NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Talquetamab for treating relapsed and refractory multiple myeloma after 3 or more treatments

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

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

The evaluation 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 age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Issue date: August 2025

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 evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using talquetamab in the NHS in England.

For further details, see NICE's manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 25 September 2025
- Second evaluation committee meeting: 14 October 2025
- Details of membership of the evaluation committee are given in section 4

1 Recommendations

1.1 Talquetamab should not be used to treat relapsed and refractory multiple myeloma in adults when:

- they have had 3 or more treatments including:
  - an immunomodulatory agent
  - a proteasome inhibitor, and
  - an anti-CD38 antibody, and
- the multiple myeloma has progressed on the last treatment.

1.2 This recommendation is not intended to affect treatment with talquetamab 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 healthcare professional consider it appropriate to stop.

What this means in practice

Talquetamab is not required to be funded and should not be used routinely in the NHS in England for the condition and population in the recommendations.

This is because there is not enough evidence to determine whether talquetamab is value for money in this population.

Why the committee made these recommendations

Teclistamab is one of the standard treatments for multiple myeloma that has relapsed (come back) and is refractory (has stopped responding to treatment) after 3 or more lines of treatment and that has progressed on the last treatment.

Talquetamab and teclistamab have not been directly compared in a clinical trial. Results from an indirect comparison with teclistamab suggest that talquetamab may increase how long people live, but this is uncertain.

There are also uncertainties in the economic model. This is because of the:

- methods used to predict how long people in the trial would live
- modelling of subsequent treatments and intravenous immunoglobulin use
- impact of side effects on quality of life.

Because of the uncertainties in the clinical evidence and in the economic model it is not possible to determine the most likely cost-effectiveness estimates for talquetamab. So, it should not be used.

2 Information about talquetamab

Marketing authorisation indication

2.1 Talquetamab (Talvey, Johnson & Johnson Innovative Medicine) is indicated 'as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least 3 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy'.

Dosage in the marketing authorisation

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

Price

2.3 The list price for talquetamab is £326.41 per 3-mg vial and £4,352.00 per 40-mg vial (excluding VAT, BNF online accessed August 2025).

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

Carbon Reduction Plan

2.5 Information on the Carbon Reduction Plan for UK carbon emissions for Johnson & Johnson Innovative Medicine will be included here when guidance is published.

3 Committee discussion

The evaluation committee considered evidence submitted by Johnson & Johnson Innovative Medicine, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Details of the condition

3.1 Multiple myeloma is an incurable and progressive condition that has a substantial impact on survival and quality of life. Complications of multiple myeloma can be significant, debilitating and painful. The relapsing–remitting nature of the condition has a huge psychological impact, because people are aware that treatment options and life expectancy reduce with each relapse. The patient expert at the committee meeting highlighted the negative impact of frequent relapses of multiple myeloma. They spoke about the anxiety around the availability of treatment options after each relapse. They also spoke about the anxiety around having to take corticosteroids, which are associated with a considerable negative impact on quality of life. The committee recognised the substantial impact that multiple myeloma has on survival and quality of life. It acknowledged the unmet need for more treatments that are effective for people with multiple myeloma who have already had several treatments.

