NICE National Institute for Health and Care Excellence

NICE guidance

Pembrolizumab for adjuvant treatment of resected stage 2B or 2C melanoma

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.

Contents

1 Recommendations

1.1 Pembrolizumab is recommended, within its marketing authorisation, as an option for the adjuvant treatment of completely resected stage 2B or 2C melanoma in people 12 years and over. It is recommended only if the company provides pembrolizumab according to the commercial arrangement.

Why the committee made these recommendations

Standard care for people with stage 2B or 2C melanoma that has been removed with surgery (resected) is routine follow-up. There is an unmet need for treatments after surgery (adjuvant treatment).

Clinical evidence shows that adjuvant pembrolizumab increases how long people live without the cancer coming back and getting worse compared with placebo. There is still not enough evidence to know how much pembrolizumab increases how long people live.

Because of this, and because introducing pembrolizumab for stage 2B or 2C melanoma is likely to change the treatment pathway, there is some uncertainty in the cost-effectiveness estimates. But despite the uncertainty, they are within what NICE considers an acceptable use of NHS resources. So, pembrolizumab is recommended.

2 Information about pembrolizumab

Marketing authorisation indication

2.1 Pembrolizumab (Keytruda, MSD) is indicated 'for the adjuvant treatment of adults and adolescents aged 12 years and older with Stage 2B, 2C or 3 melanoma and who have undergone complete resection'.

2.2 Pembrolizumab is also recommended for the adjuvant treatment of resected stage 3 melanoma (NICE technology appraisal guidance 766).

Dosage in the marketing authorisation

2.3 The dosage schedule is available in the summary of product characteristics for pembrolizumab.

Price

2.4 The list price is £2,630.00 per 100 mg/4 ml concentrate for solution for infusion vial (excluding VAT; BNF online, accessed August 2022).

2.5 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.

Clinical need

People with resected stage 2B or 2C melanoma would welcome an adjuvant treatment option

3.1 Melanoma is a cancer that develops from melanocytes in the skin. There are multiple risk factors that increase the likelihood of developing melanoma, including a family history of melanoma, fair skin and hair colour, and intense or chronic exposure to ultraviolet (UV) light. Melanomas are classified by the size and depth of the melanoma and whether it has spread. Stage 2 melanoma is defined as having no evidence of spread to lymph nodes or distant metastases. Stage 2B and 2C tumours are deeply penetrating tumours, with or without ulceration, and are at high risk of recurrence. Standard care for people with stage 2B or stage 2C melanoma is complete surgical excision with wide margins. After surgery, people then have routine follow-up for 5 years, which is tailored according to individual risk. The clinical experts explained that the risk of disease recurrence is greatest in the first 3 years after surgery. There are currently no adjuvant treatment options available for stage 2 melanoma. The aim of adjuvant treatment is to remove any residual microscopic disease after surgery to reduce the risk of local recurrence or progression to metastatic disease, which is currently considered incurable. The patient expert described how people with resected stage 2B or 2C melanoma experience a substantial physical, mental and emotional burden. This is because of the fear of recurrence and uncertainty about outcomes if the cancer were to recur. The clinical experts explained that stage 2B and 2C melanoma has a similar risk of recurrence to stage 3A and stage 3B melanoma, for which adjuvant treatments are available. So, there is a similar need for adjuvant

treatment for stage 2B or stage 2C melanoma. The patient experts acknowledged that pembrolizumab may have adverse effects which can occasionally be severe and long lasting. However, they agreed the benefit in reducing the risk of recurrence outweighs the potential risk of adverse effects. The clinical experts stated that, generally, pembrolizumab is well tolerated across all ages, although about 10% of people can have permanent adverse effects. Clinicians are familiar with monitoring for adverse events in people having pembrolizumab because it is already used to treat melanoma at later disease stages. The committee concluded that there is an unmet need in this area, and that people with resected stage 2B or 2C melanoma would welcome an adjuvant treatment that reduces the risk of recurrence.

