NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Nivolumab for treating recurrent or metastatic squamous cell carcinoma of the head and neck after platinum-based chemotherapy

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using nivolumab in the NHS in England. The appraisal committee has considered the evidence submitted by the company and the views of non-company consultees and commentators, clinical experts and patient experts.

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

The appraisal committee is interested in receiving comments on the following:

Has all of the relevant evidence been taken into account?
Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
Are the recommendations sound and a suitable basis for guidance to the NHS?
Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Issue date: December 2020

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

The appraisal committee will meet again to consider the evidence, this appraisal consultation document and comments from the consultees.
At that meeting, the committee will also consider comments made by people who are not consultees.
After considering these comments, the committee will prepare the final appraisal document.

- Subject to any appeal by consultees, the final appraisal document may be used as the basis for NICE's guidance on using nivolumab in the NHS in England.

For further details, see NICE's guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 28 January 2021

Second appraisal committee meeting: TBC

Details of membership of the appraisal committee are given in section 5

1 Recommendations

1.1 Nivolumab is not recommended, within its marketing authorisation, for treating recurrent or metastatic squamous cell carcinoma of the head and neck in adults whose disease has progressed during or after platinum-based chemotherapy.

1.2 This recommendation is not intended to affect treatment with nivolumab that was started in the NHS before this guidance was published. People having treatment outside of this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

This appraisal reviews the additional evidence collected as part of the Cancer Drugs Fund managed access agreement for nivolumab for treating recurrent or metastatic squamous cell carcinoma of the head and neck after platinum-based chemotherapy (NICE technology appraisal guidance 490). If nivolumab is not recommended for routine commissioning in this indication when final guidance is published, it will no longer be available in the Cancer Drugs Fund for people to start treatment, but people already taking it will be able to continue.

The new evidence includes data from clinical trials and from patients having treatment in the NHS, while this treatment was available in the Cancer Drugs Fund in England. It shows that people who have nivolumab are likely to live up to 9 months longer than those who have docetaxel, methotrexate or cetuximab. But it is unclear whether nivolumab extends life for longer than 3 months in people who are fit enough to be offered docetaxel or for people with tumours with a low PD-L1 score. These groups of people are most likely to be offered nivolumab in the NHS. So it is unclear whether nivolumab meets NICE's criteria to be considered a life-extending treatment.

The cost-effectiveness estimates are highly uncertain. But they are likely to be at the higher end of what NICE considers an acceptable use of NHS resources, and could exceed the maximum. So nivolumab is not recommended.

2 Information about nivolumab

Marketing authorisation indication

2.1 Nivolumab (Opdivo, Bristol-Myers Squibb) as monotherapy is indicated for 'the treatment of recurrent or metastatic squamous cell cancer of the head and neck in adults progressing on or after platinum-based therapy'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics.

Price

2.3 The list price is £439 per 40-mg vial, £1,097 per 100-mg vial and £2,633 per 240-mg vial (excluding VAT; British national formulary [BNF] online accessed November 2020 and company submission). The company has a commercial arrangement. This makes nivolumab available to the NHS with a discount and it would have also applied to this indication if the technology had been recommended. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee considered evidence submitted by Bristol-Myers Squibb, a review of this submission by the evidence review group (ERG), NICE's technical report, and responses from stakeholders. See the committee papers for full details of the evidence.

This guidance review looks at data collected in the Cancer Drugs Fund to address uncertainties identified during the original appraisal. Further information about the

original appraisal is in the committee papers. As a condition of the Cancer Drugs Fund funding and the managed access arrangement, the company was required to collect updated efficacy data from the CheckMate 141 study. Data were also collected using the Systemic Anti-Cancer Therapy (SACT) dataset.

The committee recognised that there were remaining areas of uncertainty associated with the analyses presented (see technical report, page 8), and took these into account in its decision making. The committee discussed the following issues, which were outstanding after the technical engagement stage:

- the generalisability of the trial population to NHS clinical practice
- the choice of parametric models to predict overall survival
- the choice of parametric models to predict time to treatment discontinuation
- the 2-year stopping rule and the continued duration of treatment benefit if nivolumab were to be stopped at 2 years
- the choice of utility values
- the cost effectiveness in the PD-L1 subgroups.

