NICE National Institute for Health and Care Excellence

NICE guidance

# Nivolumab for previously treated advanced renal cell carcinoma

Technology appraisal guidance
Published: 23 November 2016

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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 Nivolumab is recommended, within its marketing authorisation, as an option for previously treated advanced renal cell carcinoma in adults, when the company provides nivolumab according to the commercial arrangement.

# 2 The technology

**Summary of nivolumab**

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| **Description of the technology** | Nivolumab (Opdivo, Bristol–Myers Squibb) is a human monoclonal antibody that blocks an immune checkpoint protein receptor called programmed cell death protein 1 (PD-1) to promote an anti-tumour response. |
| **Marketing authorisation** | Nivolumab 'as monotherapy is indicated for the treatment of advanced renal cell carcinoma after prior therapy in adults'.<br>Before the marketing authorisation was granted (April 2016), nivolumab was available in the NHS through the early access to medicines scheme. |
| **Adverse reactions** | The most common adverse reactions with nivolumab in clinical trials were tiredness, rash, pruritus, diarrhoea, nausea and decreased appetite (occurring in more than 10% of people). For full details of adverse reactions and contraindications, see the summary of product characteristics. |
| **Recommended dose and schedule** | 3 mg/kg given intravenously every 2 weeks. |
| **Price** | The list price is £439 per 40-mg vial or £1,097 per 100-mg vial.<br>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 Evidence

The appraisal committee considered evidence submitted by Bristol–Myers Squibb and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

# 4 Committee discussion

The appraisal committee reviewed the data available on the clinical and cost effectiveness of nivolumab, having considered evidence on the nature of renal cell carcinoma and the value placed on the benefits of nivolumab by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.

4.1 The committee considered the experience of people with advanced renal cell carcinoma. It heard from the clinical and patient experts that nivolumab could extend life and improve its quality. It heard that nivolumab was generally well tolerated, and usually caused fewer side effects than other treatments such as axitinib and everolimus. The committee noted that one of the patient experts who had had nivolumab was able to continue working. The committee recognised nivolumab is an intravenous drug whereas axitinib and everolimus are oral. The committee heard that people prefer oral treatments that they can have at home, but are willing to travel to have intravenous infusions to get more effective therapy. The committee was aware of several comments received during consultation from patients and carers who emphasised the importance of having access to nivolumab.

## Treatment pathway

4.2 The committee heard from the clinical experts that most people in the NHS with newly diagnosed advanced renal cell carcinoma would be offered one of two tyrosine kinase inhibitors; either pazopanib or sunitinib, as recommended in NICE's technology appraisal guidance on pazopanib and sunitinib. If the disease progresses and they are fit enough to have further treatment, most people are then offered a different tyrosine kinase inhibitor, axitinib, as recommended in NICE's technology appraisal guidance on axitinib. The committee understood that everolimus (a mammalian target of rapamycin [mTOR] inhibitor) is currently available through the Cancer Drugs Fund for people who have had treatment with only 1 tyrosine kinase inhibitor and for whom axitinib is contraindicated or not tolerated. It heard from the clinical experts that, if given a choice of axitinib or

everolimus for previously treated renal cell carcinoma, they would prefer axitinib because they expect a better response to a second tyrosine kinase inhibitor than an mTOR inhibitor. The committee heard that, in current practice, everolimus is offered to people who have previously had tyrosine kinase inhibitor-related adverse events such as hypertension, or who cannot tolerate axitinib, or for whom axitinib is contraindicated. The committee heard that after 2 treatments, no further treatments are available in the NHS and people are offered best supportive care.

# Comparators

4.3 The committee heard from the clinical experts that they would like to offer nivolumab to people who have had 1 or 2 previous treatments. The experts also advised that a small number of people cannot tolerate axitinib or everolimus, but may be able to have nivolumab because of its favourable toxicity profile. For people who have had 1 previous treatment, the committee agreed that the relevant comparator for nivolumab is:

- axitinib, for most people
- everolimus, for people who cannot have axitinib
- best supportive care, for people who cannot have axitinib or everolimus.

The committee further concluded that, for people who have had 2 previous treatments, best supportive care is the appropriate comparator for nivolumab.