Clinical management

Treatment pathway, positioning and comparators

3.2 According to the marketing authorisation, people having talquetamab must have had 3 or more treatments including a proteasome inhibitor, an immunomodulatory drug and an anti-CD38 monoclonal antibody. The condition must have also progressed on the last treatment. The company submission provided a comparison with teclistamab, a treatment at fourth line and beyond. Clinical advice to the EAG was that teclistamab is the most relevant comparator for this evaluation, given the company's positioning after 3 or more lines of treatment. The clinical experts at the committee meeting agreed that teclistamab is the most frequently used fourth-line treatment option for relapsed and refractory multiple myeloma and a relevant comparator to talquetamab. But the NHS England Cancer Drugs Fund clinical lead highlighted that most people have pomalidomide plus dexamethasone and daratumumab at fourth line, with teclistamab mostly being used at fifth line. They also noted that the treatment pathway was rapidly evolving and that the data informing treatment use may change as newer treatments are implemented into the pathway. The committee was aware that teclistamab was cost effective compared with pomalidomide plus dexamethasone and that NICE recommended it for use after 3 or more lines of treatment. (See NICE's technology appraisal guidance on teclistamab for treating relapsed and refractory multiple myeloma after 3 or more treatments (TA1015). The committee was also aware that elranatamab is available for treating relapsed and refractory multiple myeloma after 3 or more lines of treatment. But elranatamab is only recommended for use within the Cancer Drugs Fund (see NICE's technology appraisal guidance on elranatamab for treating relapsed and refractory multiple myeloma after 3 or more treatments). So, it cannot be considered a comparator to talquetamab in this appraisal. The committee concluded that teclistamab is the most relevant comparator to talquetamab for this evaluation.

Clinical effectiveness

Talquetamab clinical trial data

3.3 The key clinical-effectiveness evidence for talquetamab came from the MonumenTAL-1 trial. This is an ongoing phase 1 and 2, single-arm, open-label, multicentre study. People in the trial have triple-class-exposed relapsed and refractory multiple myeloma that is refractory to at least 1 proteasome inhibitor, 1 immunomodulatory drug and 1 anti-CD38 monoclonal antibody. The company presented data for cohort C only (n=154). The company said that it had had clinical advice that the majority (90%) of people in UK clinical practice will have talquetamab once every 2 weeks (cohort C) with 10% having it once weekly (cohort A). It presented data from the September 2024 data cut, with a median follow up of 31.2 months. The overall response rate was 69.5%. Median overall survival was not estimable and median progression-free survival was 11.2 months. The committee was aware that the marketing authorisation allowed talquetamab to be used once weekly or once every 2 weeks. So, it questioned whether the clinical-effectiveness evidence from cohort A was appropriately captured in the company submission, and noted that median progression-free survival was worse for cohort A (7.5 months) than for cohort C. The company said that the once every 2 weeks dosage in cohort C is more convenient and should increase the cost effectiveness. A clinical expert said that approximately 90% of people have the once every 2 weeks dosage in NHS clinical practice because of its convenience over the once weekly dosing regimen. The committee was aware that the company had provided a scenario analysis using a weighted split of 90% for cohort C and 10% for cohort A. It considered that it may be appropriate to model resource use according to 90% of dosing regimens being once every 2 weeks and 10% being once weekly. But the committee was unclear why the clinical efficacy would differ markedly between these 2 dosing regimens. So, it decided that it would also like to see clinical and cost-effectiveness analyses on pooled data. The committee concluded

that the clinical-effectiveness evidence for talquetamab from MonumenTAL-1 was appropriate. But it said that it would also like to see results from clinical-effectiveness analyses of all cohort A and cohort C data from MonumenTAL-1 pooled, and the related economic analyses.

Comparing talquetamab with teclistamab

Indirect treatment comparison methods and results

3.4 In the absence of direct clinical trial evidence comparing talquetamab with teclistamab, the company did indirect treatment comparisons to estimate the comparative effectiveness for the relevant patient population. The clinical-effectiveness evidence for teclistamab came from MajesTEC-1, an ongoing phase 1 and 2, single-arm, open-label, multicentre trial. People in the trial have triple-class-exposed relapsed and refractory multiple myeloma that is refractory to at least 1 proteasome inhibitor, 1 immunomodulatory drug and 1 anti-CD38 monoclonal antibody. The company presented data from the phase 1 part 2 cohort and the phase 2 cohort A of the study (n=165). It presented data from the August 2023 data cut, with a median follow up of 30.4 months. The overall response rate was 63%. Median overall survival was 22.2 months and median progression-free survival was 11.4 months. For the indirect treatment comparison, 17 covariates were identified, of which 5 were considered priority prognostic factors and were adjusted for using inverse probability of treatment weighting (IPTW). The company used the average treatment effect for the treated (ATT) method to re-weight the baseline characteristics of the MajesTEC-1 cohort to match those of MonumenTAL-1. The results of the indirect treatment comparison for progression-free survival showed that talquetamab had a non-significant improvement compared with teclistamab. (The hazard ratio for progression-free survival is considered confidential by the company and cannot be reported here.) For the overall-survival analyses from the indirect treatment comparison, MonumenTAL-1 and MajesTEC-1 data was adjusted using a 2-stage adjustment. This was done to remove the

