NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Tebentafusp for treating advanced uveal melanoma

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using tebentafusp 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, sex, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Issue date: June 2022

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 tebentafusp 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: 12 July 2022

Second appraisal committee meeting: TBC

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

1 Recommendations

1.1 Tebentafusp is not recommended, within its marketing authorisation, for treating HLA-A*02:01-positive unresectable or metastatic uveal melanoma in adults.

1.2 This recommendation is not intended to affect treatment with tebentafusp that was started in the NHS before this guidance was published. People having treatment outside 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

There is no standard treatment for HLA-A*02:01-positive advanced uveal melanoma. Usually people are offered immunotherapies licensed for treating cutaneous melanoma, such as pembrolizumab, or chemotherapy. Tebentafusp aims to treat the specific features of HLA-A*02:01-positive uveal melanoma.

Clinical trial evidence suggests that tebentafusp could increase how long people live and the length of time before their cancer gets worse compared with the usual treatments offered, but this is uncertain.

Tebentafusp meets the criteria for a life-extending treatment at the end of life. Because of the clinical uncertainty, the cost-effectiveness estimates are uncertain. They are also all higher than what NICE considers an acceptable use of NHS resources for end of life treatments. So, tebentafusp is not recommended.

2 Information about tebentafusp

Marketing authorisation indication

2.1 Tebentafusp (Kimmtrak, Immunocore) is ‘indicated as monotherapy for the treatment of human leukocyte antigen (HLA)-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma’.

Dosage in the marketing authorisation

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

Price

2.3 The company has marked the list price of tebentafusp as confidential.

The company has a commercial arrangement, which would have applied if the technology had been recommended.

3 Committee discussion

The appraisal committee considered evidence submitted by Immunocore, a review of this submission by the evidence review group (ERG), and responses from stakeholders. See the committee papers for full details of the evidence.

Treatment pathway

Tebentafusp would be a welcome new treatment option

3.1 The patient experts explained that uveal melanoma is a rare and aggressive disease with a poor prognosis. They explained that around 50% of people diagnosed with the condition will develop metastases. So many people with uveal melanoma live with the fear that they will be diagnosed with advanced disease. This is made more distressing by the prospect that once the cancer has metastasised, life expectancy is usually short. There are few treatment options for advanced disease, and those that are available have limited effect (see section 3.2). The patient experts explained that symptoms may not affect a person's quality of life until the late stages of the disease. However, the psychological burden of waiting for 6-monthly scans is immense, because a finding on a scan could mean prognosis suddenly worsens. People want treatments that could potentially decrease tumour burden and increase overall survival. The patient experts explained that the addition of tebentafusp as a treatment option would bring significant hope to people with uveal melanoma,

including people with localised disease who fear metastatic disease. The committee concluded that people would welcome tebentafusp in this disease area, which has very limited effective treatment options.

There is no standard care for treating advanced uveal melanoma

3.2 The patient and clinical experts explained that there is no standard care for treating advanced uveal melanoma. The clinical experts explained that the treatments used are those licensed for melanoma (based on evidence for their clinical effectiveness in treating cutaneous melanoma), including pembrolizumab, nivolumab and ipilimumab immunotherapies, and dacarbazine chemotherapy. Most people with advanced uveal melanoma are offered pembrolizumab, some people are offered ipilimumab with or without nivolumab and a small minority who cannot take immunotherapies are offered dacarbazine. The clinical experts explained that uveal melanoma is biologically distinct from cutaneous melanoma, and that there is no evidence for the effectiveness of immunotherapies for treating uveal melanoma. A clinical expert noted that the nivolumab and ipilimumab combination has a higher toxicity profile than pembrolizumab or ipilimumab, so it is not used as often as other immunotherapies. They also explained that nivolumab monotherapy is not used in clinical practice because people find the dosing schedule of pembrolizumab more convenient. The committee concluded that although pembrolizumab is the most common treatment option, there is no standard care for treating advanced uveal melanoma.