The condition and clinical management

Squamous cell carcinoma of the head and neck is a debilitating condition with an unmet need for effective treatment options

3.1 Recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) that has progressed during or after platinum-based chemotherapy has a poor prognosis. The patient experts described SCCHN as a debilitating condition with multiple distressing symptoms such as disfigurement, a dry and sore mouth, weight loss and decreased appetite. They explained that the disease affects all aspects of life including mental wellbeing, social functioning, mobility and work. The clinical expert explained that people have limited treatment options and their disease is generally considered incurable at this stage. Existing treatments are taxane-based chemotherapies such as docetaxel or paclitaxel, which can cause significant adverse reactions. The patient

expert stated that the outlook is poor for patients with recurrent or metastatic SCCHN that has relapsed on or after platinum-based chemotherapy. The committee noted that improved quality of life both during and after treatment is most important to this patient group, as is extending life. The committee concluded that there is an unmet need for effective treatment options for people with recurrent or metastatic SCCHN that has progressed on or after platinum-based chemotherapy.

Docetaxel is the most appropriate comparator for people fit enough to have it

3.2 The committee noted that the treatment pathway for recurrent or metastatic SCCHN had changed since the publication of the original appraisal of nivolumab. This is because cetuximab combination therapy and pembrolizumab monotherapy have been recommended for treating recurrent or metastatic SCCHN (see NICE's technology appraisal guidance on cetuximab for treating recurrent or metastatic squamous cell cancer of the head and neck and pembrolizumab for untreated metastatic or unresectable recurrent head and neck squamous cell carcinoma). The committee noted that both these treatments are used earlier in the treatment pathway than nivolumab. It also noted that there are potential implications for using nivolumab to treat SCCHN that has progressed within 6 months of platinum-based chemotherapy. Pembrolizumab is recommended for untreated metastatic or unresectable recurrent SCCHN in adults whose tumours express PD-L1 with a combined positive score of 1 or more. But in NHS clinical practice, people would only have immunotherapy once during the treatment pathway. Therefore, the committee agreed that most people who will be eligible for immunotherapy in later lines of treatment will have tumours that have a PD-L1 score of less than 1. At the time of the original appraisal of nivolumab, treatment options in clinical practice in England included taxane-based chemotherapies (such as docetaxel and paclitaxel) or methotrexate. In the original appraisal, the clinical experts agreed that although there was no

evidence of difference in efficacy between docetaxel and paclitaxel, docetaxel would be the standard single-agent chemotherapy used for recurrent or metastatic SCCHN that progressed during or after platinum-based therapy in the NHS (most often prescribed as a 3-weekly treatment regimen), and that the use of paclitaxel in clinical practice is limited. They also stated that methotrexate is normally only offered to people with a poor performance status who are not fit enough to have a taxane, or as subsequent therapy for people who have had a single-agent taxane. The committee concluded in the original appraisal that docetaxel would be the most appropriate comparator for people fit enough to have it. For this guidance review, the committee concluded that docetaxel was still the most appropriate comparator for its decision making.

Clinical effectiveness

The docetaxel subgroup from CheckMate 141 is most relevant to UK clinical practice

3.3 The clinical-effectiveness evidence for nivolumab came from 1 study (CheckMate 141) that compared nivolumab with the investigator's choice of therapy. Patients randomised to the investigator-choice arm had 1 of 3 possible weekly therapies (docetaxel [47% of patients], methotrexate [41%] and cetuximab [12%]). In the original appraisal, the committee concluded that excluding paclitaxel from the trial and including cetuximab, a drug not used in clinical practice at that time and therefore not included in the NICE scope, introduced uncertainty about the relevance of CheckMate 141 to UK clinical practice. The committee also concluded, based on the testimony of the clinical experts, that it was valid to assume that docetaxel and paclitaxel were equivalent. But it was not persuaded by the company's assumption that docetaxel is equivalent to methotrexate. For this guidance review, the clinical expert acknowledged that the trial took place in several countries where standard care differs from NHS clinical practice. He suggested that the investigator-choice arm of the trial was an appropriate comparison even though cetuximab is not standard

care in NHS clinical practice and methotrexate is only offered to people with poor performance status and may be less effective. The Cancer Drugs Fund Clinical Lead stated that people in the trial (who had an Eastern Cooperative Oncology Group performance status of 0 or 1) would have been fit enough to get docetaxel in NHS clinical practice, and therefore the investigator-choice arm would not be a relevant comparator. The committee noted that the company had presented results for an analysis comparing nivolumab and docetaxel in patients who would have docetaxel (referred to as the 'docetaxel subgroup') in CheckMate 141. The company highlighted that the trial was not powered to detect differences between nivolumab and docetaxel alone and therefore any results had to be treated with caution. The committee acknowledged that this was not a prespecified subgroup analysis and such a comparison was less robust than using the intention-to-treat population, because of the smaller sample size. The committee agreed that there was uncertainty about the relevance of the comparator arm of CheckMate 141 to UK clinical practice. It concluded that the docetaxel subgroup was the most appropriate data source for this guidance review because it was most relevant to NHS clinical practice.