effects of the subsequent treatments not routinely available in UK clinical practice (see section 3.10). The results of the indirect treatment comparison showed a significant improvement in overall survival for talquetamab compared with teclistamab. (The hazard ratio for overall survival is considered confidential by the company and cannot be reported here.) The EAG considered that the company's indirect treatment comparison results, particularly the overall-survival hazard ratio were very uncertain and noted limitations, including that:

- There is notable separation from the start of the overall-survival Kaplan–Meier curves for talquetamab and teclistamab. This is not the case for the progression-free survival Kaplan–Meier curves for talquetamab and teclistamab from the indirect treatment comparison, which are similar to each other and close together (see section 3.5).
- Regression-analysis studies on overall survival and progression-free survival (Etekal et al. 2023 and Cartier et al. 2015) indicate that the company's overall-survival hazard ratio is an outlier and is more favourable to talquetamab than would be expected given the progression-free survival hazard ratio (see section 3.6).
- The impact of COVID-19 on the overall survival of the unvaccinated MajesTEC-1 population (MajesTEC-1 was recruited to earlier in the pandemic) is not adjusted for and is likely to introduce some confounding (see section 3.7).

In the absence of access to patient-level overall-survival data from the clinical trials, the EAG could not run its own analyses. So it used the overall-survival hazard ratio from the indirect treatment comparison in its base case. But the EAG highlighted that the clinical effectiveness of talquetamab compared with teclistamab, particularly the overall-survival hazard ratio, was highly uncertain and should be interpreted with caution. It provided scenario analyses that varied the overall-survival

hazard ratio to demonstrate the impact on the cost-effectiveness results.

Plausibility of overall-survival clinical trial data

3.5 The committee noted that the indirect treatment comparison results demonstrate a significantly large benefit in overall survival with talquetamab compared with teclistamab. It noted that this was despite there being no statistically significant benefit in duration of response or progression-free survival. The company said that the overall-survival benefit for talquetamab is driven by the difference in antibody drug target, with there being significantly fewer infections associated with talquetamab compared with teclistamab. The company also said that people in MonumenTAL-1 were fitter than in MajesTEC-1. So, people were more likely to have subsequent treatments after talquetamab than after teclistamab. The company also said that there were fewer adverse-event related deaths in MonumenTAL-1 compared with MajecTEC-1. The EAG explained that it had received clinical advice that the overall-survival benefit with talquetamab was implausible. The clinical experts at the committee meeting explained that the overall-survival benefit is likely associated with people being fitter in MonumenTAL-1 than in MajesTEC-1 and having considerably fewer infections with talquetamab compared with teclistamab. The clinical experts also highlighted the current difficulty in managing multiple myeloma that does not respond to treatment with teclistamab compared to if people could move on to have talquetamab. They said that this is reflected in the higher overall-survival benefit seen in MonumenTAL-1 compared with in MajesTEC-1. But the clinical experts acknowledged that a large overall-survival benefit early in the clinical data is unusual and they would normally expect to see this later. The committee concluded that there was no clear explanation for the early separation of the overall-survival curves despite minimal separation in the curves for duration of response and progression-free survival, and that this added uncertainty.