# Clinical effectiveness

## Survival benefit of nivolumab compared with everolimus

4.4 The committee noted that the evidence for nivolumab mostly came from CheckMate 025, a well-conducted open-label randomised controlled trial with 821 patients that compared nivolumab with everolimus. Overall survival was the

primary outcome. The committee noted that, in CheckMate 025, patients randomised to nivolumab lived longer (median 25.0 months) than patients randomised to everolimus (median 19.6 months; 95% confidence interval [CI] 17.6 to 23.1), resulting in a hazard ratio of 0.73 (98.5% CI 0.57 to 0.93; p=0.002). The committee noted that the CheckMate 025 trial showed no difference in progression-free survival between nivolumab and everolimus. The committee concluded that, compared with everolimus, nivolumab extended overall survival, but not progression-free survival.

4.5 The committee considered the extent to which nivolumab extends survival when compared with everolimus:

- The committee considered the survival data from CheckMate 025 to be immature because, at the time of the interim analysis that led to the study stopping (July 2015), 398 out of 821 (48%) patients had died and median follow-up was only about 18 months.
- The company's submission stated that, when nivolumab is used to treat melanoma, survival curves show 'long tails' for overall survival meaning that some patients survive for a long time. The clinical experts advised that it was plausible that an overall survival curve with a 'long tail' would also be shown for renal cell carcinoma treated with nivolumab. The committee noted that this opinion was reiterated in the company's consultation response, which contained advice from 2 consultant oncologists.

  The committee concluded that the most robust results came from the larger CheckMate 025 trial, which showed that nivolumab extended life by a median of 5.4 months compared with everolimus, but also concluded that there was uncertainty about the extent of the survival benefit when measured over the long term.

## Generalisability of the CheckMate 025 population

4.6 The committee heard from the clinical experts that the characteristics of the patients in CheckMate 025 were similar to those of the people in their NHS clinics. The committee concluded the trial results were generalisable to the NHS.

## Subgroups with 1 or 2 previous treatments

4.7 The committee recognised that the trial included a mix of people who had had 1 previous treatment with a tyrosine kinase inhibitor (72% of patients) and people who had had 2 previous tyrosine kinase inhibitors (28%). During consultation the company clarified that a subgroup analysis based on number of previous treatments showed that the treatment effect of nivolumab compared with everolimus was clinically and statistically significant both for patients who had 1 previous tyrosine kinase inhibitor (hazard ratio 0.79; 95% CI 0.63 to 0.99) and patients who had 2 previous tyrosine kinase inhibitors (hazard ratio 0.65; 95% CI 0.43 to 0.99). The committee concluded that nivolumab prolonged overall survival compared with everolimus both for people who had had 1 previous treatment and people who had had 2 previous treatments.

## Subsequent treatments in CheckMate 025

4.8 The committee was aware that people generally continue having nivolumab until disease progression, or some time beyond it, after which some people then try other therapies. The committee heard from the company that the trial protocol prohibited patients from switching treatments during the trial (that is, patients randomised to everolimus could not have nivolumab after progression), yet patients in both the nivolumab and everolimus groups had subsequent treatments including everolimus and tyrosine kinase inhibitors. The committee heard from the clinical experts that these subsequent treatments extend survival, but that they are not given in NHS practice after people have had 2 treatments. The committee recognised the use of these treatments was unlikely to have been equal between both groups in CheckMate 025, which may have confounded the results, although the direction of the bias was not clear. The committee concluded that this should be taken into account in any analyses.

## Duration of nivolumab treatment

4.9 The committee noted that the summary of product characteristics allows for nivolumab treatment to continue after disease progression, as did the trial. It heard from the clinical experts that about 10% of people have nivolumab for a

short time after disease progression. The committee concluded that treatment after disease progression was likely to reflect NHS practice, and that the company had appropriately included this in its economic model.