The clinical benefit of nivolumab compared with docetaxel alone is not clear

3.4 For this guidance review, the company provided an additional 37 months of data (up to October 2019) from Checkmate 141. The results for the intention-to-treat population showed that people who had nivolumab lived longer than people who had the investigator-choice treatment (median overall survival for nivolumab was 7.7 months, 95% confidence interval 5.7 to 8.7 months; investigator choice was 5.1 months, 95% confidence interval 4.0 to 6.2 months; hazard ratio 0.69, 95% confidence interval 0.55 to 0.86). The Cancer Drugs Fund Clinical Lead referred to an amendment update of the clinical protocol for CheckMate 141, which meant that people in the investigator-choice arm could have had nivolumab in the extension phase of the trial. The company did not provide data on how

many people switched from investigator choice to nivolumab. It is therefore unclear how a treatment switch would have affected overall survival, which could potentially bias the results against nivolumab. The company provided results for the docetaxel subgroup that showed a numerical survival benefit for nivolumab compared with docetaxel, but this was not statistically significant (the exact data are confidential and cannot be reported here). The committee acknowledged that there was uncertainty associated with the results from the docetaxel subgroup because of the small number of people in the subgroup analysis, and because the effect of treatment switching was unknown. However, it agreed that the subgroup analysis was relevant for its decision making (see section 3.4). It concluded, based on the evidence that had been presented to date, that it was uncertain whether nivolumab was clinically effective compared with docetaxel alone.

There is evidence of nivolumab's benefit for tumours with a PD-L1 score of 1% or higher, but at a lower PD-L1 score the benefit is not clear

3.5 In the original appraisal, the committee concluded that there was evidence of nivolumab's benefit for tumours expressing 1% or more PD-L1 protein, but at lower expression levels the benefit was not clear. For this guidance review, the company provided subgroup analyses based on the latest available data (up to 15th October 2019) for PD-L1 of 1% and above and PD-L1 of less than 1% subgroups in the intention-to-treat population of CheckMate 141. For the subgroup with a PD-L1 score of 1% and above, the median overall-survival gain was 3.6 months with nivolumab compared with investigator choice (hazard ratio of 0.54, 95% confidence interval 0.39 to 0.76). For the less than 1% PD-L1 group, the median overall-survival gain was 1 month (hazard ratio 0.74, 95% confidence interval 0.50 to 1.10). The clinical expert explained that in clinical practice the availability of PD-L1 testing varies across the NHS in England, and that PD-L1 scores might not be available for all people at the time when treatment is started. The clinical expert also suggested that the PD-L1 score may not be as good a predictor of treatment outcome as previously

thought. The committee noted that PD-L1 testing in SCCHN would become routine in the NHS now that pembrolizumab is recommended for treating PD-L1 in adults whose tumours express 1% or more PD-L1. It acknowledged that there was uncertainty associated with the results from the subgroup analyses based on PD-L1 expression because of the small number of people in the subgroup analysis. However, it considered it was important to explore them because of NICE's recent recommendation for using pembrolizumab earlier in the treatment pathway, which means that nivolumab is likely to be used to treat SCCHN with a low PD-L1 score (see section 3.2). It concluded that there was evidence that nivolumab is clinically beneficial for tumours with a PD-L1 score of 1% and above but the benefit for those with a low PD-L1 score was less certain.