Etekal et al. regression analysis

3.6 The committee noted that the Etekal et al. regression analysis, which included treatments for relapsed or refractory multiple myeloma, identified a correlation of 0.76 (95% confidence interval [CI] 0.42 to 0.91). This indicated a medium association between progression-free survival and overall survival. The committee recalled the non-significant progression-free survival hazard ratio of close to 1 from the company's indirect treatment comparison. It questioned how this translates to a large statistically significant overall-survival hazard ratio for talquetamab compared with teclistamab. The clinical experts explained that the studies in the Etekal et al. regression analysis predate bispecific treatments such as teclistamab and talquetamab with their novel mechanism of action. So, they said that the Etekal et al. regression analysis may not be applicable. The clinical experts further highlighted that the overall-survival hazard ratio for teclistamab compared with pomalidomide plus dexamethasone from TA1015 is also an outlier. But the committee remained concerned because it is very rare to see a large overall-survival benefit with a treatment that has little demonstrated difference in progression-free survival. It also considered that progression-free survival is likely to have a more direct impact on overall survival in the later phases of multiple myeloma treatment, which Etekal et al. showed. The committee concluded that there was no clear explanation for the lack of correlation between the progression-free survival and overall-survival results from the indirect treatment comparison and that this added uncertainty.

Impact of COVID-19

3.7 The committee also noted the different timepoints at which the MajesTEC-1 and MonumenTAL-1 trials were done and the large difference in number of COVID-19-related deaths in the 2 trials. It questioned whether the timing of these trials in relation to COVID-19 accounted for the large overall-survival benefit seen with talquetamab. The clinical expert highlighted that there was likely a difference in the availability of COVID-

19 vaccinations accounting for the higher number of all infections in MajesTEC-1 than in MonumenTAL-1. But the expert explained that 76 of 94 deaths in MajesTEC-1 were not related to COVID-19, and that most of these were related to disease progression. So, COVID-19-related infections might not explain all of the survival benefit seen with talquetamab. The committee was made aware by the company that the survival benefit, despite a small increase in the hazard ratio, was maintained for talquetamab in an analysis censoring all COVID-19-related deaths. But the committee decided that because this analysis had not been formally submitted as part of the company submission it could not be considered in its decision making. The committee was aware that the company in TA1015 qualitatively considered that the overall-survival benefit for teclistamab in MajesTEC-1 may be underestimated. It said that this was because the trial was done during the height of the pandemic before widespread COVID-19 vaccinations were available. The committee also recalled its conclusion in section 3.3 that it would like to see the clinical and cost-effectiveness evidence of talquetamab using analyses that include all data from MonumenTAL-1 cohort A and cohort C pooled. The committee concluded that the overall-survival hazard ratio for talquetamab compared with teclistamab from the indirect treatment comparison is highly uncertain. It requested that the company provide:

- indirect treatment comparisons for the clinical effectiveness of talquetamab informed using analyses of all data from MonumenTAL-1 cohort A and cohort C pooled
- a survival analysis censoring for deaths related to COVID-19.

Economic model

Company's modelling approach

3.8 The company used a partitioned survival model with 3 health states:

- pre-progression

- post-progression
- death.

The cycle length was 1 week and the time horizon was 40 years. The EAG was broadly satisfied with the company's model structure. It noted that the company discounted costs and quality-adjusted life years (QALYs) in the first year of the model and applied a half-cycle correction to account for mid-cycle transitions in the model. The EAG considered that discounting for costs and benefits was inappropriate in the first year. It also thought that the cycle length was not long enough to apply half-cycle corrections in the model. So, the EAG discounted costs and QALYs from year 2 onward and excluded the half-cycle correction in its base-case model. The EAG also had reservations about several assumptions and the parameter selections used in the economic model (see section 3.4 and sections 3.9 to 3.12). The committee noted that the company's model was similar to previous models used for multiple myeloma. But it considered the EAG's approach to discounting from year 2 onward and the exclusion of the half-cycle correction appropriate. The committee concluded that overall, the model structure was appropriate for decision making.