Tebentafusp

Tebentafusp is a new drug with a novel mechanism of action

3.3 The clinical experts explained that tebentafusp is a new drug which works differently to checkpoint inhibitors such as pembrolizumab, ipilimumab and nivolumab and other immunotherapies used to treat cancer. They explained that tebentafusp acts as a molecular bridge to link cancer cells to T-cells in the individual's immune system, allowing T-cells to target and

destroy cancer cells. This bridge is formed through an interaction between tebentafusp and a protein called gp100, which is almost always found on the surface of uveal melanoma cells. They explained that any cancer cell with gp100 proteins could be targeted by tebentafusp, potentially also cutaneous melanoma. But uveal melanoma is particularly susceptible because its tumour cells have a particularly high amount of gp100 proteins. The clinical experts explained that the second half of the molecular bridge is formed by tebentafusp binding to a marker on T-cells in a person's immune system called human leukocyte antigen-A*02:01 (HLA-A*02:01). They explained that the presence of HLA-A*02:01 markers is necessary for tebentafusp to work and that these are present on T-cells in approximately 50% of the uveal melanoma population. The committee concluded that tebentafusp is a new drug with a novel mechanism of action.

Tebentafusp would be used primarily as a first-line treatment for advanced uveal melanoma in line with the IMCgp100-202 trial

3.4 IMCgp100-202 is an open-label randomised controlled trial investigating the effectiveness of tebentafusp as a first-line treatment for advanced uveal melanoma (n=378). IMCgp100-102 is a single-arm trial of tebentafusp for treating advanced uveal melanoma in people who have had 1 or more lines of treatment for advanced disease (n=146). The clinical experts noted that tebentafusp would be used primarily as a first-line treatment based on evidence from IMCgp100-202. But they noted that the results from IMCgp100-102 showed the potential clinical benefit of tebentafusp as a second-line treatment for advanced disease. So the clinical experts considered it could be used as a second-line treatment. In its response to the ERG's clarification questions on the company submission, the company noted that tebentafusp was positioned as a first-line treatment. It explained that if tebentafusp were recommended by NICE, only people already having treatment for advanced uveal melanoma would be likely to have it second line. The committee accepted

that some people may have tebentafusp as a second-line treatment, although the numbers would decrease over time if tebentafusp was used as a first-line treatment. The committee concluded that tebentafusp would be used primarily as a first-line treatment for advanced uveal melanoma, in line with the IMCgp100-202 trial.

Generalisability of the clinical evidence

The IMCgp100-202 trial is generalisable to NHS practice for HLA-A*02:01-positive advanced uveal melanoma

3.5 IMCgp100-202 assessed the clinical effectiveness of tebentafusp compared with investigator's choice (either pembrolizumab, ipilimumab or dacarbazine) in HLA-A*02:01-positive advanced uveal melanoma. Pembrolizumab was the most used treatment in the comparator arm (82%), then ipilimumab (13%), then dacarbazine (6%). The ERG highlighted that not all the comparators in the NICE scope had been included in the investigator's choice arm. The clinical expert, who was also the principal investigator in the trial, noted that the use of investigator's choice as the comparator in the trial reflected the lack of standard care for uveal melanoma (see section 3.2). The mean age of people in the IMCgp100-202 trial was 62 years. The patient experts explained that some people are diagnosed with uveal melanoma in their 30s. The clinical experts explained that they would expect the median age of the treated population in practice to be around 62 years or younger. They noted that tebentafusp is not suitable for some older people who might not be fit enough to have treatment. The committee also noted that it would only be suitable for people with HLA-A*02:01 (around 50% of the uveal melanoma population) as specified in the trial (see section 3.3). The committee concluded that the investigator's choice arm reflected the treatment usually used for advanced uveal melanoma, and the population of the trial was generalisable to NHS practice.

Clinical evidence results

Tebentafusp improves overall survival and seems to have a benefit after disease progression but the reason for this is unclear