Clinical experience with nivolumab in the Cancer Drugs Fund reflects the trial results

3.6 As well as new data from the CheckMate 141 study, there were Systemic Anti-Cancer Therapy (SACT) data available for this review. These were collected from 506 people who had nivolumab through the Cancer Drugs Fund between October 2017 and October 2019. The clinical expert explained that the clinical experience with nivolumab is positive and that outcomes are reflective of what was seen in the clinical trials. The 1-year overall survival was similar between the nivolumab arm of the intention-to-treat population in the trial and the SACT data (trial 33.4%, 95% confidence interval 27.5 to 39.5; SACT data 34%, 95% confidence interval 29% to 38%). The median overall survival in the trial was longer (7.7 months, 95% confidence interval 5.7 to 8.7 months) than in the SACT data (6.5 months, 95% confidence interval 5.6 to 7.6 months). However, the 95% confidence intervals overlapped. The time to treatment discontinuation in the SACT data was 3.0 months (95% confidence interval 2.7 to 3.3 months), which is longer than in the trial (results are confidential and cannot be reported). The committee noted that the SACT data had a median follow-up of 6.2 months compared with a minimum follow up of 48.2 months in the trial.

Modelling overall survival and time to treatment discontinuation

The most plausible extrapolation method for overall survival for the docetaxel subgroup is unknown

3.7 In the original appraisal, the committee accepted that a piecewise model was appropriate for estimating overall survival in the intention-to-treat population. The model used Kaplan–Meier data followed by a log-normal distribution, but the time point from which to extrapolate was uncertain. For this guidance review, the company used data from the intention-to-treat population of the trial. It extrapolated from 96 weeks in line with the median follow up of the trial. This resulted in a 5-year survival of 5.7% and a 10-year survival of 2.6%. The clinical expert estimated that it was plausible that between 1% and 5% of people having nivolumab will be alive at 5 years, and that few people survive up to 10 years. In its response to technical engagement, the company used the same extrapolation method for the docetaxel subgroup. It did not present evidence of the goodness of fit for this method to the subgroup data, and it did not explore alternative methods. The committee considered the docetaxel subgroup to be the most appropriate data source for this guidance review because it was the most relevant population to NHS clinical practice. But it agreed that the extrapolation of overall survival for the docetaxel subgroup was uncertain because the assumptions had not been validated and reported with sufficient transparency.

The most plausible extrapolation method for time to treatment discontinuation for the docetaxel subgroup is unknown

3.8 In the original appraisal, using the intention-to-treat population, the committee concluded that none of the parametric distributions fitted the time to treatment-discontinuation data well. It preferred the generalised gamma distribution for both arms in the model for this population. In this guidance review, the company presented an alternative approach using different distributions for the 2 treatment arms. It used the 2-spline normal

distribution for the nivolumab arm, because it had a better statistical and visual fit to the data than the generalised gamma distribution. The method used for the investigator-choice arm is confidential and cannot be reported here. The ERG preferred to use the generalised gamma distribution for both arms as in the original appraisal and in line with the NICE Decision Support Unit's technical support document 14. In its response to technical engagement, the company used the same extrapolation method for the docetaxel subgroup. It did not present evidence of the goodness of fit for this method to the subgroup data and it did not explore alternative methods. The committee considered the docetaxel subgroup to be the most appropriate data source for this review because it was the most relevant population to NHS clinical practice. But it agreed that the time to treatment discontinuation for the docetaxel subgroup was uncertain.

Stopping rule and continued treatment effect

Analyses without a stopping rule are more appropriate for decision making

3.9 In the original appraisal, the committee concluded that analyses without a nivolumab stopping rule are more appropriate for decision-making than analyses that included a stopping rule. The 2-year stopping rule was only accepted in the context of the Cancer Drugs Fund. In this guidance review, the patient experts and the clinical expert agreed that people might be disappointed if treatment was beneficial but was stopped at 2 years. The clinical expert confirmed that people who tolerate and benefit from treatment should be able to have it until their disease progresses, or they have intolerable side effects or choose to stop. People who stopped nivolumab after 2 years but whose disease has not progressed would be offered platinum-based chemotherapy. The clinical expert explained that people who are alive 5 years after treatment started are considered 'cured' from the disease. The committee noted that there was no stopping rule included in the trial, and that some people were still taking nivolumab after 2 years. It noted that a stopping rule had been accepted in previous

appraisals for nivolumab and other similar drugs, whether or not it was included in the trial. However, in this instance, the committee concluded that a 2-year stopping rule was not appropriate.