Long-term extrapolations of overall survival, progression-free survival and time to treatment discontinuation

3.9 To estimate long-term overall survival, progression-free survival and time to treatment discontinuation beyond the trial follow-up period, the company fitted parametric models to the MajesTEC-1 individual patient data for teclistamab. The company selected a log-normal model for all 3 outcomes and calibrated it to clinical-expert estimates for these outcomes at 10 and 15 years in line with TA1015. The hazard ratios from the indirect treatment comparison for each outcome were then applied to the calibrated log-normal models for teclistamab. This was done to predict long-term overall survival, progression-free survival and time to treatment

discontinuation for talquetamab. Long-term overall survival for talquetamab was then capped to the general population mortality. With differing hazard profiles for overall survival, progression-free survival and time to treatment discontinuation, the EAG noted that the same parametric model did not need to be selected for all 3 outcomes. It highlighted that extrapolating using the log-normal model produces implausible long-term overall-survival estimates. It said that in order to produce plausible overall-survival curves, the company had to force it in to plausibility using clinical-expert estimates. The EAG also said that it did not think that the proportional hazards assumption was compatible with the selected log-normal models. So, the EAG selected the Weibull model which does not need to be adjusted to produce clinically plausible estimates. The committee did not agree with the company's choice of using the log-normal model for overall survival, progression-free survival and time to treatment discontinuation given their different hazard profiles. It also questioned the need to calibrate the log-normal models when there are other parametric models that would not need calibration. The company explained that selecting log-normal models for all 3 outcomes and calibrating them to meet clinical-expert estimates was consistent with the approach accepted by the committee in TA1015. The company further explained that aligning with TA1015 ensures internal and external validity. But the committee was aware that the calibrated log-normal model for progression-free survival and time to treatment discontinuation did not fit the observed Kaplan–Meier curves well despite having mature Kaplan–Meier data. So it thought that the calibrated log-normal model lacked internal validity. The committee was also aware of the availability of individual patient data for both treatments. It said that using the IPTW method in the indirect treatment comparison would allow independent models to be fitted that would not need an assumption of proportional hazards. The committee thought that the EAG's approach using the uncalibrated Weibull model was more appropriate because it had not needed calibration. But it considered that it would prefer to see

independent curves modelled rather than applying the indirect treatment comparison hazard ratio. The committee concluded that it would like to see the long-term overall survival, progression-free survival and time to treatment discontinuation extrapolations modelled independently for both teclistamab and talquetamab without calibrating to clinical-expert estimates.

Subsequent treatments

3.10 Some people in MonumenTAL-1 and MajesTEC-1 had subsequent treatments not routinely available in the NHS. To account for this, the company adjusted the overall-survival hazard ratio by removing the effects of these treatments using the 2-stage approach as per NICE Decision Support Unit's Technical Support Document 16. The company included subsequent teclistamab after talquetamab but excluded subsequent talquetamab after teclistamab in its base case. The company also provided a scenario analysis with people having subsequent talquetamab after initial teclistamab and subsequent teclistamab after initial talquetamab. The EAG thought that the company's base-case approach was not equitable and did not allow for a fair comparison of talquetamab with teclistamab. The EAG highlighted that this approach affects both costs and QALYs and favours the talquetamab arm. To allow for a fair comparison, the EAG included both talquetamab and teclistamab as subsequent treatments after initial treatment. The clinical experts at the committee meeting highlighted that if talquetamab is recommended, some people will start talquetamab or teclistamab and then have the other treatment after disease progression. Whether to have treatment with talquetamab or teclistamab first would be a decision between people with multiple myeloma and their healthcare practitioner. The committee noted the lack of detail in the company submission on how it adjusted for subsequent treatments not available in the NHS. It also noted that the company only used the Weibull model when adjusting for subsequent treatments using the 2-stage adjustment approach. The committee

considered that other parametric distributions could have been explored in scenario analyses. The committee concluded that the costs and benefits of both subsequent talquetamab and subsequent teclistamab following initial treatment should be modelled. It said that this is because this reflects how they would be used in NHS clinical practice. The committee also concluded that it would like the company to provide a more detailed explanation of overall methods used to adjust for subsequent treatments not available in the NHS. It also concluded that it would like to see analyses using parametric models, other than the Weibull model, when adjusting for subsequent treatments using the 2-stage adjustment approach.