Current treatment pathway

Adjuvant pembrolizumab is a step change in managing stage 2B or 2C melanoma and may change the treatment pathway

3.2 People with stage 2B or 2C melanoma can have a locoregional recurrence after surgery. This means they can have a recurrence at the same site (stage 2B or 2C recurrence), or in the local lymph nodes (stage 3 melanoma). Currently, stage 3 melanoma is treated with complete surgical excision with wide margins, followed by adjuvant treatment with pembrolizumab, nivolumab or dabrafenib plus trametinib (see NICE's technology appraisal guidance on pembrolizumab, nivolumab and dabrafenib plus trametinib). The committee considered whether people would have adjuvant treatment again for stage 3 melanoma if they had had it for stage 2B or 2C. The clinical experts explained that people whose cancer recurs when having adjuvant pembrolizumab are likely to have immunotherapy-resistant cancer, so are unlikely to benefit from further adjuvant immunotherapies (such as pembrolizumab or nivolumab). But people who have a BRAF gene mutation could still benefit from BRAF-targeted adjuvant treatment with dabrafenib plus trametinib. The committee noted that all people with melanoma at high risk of recurrence (including stage 2B or 2C) will have testing to see if they have a BRAF mutation. The committee heard that about 45% of people will have a BRAF mutation. The clinical experts noted that

restrictions from NHS England may affect access to further adjuvant immunotherapies after adjuvant pembrolizumab for stage 2B or 2C melanoma. In other indications, NHS England only permits the use of adjuvant immunotherapies at one point in the treatment pathway. The Cancer Drugs Fund clinical lead noted that this is an area of uncertainty and there is no evidence of the efficacy of further adjuvant immunotherapy for people who have already had it. The committee then discussed the treatment pathway for stage 2B or 2C melanoma with distant metastasis (advanced melanoma). For advanced melanoma, NICE recommends immunotherapies in combination (see NICE's technology appraisal guidance on nivolumab plus ipilimumab) or as monotherapy (see NICE's technology appraisal guidance on pembrolizumab, pembrolizumab after ipilimumab, nivolumab and ipilimumab). It also recommends targeted treatments for BRAF V600 mutation-positive advanced melanoma (see NICE's technology appraisal guidance on dabrafenib plus trametinib, trametinib plus dabrafenib, encorafenib plus binimetinib, vemurafenib and dabrafenib). NICE's guideline on melanoma also states that chemotherapy (dacarbazine) or best supportive care should be considered if immunotherapies or targeted therapies for BRAF V600 mutation-positive advanced melanoma are not appropriate. The Cancer Drugs Fund clinical lead noted that the objective of treatment for advanced melanoma is different to that of adjuvant treatment. Adjuvant treatment is used to prevent recurrence or metastases, but once there is metastatic spread the aim is to extend overall survival. The clinical experts noted that most people with advanced melanoma would have immunotherapies in combination. Or, if they had a BRAF V600 mutation, they would have targeted treatment. They further noted that if BRAF V600 mutation-positive melanoma had not responded to adjuvant immunotherapy monotherapy, it may respond to combination immunotherapy. The committee concluded that adjuvant pembrolizumab is an important step change in managing stage 2B or 2C melanoma but may change whether adjuvant treatment options are used later in the pathway.