3.6 IMCgp100-202 is an ongoing trial. At the October 2020 data cut, the median overall survival was longer in the tebentafusp arm (21.7 months) than in the investigator's choice arm (16.0 months). The difference in median overall survival was 5.7 months (hazard ratio 0.51, 95% confidence interval [CI] 0.37 to 0.71). Trial results for the most recent August 2021 and February 2022 data cuts are academic in confidence and cannot be reported here. The committee noted that the overall survival data used in the model (from the August 2021 data cut) included some people who had crossed over from the investigator's choice arm to have tebentafusp, but the results had not been adjusted. This contributed to some uncertainty in the results so it would have preferred the crossover to have been adjusted for. However, the company did not consider adjusting for crossover was feasible using standard methods because the trial protocol did not mandate crossover. At the October 2020 data cut, median progression-free survival was also longer in the tebentafusp arm than the investigator's choice arm. But the extent of benefit with tebentafusp on progression-free survival appeared to be lower than that on overall survival. Median progression-free survival was 3.3 months in the tebentafusp arm and 2.9 months in the investigator's choice arm. The difference in median progression-free survival was 0.4 months (hazard ratio 0.73, 95% CI 0.58 to 0.94). The committee noted the difference in the benefit shown for overall survival and progression-free survival. The clinical experts explained that disease progression was measured with the RECIST criteria (a radiographic measure of disease progression) in the trial. But they explained that the benefits of tebentafusp may not stop after disease progression as measured in the trial, possibly due to changes in the tumour microenvironment caused by tebentafusp. The committee concluded that although the progression-free survival benefit with

tebentafusp is limited, tebentafusp does improve overall survival for people with advanced uveal melanoma. The committee further concluded that there seems to be a benefit with tebentafusp after disease progression according to RECIST criteria, but the reasons for this are unclear.

The clinical effectiveness results for the 82% of people who had pembrolizumab in the trial are the most relevant to NHS clinical practice

3.7 The comparators in the scope for first-line treatment of advanced uveal melanoma were pembrolizumab, ipilimumab, nivolumab alone or with ipilimumab, and dacarbazine. For previously treated disease the comparator in the scope was best supportive care. The committee agreed that tebentafusp would be used primarily as a first-line treatment (see section 3.4) so the appropriate comparator should be active treatment. The ERG stated that all the comparators included in the scope should be included in the model. The clinical experts noted that pembrolizumab is the most frequently used treatment for advanced uveal melanoma (see section 3.2). The committee noted that in the investigator's choice arm of IMCgp100-202 a large proportion of people were taking pembrolizumab. It considered that this population drives the outcomes for this arm. Subgroup data suggested worse outcomes with dacarbazine, and better outcomes for ipilimumab compared with pembrolizumab. But the data for dacarbazine and ipilimumab came from very small groups of people in the trial so was highly uncertain. The committee acknowledged that other treatments are sometimes used for treating advanced uveal melanoma, but agreed that pembrolizumab was the most relevant comparator. It concluded that data from the large subgroup of people who had pembrolizumab, making up 82% of the investigator's choice arm in the trial, was suitable to assess the clinical effectiveness of tebentafusp.

Tebentafusp is associated with more adverse events than the usual treatments, but side effects are short in duration

3.8 In IMCgp100-202 the number of people having any grade 3 or above treatment-emergent adverse event was higher in the tebentafusp arm than in the investigator's choice arm. This data is academic in confidence so cannot be reported here. The most common adverse event reported in the tebentafusp arm was adjudicated cytokine release syndrome of any grade. The marketing authorisation for tebentafusp states that people should be monitored overnight for cytokine release syndrome after each of the first 3 doses. Other adverse events reported more often by people in the tebentafusp arm included rash, pyrexia (fever), pruritus (itchy skin) and fatigue. The clinical experts explained that although there can be adverse events associated with tebentafusp, these are usually limited to the first 4 weeks of treatment. They explained that if tebentafusp is tolerated beyond this point, toxicity throughout the rest of treatment is very low and quality of life is often improved compared with before treatment started. The patient experts agreed that the adverse event profile of tebentafusp was better compared with other treatment options and that the adverse events that did occur were tolerable. They explained that while on tebentafusp, many people could continue life as they had done before treatment. The committee concluded that although the trial evidence suggests that the number of adverse events associated with tebentafusp is greater than with the usual treatments, these are likely to happen within the first month and after this tebentafusp is well tolerated.

The economic model

The company's model structure is acceptable for decision making

3.9 The company presented a 3-state partitioned survival model to estimate the cost effectiveness of tebentafusp compared with current treatment. The 3 health states were progression-free, progressed disease and death. The starting age in the model was 62 years, in line with the mean age in

the clinical trial (see section 3.5). A time horizon of 38 years, equating to a lifetime, was used. The committee concluded that the partitioned survival model presented by the company was acceptable for decision making.

