NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Avelumab for treating metastatic Merkel cell carcinoma

The Department of Health has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using avelumab 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: November 2017

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 determination.
- Subject to any appeal by consultees, the final appraisal determination may be used as the basis for NICE's guidance on using avelumab 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: 18 December 2017

Second appraisal committee meeting: 16 January 2018

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

1 Recommendations

1.1 The committee is minded not to recommend avelumab for routine commissioning for treating metastatic Merkel cell carcinoma in adults. However the committee recognised the promising nature of this technology and saw its potential as a suitable candidate for use in the Cancer Drugs Fund. Therefore the company is invited to submit a proposal for including avelumab in the Cancer Drugs Fund for this indication. This proposal should:

- detail any commercial access arrangements
- show plausible potential for cost effectiveness
- detail how data collection will address the key clinical uncertainties described in section 3

- state the likelihood that additional research will reduce uncertainty enough to support positive guidance in the future
- state the proposed data collection approach and current status
- state the timeframe for availability of the results
- if appropriate data collection is ongoing, summarise the study protocol
- if appropriate data collection is not ongoing, and therefore data collection would be started to address the key areas of uncertainty, summarise the proposed data collection protocol specifying:
  - methodology
  - study governance details (information governance, patient consent, ethical approval)
  - analysis plans
  - data access and accountability for disseminating results
  - accountability for monitoring and validation
  - any funding arrangements.

Why the committee made these recommendations

Treatment options for metastatic Merkel cell carcinoma are limited. People are usually offered chemotherapy or best supportive care. Avelumab could be offered either as the first treatment for metastatic Merkel cell carcinoma or after chemotherapy.

Clinical trial evidence shows that avelumab may improve overall survival compared with chemotherapy. But the evidence is from only 1 trial of a small number of people and the data are still being collected, so the results are highly uncertain.

Avelumab meets NICE's criteria to be considered a life-extending end-of-life treatment.

Avelumab as a first treatment is not recommended because the cost-effectiveness estimate is uncertain. The current estimate is higher than what NICE normally considers acceptable for end-of-life treatments.

Avelumab after chemotherapy is not recommended because, although the current cost-effectiveness estimate is likely to be below the maximum value NICE normally considers acceptable for end-of-life treatments, this estimate is uncertain.

Avelumab is a promising treatment and has the potential to be cost effective. To address the uncertainty about survival estimates and cost effectiveness, the company is invited to submit a proposal for including avelumab in the Cancer Drugs Fund for metastatic Merkel cell carcinoma.

2 The technology

Marketing authorisation indication	Avelumab (Bavencio, Merck) is indicated as monotherapy for 'the treatment of adult patients with metastatic Merkel cell carcinoma'.
Dosage in the marketing authorisation	10 mg/kg every 2 weeks by intravenous infusion over 60 minutes. Avelumab should be continued until there is disease progression or unacceptable toxicity. Patients could continue treatment if they have radiological disease progression that is not associated with significant clinical deterioration (defined as no new or worsening symptoms, no change in performance status for more than 2 weeks and no need for salvage therapy).
Price	£768 per 200 mg vial (excluding VAT; British national formulary [BNF] online [accessed November 2017]). The average cost of treatment per patient is £65,086 based on the list price. Costs may vary in different settings because of negotiated procurement discounts.

3 Committee discussion

The appraisal committee (section 5) considered evidence submitted by Merck and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

Merkel cell carcinoma

People with metastatic Merkel cell carcinoma would welcome avelumab as a treatment option

3.1 Merkel cell carcinoma is a rare and aggressive cancer with limited treatment options. There is an unmet clinical need for people with the

disease. The patient experts explained that Merkel cell carcinoma often progresses rapidly, and can be frightening for both patients and families. The disease can start off as a small bump and then grow rapidly, spreading to other parts of the body (metastatic disease). Because it affects the surface of the skin it is a very visible disease that can become oozing and unsightly. When it spreads to other parts of the body, patients are currently offered chemotherapy. The initial response rates are relatively high, but the disease often relapses relatively quickly. The main benefit of avelumab is the potential for both good response rates and longer disease control than seen with chemotherapy. The patient experts stated that avelumab has shown very rapid responses in some cases, with fewer side effects than chemotherapy. The clinical experts indicated that avelumab could be used either as a first treatment or after chemotherapy, but should ideally be used as early as possible in the treatment pathway for maximum clinical benefit. Avelumab could also be an option for people who cannot have not chemotherapy. The committee concluded that avelumab offers a promising treatment option for people with metastatic Merkel cell carcinoma.