## Network meta-analysis

4.10 The committee understood that, because there were no head-to-head trials comparing nivolumab with axitinib or best supportive care, the company had done a network meta-analysis to compare the treatments indirectly. To compare nivolumab with best supportive care, the network linked CheckMate 025 (nivolumab compared with everolimus) with the RECORD-1 trial (everolimus compared with best supportive care) using everolimus as a common comparator. To compare nivolumab with axitinib, the network joined these 2 trials to 2 other trials (TARGET, sorafenib compared with best supportive care; AXIS, axitinib compared with sorafenib). It noted advice from the evidence review group (ERG) that the results were likely to be biased because of differences between trials:

- **Number of previous treatments**: CheckMate 025 and RECORD-1 recruited patients who had had 1 or 2 previous tyrosine kinase inhibitors, while AXIS and TARGET recruited patients who had only had 1 previous treatment with a tyrosine kinase inhibitor.
- **Choice of previous treatments**: The committee heard from the clinical experts that previous therapy affects response to subsequent treatments. The committee acknowledged that the company had partly addressed this by only using data from the subgroup of patients in the AXIS trial who previously had sunitinib. But the trials still differed in the choice of previous treatments.
- **Prognosis of patients at baseline**: The committee noted that patients in AXIS had a poorer prognosis than those in CheckMate 025, measured using the Memorial Sloan Kettering Cancer Center (MSKCC) tool for predicting renal cancer prognosis. The committee heard from the company that both trials used the MSKCC tool, but that 1 component (performance status) was measured using different tools in each trial. The company stated that this explained the difference in prognosis and that the trial populations were similar. The committee concluded that there was no way to assess whether the prognosis of the trial patients was similar.

- **Subsequent treatments**: The ERG noted that Motzer et al. (2013) raised concerns that the results of the AXIS trial may have been confounded by differences between treatment groups with respect to subsequent treatments. The committee was concerned that the company had not explored whether an imbalance in the choice of subsequent treatments, which extended life and were not routinely available in the NHS, could have biased the AXIS results and hence the company's network meta-analysis.

4.11 The committee assessed the effect of the limitations in the network meta-analysis. It heard from the ERG that in its opinion the poorer prognosis of patients in AXIS, and the impact of subsequent treatments in that trial, meant that the results were likely to have underestimated the effectiveness of axitinib, and so overestimated the relative effectiveness of nivolumab with respect to overall survival. The committee concluded that the company's network meta-analysis could potentially have been biased in favour of nivolumab.

## Effectiveness of axitinib compared with everolimus (and, by extension, nivolumab)

4.12 The committee was aware that to be able to estimate the relative effectiveness of nivolumab compared with axitinib, the company's original model used the results of CheckMate 025 (nivolumab compared with everolimus) but adjusted the everolimus arm, using the network meta-analysis results to represent the effectiveness of axitinib. Two key inputs to the economic model were therefore the hazard ratios for progression-free survival and overall survival comparing axitinib with everolimus. The committee noted that the company's network meta-analysis showed axitinib was less effective than everolimus (the results are academic-in-confidence and cannot be reported here). The committee questioned the face-validity of this result.

- It heard from clinical experts that in their experience, axitinib and everolimus have similar treatment effects.
- The committee also heard that clinicians would usually choose axitinib over everolimus (unless a person could not tolerate tyrosine kinase inhibitors) because they expected a better response with a second tyrosine kinase

inhibitor than with an mTOR inhibitor.

- The committee noted that a published indirect treatment comparison of axitinib and everolimus showed no difference in progression-free survival (Sherman et al. 2015).

  The committee acknowledged the limited evidence, but concluded that axitinib and everolimus were likely to have similar effectiveness and that it was appropriate to use a hazard ratio of 1 for overall survival and progression-free survival in the model. Both the company and ERG used hazard ratios of 1 in their revised base-case analyses submitted after consultation.

# Cost effectiveness

4.13 The committee agreed that the structure of the 6-stage, partitioned-survival economic model was appropriate. It noted that the model represented patients who had had either 1 or 2 previous tyrosine kinase inhibitors. The committee would have preferred to consider separate analyses for patients who had 1 previous tyrosine kinase inhibitor and patients who had 2 previous tyrosine kinase inhibitors because the comparators that reflect NHS practice differ for each group (see section 4.3) and the patients in the groups likely differ in ways that might affect treatment effectiveness. However, neither the company nor the ERG presented subgroup analyses. The committee accepted that the analyses for the overall population (representing patients who had had either 1 or 2 previous tyrosine kinase inhibitors) were suitable for decision-making.