Survival modelling

Overall survival modelling is highly uncertain but standard parametric approaches are the most appropriate

3.10 The company modelled overall survival based on extrapolation of data from IMCgp100-202. It used a 3-knot spline model for extrapolation of overall survival in the tebentafusp arm and a Weibull model for extrapolation in the investigator's choice arm. The company noted that the choice to use a spline model was due to a change in survival profile which could not be captured by a standard parametric model. The ERG preferred standard parametric models applied to both arms to extrapolate overall survival from the trial data. This was because the company had not fully justified:

- using a different approach in each treatment arm given the observed proportional overall survival hazards from the trial
- using a spline model rather than a standard parametric model.
- the points at which it considered the risk of dying would change (the knots).

The committee noted that:

- the company's spline model for tebentafusp followed the observed trial Kaplan Meier data closely at first, but at the end of the observed data it plateaued above the Kaplan Meier curve
- the ERG's preferred log-logistic or generalised gamma curves did not have a plateau for the period after the observed trial data and resulted in a much lower modelled mean overall survival for tebentafusp.

The clinical experts explained tebentafusp has a novel mechanism of action. So, it is reasonable to assume that post-progression survival is different after tebentafusp than after immunotherapy, so using a different modelling approach in each arm may be reasonable. But they noted that follow up is not currently long enough to assess this. The clinical experts explained that the overall survival estimates from the company's model were plausible. However, they also suggested that uveal melanoma is an aggressive disease and that there is no expectation that tebentafusp would be curative. So it is not expected that the overall survival curve would plateau, indicating disease cure, as suggested by the company's approach. The committee noted that most of the gains in overall survival made in the economic model are accumulated beyond the observed trial data. So the model is driven by the extrapolation of trial data, which is associated with uncertainty. Also the committee was aware that the choice of overall survival extrapolation has a large impact on the modelled overall survival and the cost-effectiveness results. The committee considered that:

- Tebentafusp is not expected to be curative and the company's spline model appears to suggest a high proportion of people who survive long term. It considered that standard parametric curves should be the starting point for modelling and could be used for this treatment. There are some functions in standard parametric models which do allow a proportion of people with long-term survival to be modelled (should longer follow-up data show this to be the case for tebentafusp).
- Data from the single-arm trial of tebentafusp as second-line treatment (IMCgp100-102; see section 3.4) could be used to provide external validation of the overall survival extrapolations.
- Longer-term evidence available in the future from IMCgp100-202 with up to 5-years follow up would help reduce the uncertainty associated with the overall survival extrapolation, but it acknowledged that this was not yet available.

- Although using different extrapolation curves for modelling overall survival in each treatment arm may be reasonable, this was not fully justified by the company.

The committee concluded that the overall survival modelling was highly uncertain, but the company's approach appeared to over-estimate the proportion of long-term survivors. On balance using a standard parametric approach to extrapolate the data in both treatment arms was preferable.

Either piecewise or fully parametric models are reasonable for estimating progression-free survival and time on treatment

3.11 The company used a piecewise modelling approach to estimate progression-free survival and time on treatment in both arms. For progression-free survival it used Kaplan Meier data and an extrapolated generalised gamma tail at the point where only 15% of the population remained at risk. For time on treatment it used Kaplan Meier data with an exponential model tail from the point where only 15% of the population remained at risk in the investigator's choice arm, and from where only 25% remained at risk in the tebentafusp arm. The ERG suggested that the use of Kaplan Meier data may overfit the trial data and that the cut-points chosen by the company for extrapolation were arbitrary. It preferred to use a fully parametric generalised gamma extrapolation for both arms for estimating both outcomes. The clinical experts explained that the time on treatment was reflective of the time to progression as tebentafusp was stopped in the trial when progression was confirmed. They noted that the mean tebentafusp treatment duration in the trial was in line with the estimated progression-free survival in the company's model. Given that the progression-free survival data in the trial is mature, the impact on the cost-effectiveness results of using different methods of extrapolation was minimal. The committee concluded that the company and the ERG had different approaches to estimating progression-free survival and time on treatment but agreed that the differences had little impact on the cost effectiveness results.

