0.2% predicted by the ERG's preferred generalised gamma distribution.
- Applying the ERG's 5-year treatment waning scenario to the ERG approach using the Gompertz distribution predicted that 3.1% of people in the nivolumab plus XELOX arm would be alive at 20 years.
- The company's approach using a Gompertz distribution predicted that slightly fewer people would be alive at 20 years than predicted using the ERG's approach with a Gompertz distribution. Applying the 5-year cut-off and 6.5-year cut-off for treatment waning resulted in just under 3% and just over 3% of people predicted to be alive at 20 years, respectively (the precise estimates are academic in confidence and cannot be presented here).

Of the 20-year survival estimates for nivolumab plus XELOX (5.9% Gompertz, 3.1% Gompertz with treatment waning, and 0.5% generalised gamma), the clinical experts considered those using the Gompertz distribution and including waning were plausible. The committee noted consultation comments on the second appraisal consultation document that stated that, for most people with this type of cancer, life expectancy is short and the focus should not be on a small proportion of people alive at 20 years. The committee agreed that long-term projections affecting only a few people were highly uncertain. However, differences in the cost-effectiveness estimates were driven by the effect of

different modelling assumptions on these long-term predictions and it needed to reach a decision on what was plausible. The committee concluded that both the company's and ERG's approaches using a Gompertz distribution and assuming treatment waning gave potentially plausible results at 20 years, but these were uncertain.

Other assumptions and inputs in the economic model

Utility values, model baseline age and adjustments for missed doses are appropriate for decision making

3.12 After technical engagement both the company and ERG made several changes to the model and agreed on the following assumptions and inputs:

- applying the company's new adjustment of costs for chemotherapy and nivolumab for missed doses
- setting the model's mean baseline age to 64.15 years based on Cancer Research UK data, instead of CheckMate 649 data
- using the company's utility values based on CheckMate 649 data.

The CheckMate 649 data that was used to inform utility values cannot be reported here because it is academic in confidence. The clinical experts agreed with the company's and ERG's approach. The committee concluded that the utility values, model baseline age and adjustments for missed doses used in the model were appropriate for decision making.

Cost-effectiveness estimates

The company's base-case ICERS using the 5- and 6.5-year treatment waning assumptions are potentially plausible, but are still uncertain

3.13 The cost-effectiveness results include nivolumab's confidential discount (see [section 2.4](#)). At the third meeting:

- the company's base case (using a Gompertz distribution to model overall survival) without treatment waning provided a probabilistic incremental cost-effectiveness ratio (ICER) of £46,221 per quality-adjusted life year (QALY) gained for nivolumab plus XELOX compared with XELOX alone
- the company's base case using a 6.5-year treatment waning assumption provided a probabilistic ICER of £49,365 per QALY gained
- the company's scenario using a 5-year treatment waning assumption provided a probabilistic ICER of £51,331 per QALY gained
- the ERG's approach to modelling overall survival using a Gompertz distribution without treatment waning provided a probabilistic ICER of £41,527 per QALY gained
- the ERG's approach using a Gompertz distribution with 5-year treatment waning applied provided a probabilistic ICER of £49,869 per QALY gained.

The committee considered the ICERs resulting from scenarios using a Gompertz distribution with the 5- or 6.5-year treatment waning assumptions were potentially plausible but were still uncertain. After the third committee meeting the company updated its commercial arrangement and submitted updated results for the company and ERG scenarios which included an assumption of treatment waning at both 5-years and 6.5 years. The change to the commercial arrangement resulted in ICERs that were well below £50,000 per QALY gained.

End of life

End of life criteria are met

- 3.14 The committee considered the advice about life-extending treatments for people with a short life expectancy in [NICE's guide to the methods of technology appraisal](#). It considered whether nivolumab with platinum- and fluoropyrimidine-based combination chemotherapy meets the end of life criteria for people with untreated HER2-negative advanced gastric, gastro-oesophageal junction or oesophageal adenocarcinoma that expresses PD-L1 with a CPS of 5 or more. The company and ERG both agreed, based on their analyses, that average life expectancy in this population is less than 24 months. The observed median overall survival benefit with nivolumab plus XELOX or FOLFOX in CheckMate 649 was larger than the additional 3-month extension to life needed by the criteria (the data cannot be reported here because it is academic in confidence). The committee concluded that nivolumab met the end of life criteria.

Because of the uncertainty, an ICER well below £50,000 per QALY gained is needed for this technology to be considered cost effective

- 3.15 [NICE's guide to the methods of technology appraisal](#) notes that the appraisal committee does not use a precise maximum acceptable ICER above which a technology would automatically be defined as not cost effective, or below which it would. Also, consideration of the cost effectiveness of a technology is necessary, but is not the sole basis for decision making. Therefore, NICE considers that the influence of other factors upon the decision to recommend a technology is greater when the ICER is closer to the top of the acceptable range. 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. The committee had concluded that end of life criteria applied (see [section 3.14](#)). At the second committee meeting the committee stated that the ICER should sit

comfortably below £50,000 for nivolumab plus XELOX to be considered a cost-effective use of NHS resources. This was because of high levels of uncertainty around long-term survival and treatment effect waning. The committee was aware that there is an unmet need (see [section 3.2](#)) and that the company had provided an updated patient access scheme for the third committee meeting. It had not been presented with any evidence to reduce the uncertainty about long-term survival and treatment effect waning, so its conclusions on an acceptable ICER remained the same. Following the third meeting the company's updated commercial arrangement reduced the ICERs from the company and ERG approaches (see [section 3.13](#)) to comfortably below £50,000 per QALY gained.

Equalities

There are no equality issues relevant to the recommendations

3.16 No equality or social value judgement issues were identified.

Conclusion

Nivolumab is recommended for use in the NHS

3.17 Extrapolation of CheckMate 649 overall survival data using a semi-parametric approach with a Gompertz distribution and accounting for treatment waning produced plausible 20-year survival outcomes. However, the most appropriate method to model overall survival remains unclear and the long-term survival estimates are highly uncertain. End of life criteria applied. The committee concluded that nivolumab is a cost-effective use of NHS resources because the most plausible scenarios resulted in ICERs comfortably below £50,000 per QALY gained (see [section 3.15](#)). The committee concluded that nivolumab with platinum- and fluoropyrimidine-based chemotherapy is recommended for treating HER2-negative, advanced or metastatic gastric, gastro-oesophageal junction or oesophageal adenocarcinoma that expresses PD-L1 with a CPS of 5 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 HER2-negative, advanced or metastatic gastric, gastro-oesophageal junction or oesophageal adenocarcinoma and the doctor responsible for their care thinks that nivolumab with platinum- and fluoropyrimidine-based chemotherapy 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.

Chair

Jane Adam

Chair, technology appraisal committee A

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.

Anne Murray, Cara Gibbons and Marcela Haasová

Technical leads

Mary Hughes

Technical adviser

Thomas Feist

Project manager

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