Clinical evidence

The population in KEYNOTE-716 adequately reflects the

population in NHS practice

3.3 KEYNOTE-716 is an ongoing multinational 2-part phase 3 study. Part 1 is a double-blind placebo-controlled study that randomised 976 adults and young people with resected stage 2B or 2C melanoma to adjuvant pembrolizumab or placebo. Baseline characteristics were well balanced between the 2 treatment arms. Most people included in KEYNOTE-716 were white, which is expected because fair skin is a risk factor for melanoma. Across both arms of the trial, 64.0% of people had stage 2B melanoma and 34.8% had stage 2C melanoma. The ERG noted that a larger proportion of people in KEYNOTE-716 had stage 2B melanoma than is expected in England (using data from Public Health England in which 57% of people had stage 2B melanoma and 43% had stage 2C melanoma). Stage 2B melanoma has a better prognosis than stage 2C melanoma. Subgroup analyses from KEYNOTE-716 appear to show a better outcome with pembrolizumab for stage 2B melanoma compared with stage 2C melanoma. The clinical experts stated that they did not consider that there was much difference between the trial and the Public Health England data, and that melanoma is increasingly being diagnosed earlier. So they considered the population in KEYNOTE-716 to be generalisable to the eligible population in the NHS. The clinical experts also stated that they would expect pembrolizumab to work relatively similarly in stage 2B and 2C melanoma. One clinical expert highlighted that stage 2C melanoma without ulceration had similar outcomes to stage 2B melanoma, but stage 2C melanoma with ulceration tended to have a worse prognosis. The clinical experts noted that subgroup analyses in KEYNOTE-716 were not statistically powered to detect differences between stage 2B and 2C melanoma and a larger trial would be needed to assess this. The committee agreed that it was more appropriate to consider the whole population rather than focusing on retrospective subgroup analyses. The committee concluded that the population included in KEYNOTE-716 adequately reflects the population who would have treatment in NHS clinical practice.

The results of KEYNOTE-716 are likely to be generalisable to young people aged 12 to 17

3.4 The median age of people in the KEYNOTE-716 trial was 60.0 years in the

pembrolizumab group and 61.0 years in the placebo group. Both groups included 1 young person (aged between 12 to 17). Because of this, the ERG noted that it is uncertain whether the trial results would be generalisable to young people. The company stated that melanoma incidence in young people is low, so there is low recruitment of young people to all melanoma trials. The European Medicines Agency has accepted that the results from KEYNOTE-716 are generalisable to young people. This is because melanoma disease biology is similar between adults and young people. Also, disease response to pembrolizumab is similar between adults and young people in other disease areas. The clinical experts stated that they would expect the efficacy and safety outcomes with pembrolizumab in young people to be similar to outcomes in adults. The committee concluded that the results of KEYNOTE-716 are likely to be generalisable to young people.

Efficacy and safety data from KEYNOTE-716 for the 3-weekly dose of pembrolizumab is likely to be generalisable to the 6-weekly dose

3.5 Pembrolizumab is licensed for treating melanoma in adults at doses of 200 mg every 3 weeks and 400 mg every 6 weeks. However, the KEYNOTE-716 trial only assessed the efficacy and safety of the 200 mg every 3 weeks dose. The company explained that the European Medicines Agency has approved the 6-weekly dosing schedule for adjuvant treatment of stage 2 melanoma because modelling of dose–exposure relationships found no significant differences in efficacy or safety between doses. Also, the 3-weekly and 6-weekly dosing schedule of pembrolizumab as monotherapy and in combination has been shown to be similar in other indications, including unresectable advanced melanoma. The clinical experts explained that the 6-weekly dosing schedule of pembrolizumab is used for other lines of treatment for melanoma. They had no concerns about the generalisability of the data from KEYNOTE-716 to NHS practice. The committee noted that the 6-weekly dosing schedule is important to manage resource use in clinics, oncology day units and pharmacies, and is the dose that would be used most frequently in clinical practice. The committee concluded that the efficacy and safety data for the 3-weekly dosing schedule of pembrolizumab from KEYNOTE-716 is likely to be generalisable to the

6-weekly dosing schedule.