Chemotherapy or best supportive care are appropriate comparators

3.2 The committee noted that the marketing authorisation for avelumab does not specify when it should be given in the treatment pathway (first treatment or after chemotherapy). The clinical experts explained that they would like to offer avelumab to patients who have had none or only 1 previous line of therapy. The committee was aware that the final scope of this appraisal includes chemotherapy as a comparator for patients who have not had any treatment for metastatic disease (referred to as first-line), and best supportive care for patients who have had 1 previous treatment (referred to as second-line). The committee concluded that the appropriate comparator for first-line treatment is chemotherapy. However it noted that some patients may be unable to have chemotherapy and are offered best supportive care instead. For second-line treatment the committee concluded that best supportive care is the most appropriate

comparator, because very few patients would be expected to have chemotherapy again. The committee noted that, because no data are available on best supportive care in metastatic Merkel cell carcinoma, the company had assumed that the efficacy of best supportive care is equivalent to chemotherapy, for which data are available.

Clinical trial evidence

Results from the JAVELIN trial should be interpreted with caution

3.3 The evidence for avelumab came from JAVELIN. This is a single-arm, non-randomised trial of patients with metastatic Merkel cell carcinoma. The trial has 2 parts:

- Part A (second-line group): 88 patients with relapse after at least 1 line of chemotherapy
- Part B (first-line group): 39 patients who had not had previous systemic therapy for metastatic disease. This part of the trial is still recruiting.

The company presented interim data from a cut-off date of March 2017, and explained that it is still collecting data for both part A and part B. The committee was concerned that the interim data from part B (first-line group) relies on a very small number of patients with a short duration of follow-up (29 patients were followed for 3 months or more, 14 were followed for 6 months or more). Follow-up in part A (second-line group) was 18 months. The committee welcomed the availability of slightly more mature data based on a larger number of patients in this group, but they noted that the results are from 1 single-arm, non-randomised trial. The committee also noted that the marketing authorisation has been granted conditionally because of the immaturity of the data. The European public assessment report (EPAR) specifies that further data cuts are expected to provide additional evidence on efficacy and toxicity. The committee concluded that the JAVELIN results should be interpreted with caution.

There are some unanswered questions about the generalisability of the JAVELIN results

3.4 The committee discussed the baseline characteristics of patients in the JAVELIN trial:

- Immunosuppressed patients were excluded from the trial. The clinical experts stated that patients with neuroendocrine tumours are generally responsive to immunotherapies such as avelumab, including immunosuppressed patients. They stated that the only immunosuppressed people who may not be offered avelumab would be post-transplant patients because of the risk of rejection, rather than because of a lower effectiveness of avelumab. Some people with chronic lymphatic leukaemia and some on very high doses of steroids may not do well on this treatment, but this represents very few patients and would be assessed on an individual basis. The committee agreed that although immunosuppressed patients are excluded from the trial, most could be offered avelumab.
- There were no study sites in England and the median age of the patients in part A is 72.5 years, which is slightly older than that expected in clinical practice in England (70 years).
- The overall survival data may be confounded by the use of subsequent treatments, and no data on subsequent treatments were recorded as part of the trial.
- The Eastern Cooperative Oncology Group (ECOG) performance score of patients was 0 to 1 in the trial. The clinical experts stated that in clinical practice they would offer immunotherapy to some patients who have an ECOG score of 2, if this was because of unrelated comorbidities that would not affect their ability to tolerate or benefit from avelumab. The clinical experts also stated that if patients have an ECOG score of 2 because of advanced Merkel cell carcinoma then immunotherapy may not be appropriate, because patients need to have a reasonable life expectancy to able to benefit from immunotherapy.

The committee concluded that there are some unanswered questions about the generalisability of the trial to UK clinical practice.