## Modelling overall survival

4.14 Because the trial data were immature (see section 4.5), the committee was concerned that a large proportion of the benefit attributed to nivolumab for extending life was based on extrapolation rather than on trial data. The committee was aware that, for predicting overall survival with nivolumab and everolimus, the company fitted a generalised gamma model to extrapolate the data from CheckMate 025. The committee noted that this model relies on the

'accelerated failure-time' assumption, but this assumption had not been formally tested by the company. In the committee's opinion, the survival curves converged suggesting that the assumption was not met. The committee noted that an alternative approach was to use independent models for each treatment group (that is, separate models for nivolumab and everolimus), as presented by the ERG in a scenario analysis requested by the committee for the second committee meeting. The committee noted that the independent log-logistic model predicted that 19% of patients treated with everolimus would be alive after 5 years, whereas the company's clinical experts predicted this would be only 10% to 12% in practice. The committee concluded that the independent log-logistic model overpredicted survival with everolimus. The committee preferred to base its decision on a single generalised gamma model to predict survival with both nivolumab and everolimus, as had been done in the company and ERG's base cases.

4.15 The committee discussed the company's scenario analysis, provided after consultation, using a 'model averaging' approach. The company gave 50% weight to the base-case model and 50% weight to a model assuming a greater long-term survival benefit for nivolumab (see section 4.5). For the latter model, based on data from CheckMate 003 and advice from 2 oncologists, the company assumed that patients whose disease was treated with nivolumab who survive for 5 years would have the same risk of death after 5 years as the age-matched general population. This scenario analysis substantially improved the cost effectiveness of nivolumab compared with all comparators. The committee considered an alternative approach presented in a scenario analysis by the ERG. The ERG used the sample sizes of CheckMate 003 and CheckMate 010 to calculate a weighting that took into account the proportion of information given by each of these trials. The ERG's scenario gave a 4% weighting to the model assuming greater long-term survival, and 96% weighting to the base-case model. The committee noted that the base-case analysis already predicted that some patients would survive for a long time with nivolumab (6% of people survived for 10 years). It noted that there was little evidence to show that the survival benefit of nivolumab was greater than predicted in the base case, and the committee could not be sure that the 'long tail' seen in melanoma would also be seen in renal cell carcinoma. The committee preferred the methods in the company's base case for predicting survival with nivolumab, but it was willing to consider scenarios with predictions of better survival in its decision-making.

## Modelling time-to-stopping treatment

4.16 The committee noted that the company fitted a complex spline model to predict time-to-stopping treatment with nivolumab and everolimus in its original submission. It considered that the simpler models used by the ERG (log normal and generalised gamma) appeared to fit the data better at the beginning of the trial, but less so at the end. Overall the committee preferred to use either a log-normal or a generalised gamma distribution to predict time-to-stopping treatment, but was not confident that any of the curves presented by the company or the ERG provided a good fit to the entire Kaplan–Meier curve. It noted that the company had used a log-normal distribution in its revised base case submitted after consultation.

## Cost of nivolumab

4.17 The committee noted that the company excluded the costs of missed doses and some of the delayed doses from its revised model. The committee heard from the company that nivolumab infusions are not prepared before the patient comes for treatment, meaning that the NHS would not pay for nivolumab drug costs for missed or delayed doses. The company further explained that if a dose was delayed for at least 7 days, the patient would be seen at the next weekly clinic and there would be at least 4 weeks between doses (in other words, delays of at least 7 days mean that patients skip a dose). Based on data from CheckMate 025, the company's revised base case excluded the costs of missed doses (2.5%) and doses that were delayed for at least 7 days (4%), resulting in a total 6.5% reduction in drug costs for nivolumab. The ERG did not agree that all of these missed and delayed doses would incur no drug costs for the NHS. In its revised base case, the ERG took the midpoint between the company's original 7.5% reduction in drug costs and no reduction in drug costs, resulting in a total 3.8% reduction. The committee remained concerned that, if a planned infusion of nivolumab was cancelled at short notice, the infusion would still be prepared and this would incur a cost for the NHS. It therefore considered both the 6.5% and 3.8% cost reductions in its decision-making, noting that the difference did not substantially affect the cost-effectiveness results.