Pembrolizumab improves recurrence-free and distant metastasis-free survival compared with placebo, but overall survival data is immature

3.6 The primary outcome of KEYNOTE-716 was recurrence-free survival. At the first interim analysis (December 2020 data cut-off), a statistically significant improvement in recurrence-free survival was seen with pembrolizumab compared with placebo (hazard ratio [HR] 0.65, 95% confidence interval [CI] 0.46 to 0.92). At technical engagement, the company shared the results of the third interim analysis of the trial data, which had a January 2022 data cut-off. The additional follow-up data from the further data cuts supports the first interim analysis for recurrence-free survival. The January 2022 data cut-off also provided data for distant metastasis-free survival. This showed that adjuvant pembrolizumab statistically significantly improved distant metastasis-free survival compared with placebo (HR 0.64, 95% CI 0.47 to 0.88; p=0.00292). At the January 2022 data cut-off most people were still alive, which meant there was not enough data to analyse overall survival. The committee concluded that pembrolizumab improves recurrence-free survival and distant metastasis-free survival compared with placebo, but overall survival data is still immature.

Improved recurrence-free and distant metastasis-free survival is likely to be associated with an overall survival benefit, but this is uncertain

3.7 The committee was aware that there are challenges in gathering and interpreting overall survival data for adjuvant treatments, such as pembrolizumab for stage 2B or 2C melanoma. This is because people have no detectable disease at the time of treatment and some people may have no remaining disease at all. A large proportion of people with resected stage 2B or 2C disease will not have a recurrence. This means that people may live for a long time, so a long follow-up would be needed to collect sufficient survival data. In the absence of overall survival data, the committee considered whether recurrence-free or distant

metastasis-free survival could be used as a surrogate for overall survival. The clinical experts explained that if a treatment makes a clinically meaningful difference to distant metastasis-free survival then it is likely that this would be reflected in an overall survival benefit. The committee concluded that, based on its earlier conclusion that pembrolizumab improves recurrence-free survival and distant metastasis-free survival compared with placebo (see section 3.6), it was likely that pembrolizumab also improved overall survival. However, given the immaturity of overall survival data, the extent of this benefit is uncertain.

Economic model

The company's model structure is acceptable for decision making

3.8 The company developed a Markov cohort state-transition model to assess the cost effectiveness of pembrolizumab for treating stage 2B or 2C melanoma. The model included 4 health states: recurrence-free, locoregional recurrence, distant metastasis and death. The distant metastasis state included 2 sub-states (pre-progression and post-progression) to include the costs and outcomes of subsequent treatments after the development of distant metastasis. The model used a lifetime time horizon (40.7 years) and a 1-week cycle length, with a half-cycle correction. Transitions from the recurrence-free and locoregional recurrence health states were modelled using recurrence-free survival and distant metastasis-free survival data from the most recent data cut of KEYNOTE-716. Transitions from the distant metastasis health states were dependent on the previous treatment for advanced melanoma, data from KEYNOTE-006 (a randomised controlled trial comparing pembrolizumab with ipilimumab in advanced melanoma) and the results of a network meta-analysis. The ERG considered the model structure reasonable. The committee noted that the structure was similar to the model used in NICE's technology appraisal guidance on adjuvant pembrolizumab for stage 3 melanoma and concluded that it was suitable for decision making.

People who have adjuvant pembrolizumab for stage 2B or 2C melanoma would probably not have further adjuvant treatment,

unless they have a BRAF mutation

3.9 The company's base assumed that people who have adjuvant pembrolizumab for resected stage 2B or 2C melanoma would not have any further adjuvant treatment for locoregional recurrence at stage 3. The company's clinical experts said that people are likely to have 'one shot' at adjuvant treatment. This is because of a lack of data and uncertainty about possible restrictions on multiple lines of adjuvant immunotherapies from NHS England (see section 3.2). The ERG stated that these assumptions were not aligned with KEYNOTE-716 data, and in its base case assumed that equal proportions of people would have subsequent treatment after locoregional recurrence in both arms. The company noted that KEYNOTE-716 is a global clinical trial and several of the treatments used after locoregional recurrence in the trial are not approved for use in the UK, so the trial may not reflect UK clinical practice. The committee recalled previous comments from the clinical experts and Cancer Drugs Fund clinical lead (see section 3.2). It agreed that there is uncertainty about the treatment pathway for stage 3 melanoma if adjuvant pembrolizumab were recommended for stage 2B or 2C melanoma. The committee agreed that it is likely that people who have adjuvant pembrolizumab at stage 2 would not have further adjuvant immunotherapy. However, it noted that people who have a BRAF V600 mutation would be able to have dabrafenib plus trametinib for the adjuvant treatment of stage 3 melanoma. So the committee considered that its preferred assumption for adjuvant treatment for locoregional recurrence would be between the ERG's and company's assumptions used in the base-case analyses. The committee concluded that the most likely assumption would align with a scenario analysis done by the company. In this scenario, people with a BRAF mutation are eligible for adjuvant treatment at stage 3 with dabrafenib plus trametinib after they have had adjuvant treatment at stage 2B or 2C, adjusted for the percentage of the overall cohort who will have no adjuvant treatment.