Assumptions in the economic model

It is not appropriate to include a 2-year stopping rule in the model

3.12 The company included a 2-year stopping rule in its model. It stated that it did not expect people to take tebentafusp for longer than 2 years in practice so it did not include the costs for treatment beyond this time. It highlighted that its model predicted that less than 5% of people were still having tebentafusp after 2 years so it was reasonable to include the stopping rule at this point. There was no 2-year stopping rule in the trial: treatment was only stopped after disease progression based on the RECIST criteria. So any benefits associated with tebentafusp treatment beyond 2 years are included in the clinical effectiveness results and the model. The patient experts suggested that tebentafusp is well tolerated so there is no logical reason to stop treatment while it is still effective. They explained that it was unlikely to be acceptable to patients to stop treatment without evidence of a sustained benefit after stopping. The clinical experts explained that there is no data on whether treatment effect would continue after stopping treatment at 2 years, or to show the impact on survival outcomes. But it is plausible that the treatment effect would not wane instantly after stopping treatment as a benefit in overall survival is seen beyond the point of stopping treatment in the trial. The committee concluded that it was not appropriate to include a stopping rule in the model because the clinical rationale for it had not been adequately justified.

The choice of approach for estimating utility values is unlikely to be a driver of the cost-effectiveness results

3.13 The company used a time-to-death approach to calculate utility values in its model. The time-to-death approach categorises utility based on the length of time before death. The utility values were taken from published values in the NICE technology appraisal guidance of pembrolizumab for advanced melanoma not previously treated with ipilimumab. The ERG

stated that EQ-5D data was available from the trial which was more appropriate to use than data from a different condition. It also disputed the use of the time-to-death approach as it is inconsistent with the model structure. This is because it included progression-free and progressed health states and produced implausibly high results for the group at least 1 year from death. The company suggested that it was more appropriate to use published utilities due to missing data in the EQ-5D data from IMCgp100-202. It also suggested that the time-to-death approach was more appropriate than utilities from on and off treatment health states. This is because disease progression is not a good marker of quality of life in people who have taken tebentafusp. The clinical and patient experts agreed that reasonably good quality of life could be maintained following progression based on the RECIST criteria. They noted that deterioration in quality of life happens quickly towards the end of life for many people with advanced uveal melanoma. The committee noted that time-to-death and on and off treatment health state utility approaches are both uncertain, and that the company and ERG both used the time to death approach in its base case analyses. It concluded that the choice of approach to estimate utility values was unlikely to be an important driver of the cost-effectiveness results.

The cost of HLA-A*02:01 testing is appropriately included in the model

3.14 The marketing authorisation for tebentafusp only includes people with HLA-A*02:01-positive uveal melanoma (see section 2.1). The clinical experts noted that people with uveal melanoma are not tested for HLA-A*02:01 in current practice and that if tebentafusp were a treatment option, all people with advanced uveal melanoma would need to have testing. They explained that HLA-A*02:01 testing is routinely done for other conditions and would be easily implementable in this setting. The company included the costs of HLA-A*02:01 testing in its model. The committee agreed that it was appropriate to include the costs of testing in the model and that this would be simple to adopt in practice.

End of life

Tebentafusp meets the end of life criteria for advanced uveal melanoma

3.15 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. Data from the October 2020 data cut of IMCgp100-202 showed that for people in the investigator's choice arm, median overall survival was 16.0 months (see section 3.10). IMCgp100-202 showed an increase in median overall survival with tebentafusp of 5.7 months. The clinical experts agreed that usually time from diagnosis to death with immunotherapy treatment was less than 2 years and that tebentafusp was expected to improve life expectancy by at least 3 months on average. The committee concluded that based on the clinical trial evidence tebentafusp meets the end of life criteria for treating advanced uveal melanoma.

Cost effectiveness

The cost-effectiveness estimates are higher than what NICE considers a cost-effective use of NHS resources

3.16 The committee discussed its preferred assumptions, which included:

- using pembrolizumab in the model as the key comparator (not included in either the company or ERG's base case; see section 3.7)
- using standard parametric curves for extrapolating overall survival (as in the ERG's base case; see section 3.10)
- not including a stopping rule in the model (as in the ERG's base case; see section 3.12).

It noted that other assumptions which differed between the company and ERG models had a limited impact on the cost-effectiveness results. These included:

- using piecewise (as in the company's base case) or fully parametric (as in the ERG's exploratory base case) progression-free survival and time on treatment extrapolation methods (see section 3.11)
- applying best supportive care costs as one-off costs (as in the company's base case) or monthly costs (as in the ERG's exploratory base case)
- assuming 95% adherence in the tebentafusp arm (as in the company's base case) or assuming the same adherence in both arms (as in the ERG's exploratory base case)
- assuming less dacarbazine use as second-line treatment than seen in the trial (as in the company's base case) or assuming second-line treatments as reported in IMCgp100-202 (as in the ERG's exploratory base case).