## Cost of subsequent treatments

4.18 The committee noted that the company's model included the costs of subsequent treatments, based on the treatments used in CheckMate 025. It recalled that these treatments are believed to have a survival benefit (see section 4.8) but are not used in the NHS. The committee would have preferred to see an analysis that excluded both the costs and the clinical benefits of subsequent treatments, but the company had not presented this analysis. The ERG presented an analysis that removed the costs of subsequent treatments, but the committee agreed that this was not appropriate because the clinical benefits were still included in the model. The committee concluded that, because all the analyses included the clinical benefits of subsequent treatments, it preferred to also include the costs of those treatments. In line with the committee's preference, the revised base cases from the company and ERG included the costs of subsequent treatments.

## Utility values

4.19 The committee was aware that CheckMate 025 collected health-related quality-of-life data using EQ-5D. In its original submission, the company took utility values for its model from CheckMate 025 for nivolumab and everolimus, and from AXIS for axitinib; the AXIS utilities were lower. The committee did not find the company's original utility values plausible because:

- The post-progression utility values for patients who had nivolumab and everolimus were higher than the pre-progression utility values for patients having axitinib or best supportive care.
- The utility values were lower for axitinib than for everolimus, but the committee heard from the clinical experts that in their experience, health-related quality of life was similar for people whose condition was being treated with these drugs.

The committee concluded that the company's utility values were not appropriate and it preferred to use the same utility values for axitinib, everolimus and best supportive care. The committee acknowledged that the company's revised base case submitted after consultation did this.

4.20 The revised base cases from both the company and the ERG took utility values for axitinib and best supportive care from the everolimus group in CheckMate 025. The committee heard from the company that this was the 'gold standard' approach to modelling because the utility values came from the main trial of nivolumab. The committee acknowledged its general preference for trial-based utilities, but also noted that the appropriate utility values are those taken from patients that most closely resemble the patients who would receive nivolumab in the NHS. The committee therefore considered the ERG's scenario analysis, which took utility values for all comparator treatments from the axitinib group in AXIS. In this scenario, the gain in utility for nivolumab compared with everolimus was taken from CheckMate 025. Compared with the ERG's base case, the scenario using AXIS utilities increased the incremental cost-effectiveness ratio (ICER) for nivolumab compared with all comparator treatments. The committee concluded that the trial population of CheckMate 025 was similar to NHS patients and so it was reasonable to use the utility values from CheckMate 025, as had been done in the base case. The committee considered that the AXIS patients may also be representative of some NHS patients who are more unwell, and therefore it was appropriate to explore scenarios using the AXIS utility values.

4.21 The company assumed in its model that, even after disease progression and stopping treatment, people treated with nivolumab have a consistently higher quality of life than people treated with axitinib or everolimus. The committee heard from the clinical experts that a post-progression treatment benefit may exist for nivolumab compared with its comparators, because the adverse effects experienced with axitinib or everolimus take some time to resolve, but that the quality-of-life benefit would only be seen for a short time. The committee remained concerned that the company assumed a continual post-treatment benefit of nivolumab and had not presented to the committee analyses that excluded this benefit.

## Results of cost-effectiveness analyses

4.22 In response to consultation, the company proposed a new simple discount patient access scheme for nivolumab. The level of discount is commercial in confidence. The committee used the results including the patient access scheme

for nivolumab for decision-making, but this document does not present precise results because the discount is confidential.

4.23 At the second committee meeting, the committee considered the company's revised pairwise comparisons, which included its preferred assumptions:

- assuming axitinib was as effective as everolimus for progression-free survival and overall survival (see section 4.11)
- using a log-normal distribution to model time-to-stopping treatment (see section 4.15)
- assuming utility values for axitinib and everolimus were equal (see sections 4.18)
- including the costs of subsequent therapy (see section 4.17)
- using the survival benefit predicted in the base-case analysis (see section 4.15).

The committee considered deterministic pairwise ICERs for nivolumab compared with axitinib, everolimus and best supportive care, using the company's revised base case (with a 6.5% cost reduction for missed and delayed doses) and the ERG's revised base case (with a 3.8% cost reduction). All analyses included the patient access schemes for nivolumab and axitinib. Most of the base-case ICERs from the company and ERG were below £50,000 per QALY gained. The committee acknowledged that the scenarios from the company and ERG using a model averaging approach with a greater long-term survival benefit with nivolumab (section 4.14) reduced the ICERs.