Continued treatment benefit up to 5 years is plausible

3.10 In the original appraisal, the committee concluded that it was plausible that the treatment benefit of nivolumab continued for 5 years after treatment started. For this guidance review, the company provided a smoothed hazard-rates plot for overall survival for the intention-to-treat population for nivolumab and investigator choice. The plot suggested that the hazard rates seemed to meet at around 5 years. This indicates that there was no difference in the treatment effect of the 2 arms at 5 years. Therefore, the ERG included treatment waning at 5 years after the start of treatment in its base-case analysis. In the trial, people in the investigator-choice arm could have had nivolumab during the extension phase of the trial (see section 3.4). The committee acknowledged that this crossover could decrease the apparent relative effectiveness of nivolumab compared with investigator choice, but it had not been presented with evidence that it could consider as part of its decision making. Conversely, the committee considered that implementing a 2-year stopping rule for nivolumab could affect the relative treatment effect and cause the hazard rates to converge more quickly. It concluded that it was plausible that nivolumab's treatment effect matches that of standard care at 5 years after treatment started.

Utility values in the economic model

The most appropriate utility values lie between the treatment-dependent and the treatment-independent estimates

3.11 In the original appraisal, the committee agreed that the most appropriate utility estimates would lie between the treatment-dependent utilities and the treatment-independent utilities. The clinical expert explained that the effect on quality of life was similar for the different treatment options

available for recurrent and metastatic SCCHN. The patient experts and the clinical expert confirmed that people's quality of life diminishes during the last months of life. Because no new evidence was presented on quality of life, the committee concluded that the most appropriate approach was to use both treatment-dependent and treatment-independent values in the base-case analysis.

End of life

Life expectancy for people with recurrent or metastatic SCCHN is less than 24 months

3.12 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. In the original appraisal, the data showed that life expectancy for people with SCCHN that has progressed within 6 months of platinum-based chemotherapy was less than 24 months. The committee did not hear any evidence to change this conclusion. Therefore, it concluded that nivolumab met the short life-expectancy criterion.

It is unclear whether nivolumab meets the end-of-life criteria when compared with docetaxel

3.13 In the latest data available for CheckMate 141, the median overall survival for the intention-to-treat population for nivolumab was 7.7 months (95% confidence interval 5.7 to 8.7 months) compared with 5.1 months (95% confidence interval 4.0 to 6.2 months) for investigator choice. The model predicted a mean survival benefit for nivolumab of between 6.8 and 9.2 months in this population. The median overall-survival results for the docetaxel subgroup are confidential and cannot be reported here. When the docetaxel subgroup data were used in the company's base-case model, the mean overall-survival benefit for nivolumab was estimated to be 6.7 months. The committee noted that the clinical effectiveness of nivolumab was uncertain in this population (see section 3.4). Also, the

extrapolation methods used for overall survival and time to treatment discontinuation were uncertain (see section 3.7 and section 3.8). Based on the evidence provided, the committee concluded that it is uncertain whether nivolumab would extend life by more than 3 months compared with NHS standard care. Therefore, it is currently uncertain if nivolumab meets the end-of-life criteria when compared with docetaxel.

Nivolumab's life-extending benefit for tumours with a low PD-L1 score is unclear

3.14 In the latest data available for CheckMate 141, nivolumab increased median overall survival by more than 3 months compared with investigator choice in people whose tumours had a PD-L1 score of 1% and above (see section 3.5). In people whose tumours had a PD-L1 score of less than 1% the increase in median survival was only 1 month, and this was not statistically significant (see section 3.5). The model estimates for the mean overall-survival benefit are 12 months for the PD-L1 1% and above subgroup, and 6.3 months for the PD-L1 less than 1% subgroup. Because of the uncertainty in the clinical evidence for the PD-L1 less than 1% subgroup, the committee concluded that it is uncertain whether the life-extending criterion was met in that subgroup.

Cost effectiveness

The company's base case does not reflect the committee's preferred assumptions

3.15 The committee agreed that its preferred approach to modelling would:

- include data from the docetaxel subgroup only
- include treatment-dependent and treatment-independent utility values
- assume no treatment benefit for nivolumab 5 years after start of treatment
- exclude the estimated utility decrements related to time before death

- exclude the stopping rule.

The company did not do exploratory analyses for the docetaxel subgroup data. And its extrapolation methods for overall survival, progression-free survival and time on treatment for this subgroup are unclear. So the ERG was unable to do exploratory analyses for the docetaxel subgroup. The committee would like to see scenarios in which the effect of different extrapolation methods are explored. Also, the committee agreed that the PD-L1 subgroups are of interest within the docetaxel population.