The proportions of subsequent treatments for metastatic disease and how long people will have these for is uncertain

3.10 In the company's base case, the proportions of people having each subsequent treatment for distant metastasis was informed by Systemic

Anti-Cancer Therapy data collected for NICE's technology appraisal guidance on adjuvant pembrolizumab for stage 3 melanoma and market share data. These proportions were adjusted to assume that 2 years after starting a 1-year course of adjuvant treatment, some people who develop metastasis may have pembrolizumab again. The ERG used the same assumptions as the company in its base-case analyses. But it noted that there is uncertainty about these inputs and did a scenario analysis assuming equal proportions of subsequent treatments after distant metastasis in both arms. This reduced the incremental cost-effectiveness ratio (ICER) by about £15,000 per quality-adjusted life year (QALY) gained. In the company's base case, the duration of first-line distant metastasis treatment was based on modelled progression-free survival for each regimen. The duration of second-line treatment was assumed to be 21 weeks for all regimens except ipilimumab, for which the duration was assumed to be 12 weeks. The ERG also used these assumptions in its base case but noted that it is unclear whether these assumptions are clinically plausible. The ERG explored this uncertainty by doing an extreme scenario analysis in which subsequent treatment acquisition costs in the distant metastasis state for both arms were excluded. This led to a substantial increase in the ICER, although the committee noted this was still below the range NICE considers a cost-effective use of NHS resources. The committee concluded that there is uncertainty about the market shares and duration of subsequent treatments in the distant metastasis health state.

Distributions used to model transition probabilities from the recurrence-free health state are uncertain but reasonable

3.11 The company's base case used a lognormal distribution to model transitions from the recurrence-free health state to the locoregional recurrence state and distant metastasis state for both arms. The company explained that the lognormal-lognormal combination was selected for the base case because it has a high ranking in terms of statistical fit. It explained that the incremental recurrence-free and distant metastasis-free survival benefit for pembrolizumab compared with observation was aligned with, or slightly below, the average incremental benefit across the other potential combinations. The ERG also used these distributions in its base case but did a scenario analysis

using the generalised gamma-lognormal distribution, which led to an increase in the ICER above £30,000 per QALY gained. The ERG explained that this scenario was done to reflect the uncertainty in transitions from the recurrence-free health state. But it noted that the distributions selected by the company are also plausible and it is difficult to determine which distribution is most appropriate. The committee asked why the statistical fit of the transition curves was based on mean squared errors, rather than using Akaike information criterion (AIC) and Bayesian information criterion (BIC) statistics. The company explained that AIC and BIC fit statistics are not suitable measures of fit when modelling competing risks, so mean squared errors were used to assess statistical fit. The ERG agreed that this approach is appropriate. The company noted that it had used the same methodology as in NICE's technology appraisal guidance on adjuvant pembrolizumab for stage 3 melanoma, and that the observed cumulative incidence function was aligned with predicted curves for the observed period. The ERG noted that a substantial proportion of the recurrence-free survival benefit was accrued beyond the observed data period. The committee concluded that there is uncertainty about the appropriate distributions to model transition probabilities from the recurrence-free health state but noted that the company's approach appears to be reasonable.