Clinical effectiveness results for avelumab in first-line are promising but should be interpreted with caution

3.5 JAVELIN showed promising response rates for avelumab in first-line treatment. The clinical expert explained that the first-line response rates in the trial have been high so far (62.11% at 3 months and 71.4% at 6 months for overall response rate), but may well be lower when more data are available from a larger number of patients. However, they anticipate that the response rate will be at least equal to, and possibly slightly better than in second-line treatment. The committee was concerned that the results are from a very small number of patients with short follow-up, and that data on progression-free survival and overall survival are not adequate for decision making. It noted that the trial provided no comparison with any other treatment. It noted that data collection is ongoing in JAVELIN. The committee concluded that the results are highly immature and should be interpreted with caution.

Clinical effectiveness results for avelumab in second-line are promising but should be interpreted with caution

3.6 JAVELIN showed favourable efficacy outcomes for avelumab when used second-line. The clinical experts explained that avelumab, as an immunotherapy agent, is expected to produce a more durable response than chemotherapy. The committee also heard that this durable progression-free survival could be reflected in a longer overall survival. It noted that the median overall survival is higher than would currently be expected for patients with metastatic Merkel cell carcinoma (the median overall survival is academic in confidence and cannot be disclosed). However, the committee noted that the overall survival data are still relatively immature. It concluded that the results for avelumab used second-line, although very promising, should be interpreted with caution.

Naive indirect comparison

Observational studies are appropriate for comparison with JAVELIN

3.7 JAVELIN is a single-arm trial with no comparator, so the company did a naive (that is, unadjusted) indirect comparison of avelumab against chemotherapy using a retrospective observational study of patients with metastatic Merkel cell carcinoma (study 100070-Obs001). The company did this study specifically for the purpose of comparing avelumab with chemotherapy. The study has 2 parts:

- Part A, done in the US: 67 patients who had systemic chemotherapy first-line, and 20 patients who had systemic chemotherapy after at least 1 line of chemotherapy
- Part B, done in the EU: 34 patients who had systemic chemotherapy after at least 2 previous lines of chemotherapy.

The company also identified a study by Iyer et al. 2016, which included patients with metastatic Merkel cell carcinoma who had systemic chemotherapy after only 1 previous line of chemotherapy (n=30) or after 2 previous lines of chemotherapy (n=62). The ERG stated that it was unclear why the Iyer study had been selected. The committee noted that both study 100070-Obs001 and Iyer et al. 2016 included immunosuppressed patients, who were excluded from JAVELIN (see section 3.4). It also noted that patients in both treatment groups in JAVELIN had better baseline ECOG performance scores than those in study 100070-Obs001. However the committee concluded that, given the lack of data for this disease, the observational studies are appropriate for comparison with JAVELIN.

The results from the naive indirect comparison are highly uncertain

3.8 The naive indirect comparison suggests that, both first-line and second-line, avelumab has improved overall response rates, progression-free survival and overall survival compared with chemotherapy. The ERG considered that results from JAVELIN and the observational studies

should have been adjusted for differences in baseline characteristics including immunosuppression, ECOG performance score and age. In its clarification response the company did regression analyses for the second-line population, but the ERG still had concerns with these analyses. The committee recalled the immaturity of the data and the small patient numbers, particularly first-line. The committee heard from the ERG that, because efficacy data are only from non-randomised single-arm studies, it cannot accurately assess how avelumab compares with chemotherapy or best supportive care. The committee concluded that the results from the naive indirect comparison should be interpreted cautiously.

Adverse events

Avelumab has an acceptable tolerability profile

3.9 The clinical experts explained that immunotherapy agents such as avelumab are generally better tolerated than chemotherapy, but immune-related adverse reactions can occur. The committee noted that no treatment-related deaths were recorded in JAVELIN, but treatment-related adverse event rates were high in both the first-line and second-line groups (79.3% and 70.5% of patients respectively). The committee would have liked to have seen long-term safety data but it appreciates that further data are being collected. The committee concluded that avelumab is generally better tolerated than chemotherapy but it can cause immune-related adverse reactions.