Because of the uncertainty an acceptable ICER is toward the lower end of the range normally considered a cost-effective use of NHS resources

3.16 NICE's guide to the methods of technology appraisal notes that above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per quality-adjusted life year (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 and whether the technology meets the criteria for special consideration as a 'life-extending treatment at the end of life'. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. The committee noted the high level of uncertainty for the docetaxel subgroup specifically regarding the clinical effectiveness (see section 3.4), appropriate extrapolation methods (see section 3.6 and section 3.7) and the end-of-life criteria (see section 3.12).

It is unclear whether nivolumab would be a cost-effective use of NHS resources

3.17 The company's base-case assumptions differed from the committee's preferred assumptions. The company's base case included a lifetime treatment benefit of nivolumab, treatment-dependent utilities and a 2-year stopping rule. Also, the time to treatment discontinuation was extrapolated using different distributions in the 2 arms. The company's base-case ICER

was £37,257 per QALY gained in the intention-to-treat population. The ICER increased by £9,304 per QALY gained, to £46,540 per QALY gained, when both the stopping rule and the time-to-death disutility decrements were removed. It increased by £17,464 per QALY gained, to £54,700 per QALY gained, when the treatment-independent utility values were also applied. The ICER was £41,888 per QALY gained when the stopping rule and the time-to-death disutility decrements were removed, and the time to treatment discontinuation was extrapolated with the same distribution in the 2 arms. When the treatment-independent utility values were also applied, the ICER was £49,233 per QALY gained. The committee noted that the deterministic and probabilistic ICERs were similar. It also noted that the ICER in the docetaxel subgroup, which used the company's base-case assumptions, was £41,695 per QALY gained. This was £4,442 per QALY gained higher than in the intention-to-treat population. The committee agreed that it was unclear how the adjusted extrapolation methods for overall survival, progression-free survival and time to treatment discontinuation would affect the cost-effectiveness estimates in the docetaxel subgroup, and what the ICER would be for this subgroup if all of its preferred assumptions were included in the model. It also agreed that the most likely ICER could be £50,000 per QALY gained or higher, and that there was high uncertainty around this ICER. It concluded that it could not recommend nivolumab for routine use in the NHS because it was not presented with all the relevant evidence to conclude that nivolumab was a cost-effective use of NHS resources.

Cancer Drugs Fund

Nivolumab cannot be recommended in the Cancer Drugs Fund

3.18 The aim of a Cancer Drugs Fund guidance review is to decide whether or not the drug can be recommended for routine use. Nivolumab for SCCHN after platinum-based chemotherapy may not remain in the Cancer Drugs Fund once the guidance review has been completed (see section 6.19 of the guide to the processes of technology appraisal).

Equality issues

The recommendations apply equally to all people with SCCHN

3.19 A patient expert questioned whether there is an equality issue regarding age. The clinical expert confirmed that there is no age limit for treatment with nivolumab. The committee heard from the Cancer Drugs Fund clinical lead that data collected by Public Health England from NHS patients in England showed that many older patients had taken nivolumab while it was available in the Cancer Drugs Fund. The committee concluded that there was no relevant equalities issue.

Other factors

3.20 The company did not highlight any additional benefits that had not been captured in the QALY calculations.

Conclusion

Nivolumab is not recommended for routine commissioning

3.21 The committee could not recommend nivolumab, within its marketing authorisation, for recurrent or metastatic SCCHN after platinum-based chemotherapy in adults. In the original appraisal, the committee concluded that docetaxel was the most relevant comparator, and that assuming clinical equivalence between some of the comparators was uncertain. This meant that using investigator-choice data to model all comparators would be likely to underestimate the effectiveness of docetaxel. In this guidance review, the company did not present a comprehensive analysis for the docetaxel subgroup. Therefore, the committee was unable to determine the most plausible ICER for this population. Based on the ICERs for the intention-to-treat population, the committee agreed that the ICERs for the docetaxel subgroup are likely to be £50,000 per QALY gained or higher. Given the uncertainty about the clinical effectiveness and life-extending benefit of nivolumab compared

with docetaxel, this ICER is above what NICE considers an acceptable use of NHS resource.

4 Proposed date for review of guidance

4.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Lindsay Smith
Chair, appraisal committee
December 2020

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 D.

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.

Verena Wolfram
Technical lead

Nicola Hay
Technical adviser

Kate Moore
Project manager

ISBN: [to be added at publication]