The data inputs for end of life care costs and post-progression utility values in the distant metastasis health state are uncertain

3.12 The economic model included intervention costs, health state costs, costs of managing adverse events and end of life care costs. These were based on NHS reference prices and prices from the BNF, Personal Social Services Research Unit and Medical Information Management System. In the company's base case, end of life care costs were applied to deaths from the distant metastasis health state only. But in the ERG's base-case end of life care costs were applied regardless of the cause of death. In the recurrence-free, locoregional recurrence and pre-progression distant metastasis states, utility values in the company's model were sourced from a regression model developed using EQ-5D data from KEYNOTE-716. In the post-progression distant metastasis health state, the company's base-case utility value was derived from Beusterien et al. 2009, which used a standard gamble approach to elicit values from the

UK general population. The ERG used a value from KEYNOTE-006, based on EQ-5D. The committee noted that the company's assumptions aligned with NICE's technology appraisal guidance on adjuvant pembrolizumab for stage 3 melanoma. But, it was aware that the different assumptions used by the company and the ERG had a limited effect on the ICER. The committee concluded that end of life care costs and post-progression utility values in the distant metastasis health state are uncertain but unlikely to significantly affect the cost-effectiveness results.

Cost-effectiveness estimates

Because of the uncertainty an acceptable ICER should be around £20,000 per QALY gained

3.13 NICE's guide to the methods of technology appraisal 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. The committee noted the uncertainties in the modelling assumptions, specifically that:

- The overall survival data for pembrolizumab is immature (see section 3.6), and that this uncertainty would not have been reflected in the cost-effectiveness results. Because the results are dependent on a surrogate relationship to estimate overall survival, the committee agreed it would have preferred to see some analyses assessing the relationship between recurrence-free survival, distant metastases-free survival and overall survival, to check the robustness of this approach.
- There is uncertainty about some of the inputs in the economic model, including the use of subsequent adjuvant treatments after adjuvant treatment with pembrolizumab for stage 2B or 2C melanoma (see section 3.9).

So it agreed that an acceptable ICER would be towards the lower end of the range normally considered a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained).

The cost-effectiveness estimates are uncertain but are likely within what NICE considers to be an acceptable use of NHS resources

3.14 The committee noted that when the confidential patient access schemes for pembrolizumab and subsequent treatments were applied, most of the ICERs were around £20,000 per QALY gained. The committee considered the uncertainty about subsequent adjuvant treatments after adjuvant pembrolizumab at stage 2 (see section 3.9). It noted that in the scenario analysis in which people who had adjuvant pembrolizumab for stage 2 disease, had a BRAF V600 mutation, and could have dabrafenib plus trametinib for adjuvant stage 3 treatment, the ICER was also around £20,000 per QALY gained. Taking all of this into account, the committee concluded that pembrolizumab was an acceptable use of NHS resources.

Other factors

Equalities

3.15 The committee did not identify any equality issues associated with using pembrolizumab in this indication.

Innovation

3.16 There are currently no adjuvant treatment options for people with stage 2 melanoma in the UK. Standard care is routine follow-up. So the committee concluded that introducing pembrolizumab as adjuvant treatment for people with stage 2B and stage 2C melanoma would be a step change in clinical management.

End of life criteria

3.17 NICE's advice about life-extending treatments for people with a short life expectancy did not apply.

Conclusion

Pembrolizumab is recommended for routine use

3.18 The committee concluded that the most plausible cost-effectiveness estimates are within what NICE considers to be an acceptable use of NHS resources. So pembrolizumab is recommended for the adjuvant treatment of resected stage 2B or 2C melanoma in people aged 12 or over.

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 resected stage 2B or 2C melanoma and the doctor responsible for their care thinks that pembrolizumab 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.

Lizzie Walker
Technical lead

Joanna Richardson
Technical adviser

Jeremy Powell
Project manager

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Accreditation