The company's economic model

The company's model structure is appropriate for decision making

3.10 The company presented a 3-state partitioned survival model comparing avelumab with chemotherapy or best supportive care in patients having first-line treatment, and comparing avelumab to best supportive care in patients having second-line treatment. Each model included 3 health states (progression-free disease, progressed disease and death) with

3 sub-health states (greater than 100 days until death, 30 to 100 days until death, and less than 30 days until death). The sub-health states applied to both the progression-free and progressed disease health states, and accounted for the deterioration in health-related quality of life when a patient approaches death. Although uncommon, the ERG considered this approach to be reasonable to capture the changes in quality of life that patients experience over their lifetime, in addition to the changes experienced after progression of the disease. The committee concluded that the model structure is appropriate for decision making.

Progression-free survival and overall survival estimates

The modelled progression-free and overall survival for second-line treatment is uncertain

3.11 The committee first discussed the second-line model, being aware that first-line survival estimates were developed and derived from the second-line modelling. In its second-line model, the company used a spline-based approach (a flexible parametric survival method) to extrapolate progression-free survival and overall survival estimates for the time horizon of the model. Because the tail observed for progression-free survival is long (suggesting a durable response) the company censored patients at 18-month follow-up. This allowed the progression-free survival estimate not to be overly influenced by a potentially optimistic estimate of durable response. The committee decided that this method is reasonable. However it noted that the estimates are based on a naive indirect comparison with small numbers of patients (see section 3.8) and an extrapolation from 18 months of follow-up to a 40-year time horizon, and are therefore highly uncertain. Because of the limitations of the naive comparison the ERG preferred a Weibull regression, adjusting for parameter differences (including immunosuppression, age and gender) between study 100070-Obs001 and JAVELIN. The committee concluded that it was not possible to confidently decide which method produces the most reliable results.

The survival estimates for first-line treatment are highly uncertain

3.12 Because of the very limited data for first-line treatment (see section 3.5), the company considered it is unreliable to use progression-free and overall survival trial data in the first-line model. Instead it used estimates derived from the second-line model. The company assumed that there is no difference in progression-free survival for avelumab in first-line and second-line treatment, and applied a hazard ratio of 1 to the progression-free survival curve for second-line treatment to estimate the benefit of first-line treatment. For overall survival, the company sought clinical experts' opinion and then applied a hazard ratio of 0.8 to the overall survival curve for second-line treatment to estimate the benefit of first-line treatment. The committee was concerned that the progression-free and overall survival estimates for first-line treatment are based on clinical assumptions, not direct evidence. This means that these estimates are highly unreliable. The ERG considered that it is more appropriate to fit distributions for avelumab to the first-line estimates, rather than generating survival curves dependent on the second-line estimates and relying on assumptions. The committee was aware that the ERG's preferred survival model did not solve the issue of the uncertainty caused by limited data. The committee heard from the ERG that the company's cost-effectiveness result for first-line treatment is most sensitive to the hazard ratio chosen for overall survival. The committee concluded that the company's progression-free survival and overall survival estimates for first-line treatment with avelumab are highly uncertain.

The estimates of progression-free survival and overall survival for chemotherapy are from pooled observational data

3.13 In the second-line model, the company used pooled patient-level data from part A and part B of study 100070-Obs001 to estimate progression-free survival and overall survival for chemotherapy. The effectiveness of best supportive care was assumed to be equivalent to chemotherapy. The committee noted that the company used chemotherapy as a proxy for best supportive care in both first-line and second-line treatment, because

of a lack of data for best supportive care. In the first-line model, the company used pooled data from study 100070-Obs001 (part A) and 6 additional studies to estimate progression-free and overall survival for chemotherapy. The committee questioned the rationale for pooling all of these data and agreed that study 100070-Obs001 (part A) provides the most appropriate comparator data.

Time-on-treatment estimates

The company's assumptions for modelling time-on-treatment are in line with clinical practice