# Innovation

4.24 The committee considered whether nivolumab was an innovative treatment. It heard from patient experts that nivolumab represented a step change in terms of extension to life and the quality of life while on treatment. The committee agreed that nivolumab was an innovative treatment in renal cell carcinoma, but noted

that it was not the first checkpoint inhibitor to gain a marketing authorisation for treating cancer. It also noted that before the marketing authorisation was granted, nivolumab was available for people in the NHS through the early access to medicines scheme, which aims to give patients access to promising innovative medicines and is granted by the UK Medicines and Healthcare products Regulatory Agency. The committee concluded that it had not been presented with any evidence of additional benefits of nivolumab that were not captured in the QALY measure.

# End-of-life considerations

4.25 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's final Cancer Drugs Fund technology appraisal process and methods.

4.26 The committee discussed whether nivolumab met the end-of-life criteria. It first discussed the life expectancy of people with previously treated advanced renal cell carcinoma having each of the 3 comparator treatments:

- Patients having axitinib lived for about 20 months (population studies, trial data).
- Patients having everolimus lived for about 19.6 months (CheckMate 025).
- Patients having best supportive care lived for less than 12 months (population studies, trial data).

  Although data on mean life expectancy were not available, on the balance of the evidence the committee concluded that average life expectancy was less than 24 months for people with advanced renal cell carcinoma and that the life-expectancy criterion was met.

4.27 The committee discussed whether nivolumab extended life by at least 3 months, noting that the relevant comparators depended on treatment history (see section 4.3). For people who had 1 previous treatment the committee compared nivolumab with axitinib, everolimus and best supportive care. For people who had had 2 previous treatments it compared nivolumab with best supportive care. The

committee recognised that the estimates of extensions to life were based on the overall trial population in CheckMate 025, which included a mixture of patients who had had 1 previous treatment and those who had had 2 previous treatments. The committee observed that CheckMate 025 had shown a median increase in survival of 5.4 months compared with everolimus. The committee had assumed axitinib was similarly effective to everolimus and so accepted that the extension to life for people having axitinib would also be greater than 3 months. The committee assumed that any extension to life would be even longer for nivolumab compared with best supportive care. The committee therefore agreed that nivolumab met the end-of-life criteria.

# Pharmaceutical Price Regulation Scheme (PPRS) 2014

4.28 The committee was aware of NICE's position statement on the Pharmaceutical Price Regulation Scheme (PPRS) 2014, and in particular the PPRS payment mechanism. It accepted the conclusion 'that the 2014 PPRS payment mechanism should not, as a matter of course, be regarded as a relevant consideration in its assessment of the cost effectiveness of branded medicines'. The committee heard nothing to suggest that there is any basis for taking a different view about the relevance of the PPRS to this appraisal. It therefore concluded that the PPRS payment mechanism was not relevant in considering the cost effectiveness of the technology in this appraisal.

# Conclusion

4.29 The committee noted that most of the revised base-case ICERs from the company and ERG were below £50,000 per QALY gained for nivolumab compared with axitinib, everolimus or best supportive care. The committee was unsure whether the survival benefit of nivolumab would be greater than assumed in the base case because there was very little long-term evidence, but it noted that scenario analyses assuming a greater benefit reduced the ICER. The committee concluded that, given the greater weight for QALYs at the end of life, nivolumab could be considered a cost-effective use of NHS resources.

# 5 Implementation

5.1 Section 7(6) 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. Because nivolumab was made available in the NHS through the early access to medicines scheme, NHS England has indicated that this guidance will be implemented 30 days after final publication.

5.2 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.

5.3 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 previously treated advanced renal cell carcinoma and the doctor responsible for their care thinks that nivolumab is the right treatment, it should be available for use, in line with NICE's recommendations.

# 6 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 B.

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.

**Anna Brett**
Technical Lead

**Rosie Lovett**
Technical Adviser

**Jeremy Powell**
Project Manager

# Update information

**Minor changes since publication**

**January 2019:** The commercial access agreement has been replaced by a patient access scheme. Sections 1.1, 2 and 5 have been updated.

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