Tebentafusp has a patient access scheme. Because of confidential commercial arrangements for comparator treatments, the incremental cost-effectiveness ratios (ICERs) are confidential and cannot be reported here. As the end of life criteria were met (see section 3.15), the committee considered that for tebentafusp to be an effective use of NHS resources, the ICER should not be above £50,000 per quality-adjusted life year (QALY) gained. Taking into account all the confidential discounts, the committee noted that the company's base case ICER was above £50,000 per QALY gained. Removing the stopping rule increased the ICER further. The ERG's exploratory base case ICERs (using either a generalised gamma or log-logistic overall survival extrapolation) were both above £250,000 per QALY gained. The committee was aware that the biggest driver of the difference between the company's and the ERG's ICERs was the choice of overall survival extrapolation (see section 3.10). The committee noted that neither the company's nor the ERG's base cases included pembrolizumab as the key comparator. The subgroup results for people taking pembrolizumab in the investigator's choice arm resulted in a more favourable hazard ratio for tebentafusp compared with the hazard ratio for the full trial population. So including the clinical effectiveness

results for this subgroup may lower the ERG's exploratory base case. The committee concluded that although the ERG's ICERs did not include its preferred assumption about the appropriate comparator, they did include its preferred assumptions of using a standard parametric modelling approach to estimate overall survival and no 2-year stopping rule. So, the ERG's ICERs reflected the committee's preferred assumptions more than the company base case.

Innovation

Tebentafusp is an innovative new treatment

3.17 The clinical experts explained that tebentafusp is a new drug with a novel mechanism of action (see section 3.3). They explained that there is no standard care for advanced uveal melanoma (see section 3.2) and that tebentafusp would be the first treatment to target the specific features of uveal melanoma. The patient experts explained that tebentafusp would be a step change in the treatment of advanced uveal melanoma. The committee concluded that tebentafusp is innovative. It considered that all the health-related quality of life gains had been captured in the QALY calculations.

Conclusion

Tebentafusp is not recommended for routine use

3.18 The committee noted that both the company's and the ERG's base case ICERs indicate that tebentafusp is not cost effective, even when considering the end of life criteria (see sections 3.15 and 3.16). The ICERs were also highly uncertain due to the uncertainty about the overall survival estimates. So tebentafusp is not recommended for use in the NHS for treating advanced uveal melanoma.

Tebentafusp is not recommended in the Cancer Drugs Fund

3.19 Having concluded that tebentafusp could not be recommended for routine use, the committee then considered if it could be recommended for treating advanced uveal melanoma within the Cancer Drugs Fund. The committee discussed the arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting NICE's Cancer Drugs Fund methods guide (addendum). It noted that:

- the company had indicated it was interested in the treatment being considered for funding through the Cancer Drugs Fund
- overall survival data used in the economic model was highly uncertain
- IMCgp100-202 is still ongoing and direct trial data could help reduce uncertainties around overall survival
- the systemic anti-cancer therapy dataset could provide additional survival data
- the economic model is suitable for decision making.

But the committee also noted that the most plausible ICER was over £250,000 per QALY gained, and that the company's ICER without the stopping rule was over £50,000 per QALY gained. So it agreed that no ICERs had been presented which showed plausible potential for tebentafusp to be cost effective. The committee was aware that if tebentafusp were to be included in the Cancer Drugs Fund, the NICE review of tebentafusp at the end of the data collection arrangement would be done following NICE's recently updated health technology evaluations process and methods manual. Using these methods, the end of life criteria would not apply and it is unknown if the severity modifier would be applicable. Based on the ICERs presented, the committee concluded that tebentafusp did not meet the criteria to be considered for inclusion in the Cancer Drugs Fund.

4 Proposed date for review of guidance

4.1 NICE proposes that the guidance on this technology is considered for review 3 years after publication of the guidance. NICE welcomes comment on this proposed date. NICE 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 A
June 2022

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.

Albany Meikle
Technical lead

Mary Hughes

Technical adviser

Thomas Feist

Project manager

ISBN: [to be added at publication]