3.14 In its second-line model the company used a log-logistic model to extrapolate, and assumed that two-thirds of patients would stop treatment after 2 years. The remaining patients are assumed to continue treatment until 5 years, at which point all patients stop treatment. The clinical experts explained that they expect 95% of patients having avelumab to stop treatment by 2 years. They explained that for many immunotherapies used in other diseases, when there is a durable response and patients remain well, treatment tends to be stopped by 2 years. At this point many patients would not want to keep coming back for further treatment. The clinical experts stated that there may be patients with a large volume of disease that was continuing to improve, who may wish to continue on treatment beyond 2 years, but this would be very few patients. In its original first-line model the company had assumed no difference in time-on-treatment compared with the second-line treatment. The ERG noted that this assumption could potentially underestimate treatment costs and considered the second approach submitted at clarification stage, a Weibull model, more plausible to model time-on-treatment. The committee heard from the ERG that the company's cost-effectiveness result for first-line treatment is sensitive to the hazard ratio chosen for time-on-treatment. Because of this, the ERG presented a scenario that fitted distributions to the first-line estimates for avelumab. The committee agreed that the company's assumptions appear to reflect clinical practice

with regard to stopping treatment. However it concluded that it would consider both the company's and the ERG's assumptions in its decision making.

Utility values in the economic model

The baseline utilities are high

3.15 JAVELIN collected health-related quality-of-life data using EQ-5D-5L and FACT-M questionnaires. The company mapped the EQ-5D-5L data to EQ-5D-3L values using a validated mapping function, in line with NICE's position statement on EQ-5D-5L. The company used a regression model to generate utilities from the mapped EQ-5D-5L. The utilities varied across 3 time periods relative to time of death; utility for greater than 100 days until death (0.77), utility for 30 to 100 days until death (0.75), and utility for less than 30 days until death (0.71). The committee was aware that the utilities included the effect of adverse reactions. The ERG noted that the company did not compare the utilities used in the model to those reported in the literature. The committee heard that the time-to-death and baseline utilities (the baseline utility is academic in confidence and cannot be disclosed) were higher than the age-matched UK population. The committee agreed that these values are implausibly high but it noted that, because the same utilities are applied regardless of treatment group, only the difference between health states matters. The committee concluded that it could accept the company's utility values but acknowledged that these are very high.

Cost of treatment in the model

Cost of premedication for avelumab was not in the company's model but was included in the ERG's analysis

3.16 The company did not include the cost of premedication for avelumab. This includes 10 mg of chlorphenamine given intravenously and 1 mg of paracetamol taken orally. The committee noted that these costs would

have very little impact on the cost-effectiveness analysis but agreed to consider them.

Administration costs were underestimated by £100 per treatment

3.17 The committee noted the NHS England submission that the company used incorrect administration costs for chemotherapy. This meant that the company's base case underestimated the total cost of treatment by £100 per treatment. The committee agreed to take this into account when considering the incremental cost-effectiveness ratios (ICERs), although the overall impact would not be large.

Cost-effectiveness estimates

Avelumab cannot be recommended as a cost-effective use of NHS resources for first-line treatment because the clinical and cost effectiveness is highly uncertain

3.18 The ERG's original base case included a scenario in which most patients would stop treatment after 5 years, rather than after 2 years. At the meeting, the committee heard that the clinical experts expect 95% of patients having avelumab to stop treatment by 2 years (see section 3.14). It therefore requested the ERG to revise their base case accordingly. The ERG's revised base case for first-line treatment was based on the following assumptions:

- using the parametric curves to model progression-free survival, overall survival and time-on-treatment (see section 3.12 and section 3.14)
- adding the cost of premedications (see section 3.16).

The ERG's original base-case ICER for avelumab compared with best supportive was £120,383 per quality-adjusted life year (QALY) gained. Its revised base-case ICER is £75,526 per QALY gained. The company's base-case ICER for avelumab compared to best supportive care is £46,148 per QALY gained. The committee noted that using the correct administration costs for avelumab increases the ICERs by around £1,000

per QALY gained. It agreed that the most plausible ICER is highly uncertain, but may well be closer to the ERG's revised base case given the uncertainties with the company's model (see section 3.12 and section 3.14). The committee was concerned about the underlying issues with the clinical data, particularly the very small number of patients in part B of JAVELIN and the uncertainties around the methods used to generate the survival estimates. It considered that the evidence will be strengthened when the company can present further clinical data based on a larger number of patients with longer follow-up. The committee concluded that it cannot recommend avelumab as a cost-effective use of NHS resources for first-line treatment.

Avelumab cannot be recommended in routine commissioning for second-line treatment because of uncertain clinical and cost effectiveness

3.19 The committee was aware that chemotherapy is a potential comparator in second-line treatment, but most patients have best supportive care. It therefore only considered the results for avelumab compared with best supportive care (see section 3.2).

3.20 The ERG's revised base case for second-line treatment, after the committee requested the ERG to revise its original base case (see section 3.18), used the following assumptions:

- using Weibull regressions to model progression-free survival and overall survival (see section 3.11)
- adding the cost of premedications (see section 3.16).

The company's base-case ICER for avelumab compared with best supportive care is £37,350 per QALY gained. The ERG's original base-case ICER was £44,914 per QALY gained, and its revised base-case ICER is £37,629 per QALY gained. The committee noted that using the correct administration costs for avelumab increases the ICER by around £1,000 per QALY gained. It noted that the ICERs are within the range that could be considered cost effective if avelumab meets the-end-of life

criteria. However it was concerned about the uncertainties in the clinical data, particularly the small number of patients and the limitations of the naive comparison (see section 3.5), and about the reliability of the long-term modelling results. The committee concluded that it cannot recommend avelumab second-line in routine commissioning.

Innovation

All potential quality-of-life benefits are accounted for in the committee's decision

3.21 The committee noted the company's view that avelumab has the potential to help address the considerable unmet clinical need of people with metastatic Merkel cell carcinoma, who currently have limited treatment options available to them at end of life. The committee heard from the clinical and patient experts that avelumab is innovative in its potential to have significant and substantial clinical benefits. It understood that avelumab is generally well-tolerated compared with chemotherapy. The committee agreed that avelumab addresses an unmet need for a debilitating condition with few treatment options, and considered that the benefits had been adequately captured in the QALY calculations.

End-of-life

Avelumab meets the end-of-life criteria

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

3.23 The committee noted the evidence presented by the company for first-line treatment. Based on the median overall survival from the pooled analysis (see section 3.13), the life expectancy of people with metastatic Merkel cell carcinoma is estimated to be 11.8 months. The modelled mean value is closer to 24 months, but it is based on very uncertain extrapolations of overall survival on first-line treatment. The trial evidence shows

considerably longer survival with avelumab compared with current NHS treatment. The committee concluded that avelumab meets the criteria to be considered a life-extending end-of-life treatment for first-line treatment of metastatic Merkel cell carcinoma.

3.24 The evidence presented by the company indicates that people with metastatic Merkel cell carcinoma on second-line treatment have a life expectancy of between 5.1 and 5.5 months, and that avelumab extends life by at least an additional 3 months compared with current NHS treatment. The committee accepted that avelumab meets the end-of-life criteria for second-line treatment of metastatic Merkel cell carcinoma.

Cancer Drugs Fund

Avelumab is a promising treatment and more data is needed to establish its clinical and cost effectiveness

3.25 Having concluded that avelumab could not be recommended for routine use, the committee then considered if it could be recommended for treating metastatic Merkel cell carcinoma within the Cancer Drugs Fund. The committee discussed the new arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting the addendum to the NICE process and methods guides. It heard from the company that it would prefer avelumab to be available through routine commissioning. The committee acknowledged that the estimated ICERs for second-line use are not particularly high. However the estimates are highly uncertain, being based on 1 single-arm trial, a small number of patents and a naive indirect comparison. For first-line use this uncertainty is even greater, and the ICER could be as high as £75,000 per QALY gained. The committee considered that avelumab is a promising treatment with the plausible potential to be cost effective. The committee's preference is that avelumab should be made available through the Cancer Drugs Fund, for both first-line and second-line treatment. This will allow further clinical data to be collected to establish whether, and for which patients, avelumab is clinically and cost effective.

Conclusion

The company is invited to submit a proposal for the Cancer Drugs Fund

3.26 The committee accepted that avelumab is a promising treatment for metastatic Merkel cell carcinoma. However it cannot recommend avelumab as a cost-effective use of NHS resources, because the estimates of clinical and cost effectiveness are uncertain. It concluded that avelumab may meet the criteria to be considered for inclusion in the Cancer Drugs Fund. The committee invited the company to submit a proposal for including avelumab in the Cancer Drugs Fund for adults with metastatic Merkel cell carcinoma.

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.

Jane Adam
Chair, appraisal committee
November 2017

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.

Aminata Thiam
Technical Lead

Joanna Richardson
Technical Adviser

Thomas Feist
Project Manager

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