Intravenous immunoglobulin use

3.11 People in MonumenTAL-1 and MajesTEC-1 could have intravenous immunoglobulin (IVIg) to prevent or treat infections. In the company's base-case analysis, IVIg use was modelled as a one-off cost in the first cycle in the talquetamab and teclistamab arms. This was in line with the observed IVIg use in the respective clinical trials. (The proportion of people having IVIg are considered confidential and cannot be reported here). The company assumed 9 doses of IVIg in both treatment arms, which aligns with TA1015. The company highlighted that because of the mechanism of action of talquetamab, people having it have less severe infections compared with teclistamab and need less IVIg. The EAG thought that modelling IVIg use as a one-off cost underestimates IVIg costs in favour of talquetamab. This is because it does not account for IVIg use by people having subsequent talquetamab and teclistamab after disease progression on the initial treatment. So the EAG included IVIg costs associated with subsequent talquetamab and teclistamab in its base case. It based the proportion of IVIg use for subsequent talquetamab and teclistamab on the observed IVIg use in the respective clinical trials. (These figures are considered confidential and cannot be reported here.) The EAG assumed 6 doses of IVIg for subsequent talquetamab and 9

doses of IVIg for subsequent teclistamab. The committee heard from the clinical experts that there is a considerable difference in the use of IVIg between talquetamab and teclistamab treatments in clinical practice. This is likely because there are fewer infections associated with talquetamab because of its novel mechanism of action compared with teclistamab. The experts agreed that the proportions used in the company's base case are broadly reflective of NHS practice. The clinical experts also agreed that people having subsequent talquetamab and teclistamab would also need IVIg. The committee concluded that the proportion of IVIg use in the talquetamab arm based on MonumenTAL-1 and in the teclistamab arm based on MajesTEC-1 is appropriate. It also concluded that IVIg use should be modelled for subsequent talquetamab and teclistamab treatments.

Adverse-event disutilities

3.12 In its base case, the company applied a one-off utility decrement in the first cycle of the model for grade 3 or higher treatment-related adverse events which happened for at least 5% of people who had talquetamab or teclistamab. A higher utility decrement was applied in the teclistamab arm compared with the talquetamab arm because teclistamab was associated with more grade 3 or higher treatment-related adverse events. The EAG considered that including a utility decrement for adverse events may lead to double counting. This is because the effect of adverse events on health-related quality of life was likely captured in the patient-reported outcomes data collected in the trial, which was used to estimate the health-state utility values in the model. So the EAG excluded modelling the utility decrement for adverse events separately to the health-state utility values. The committee heard from the patient experts that talquetamab is associated with altered taste in the first few months of starting talquetamab, which may result in subsequent weight loss. But the patient and clinical experts explained that these side effects are manageable, with weight loss being managed with dietitian support. A

patient expert also highlighted that other treatments have more profound side effects, particularly fatigue and gastrointestinal side effects which impact day-to-day life. The committee considered that altered taste and subsequent weight loss is likely to impact quality of life. But it noted that this had not been accounted for in the utility decrement applied for adverse events in the talquetamab arm because changes in taste are not classed as a grade 3 or 4 adverse event. The committee concluded that it would like the company to provide more explicit modelling of adverse-event disutilities and include the impact of altered taste and associated weight loss in the adverse-event disutility for talquetamab.

Cost-effectiveness estimates

Acceptable ICER

3.13 NICE's manual on health technology evaluations notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per QALY gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects including uncaptured health benefits. The committee noted the high level of uncertainty, specifically:

- the limited clinical-effectiveness evidence provided from cohort A of MonumenTAL-1 (see section 3.3)
- the indirect treatment comparison hazard ratio for overall survival (see sections 3.4 to 3.7)
- the modelling of long-term overall survival, progression-free survival and time to treatment discontinuation extrapolations for both talquetamab and teclistamab (see section 3.9)
- the lack of detail on how subsequent treatments not available in the NHS were adjusted for (see section 3.10)

- not taking into account adverse-event disutility for altered taste and associated weight loss with talquetamab treatment (see section 3.12).

The committee concluded that given the considerable uncertainties and based on the evidence and analysis it had seen at the first committee meeting, an acceptable ICER would be around £20,000 per QALY gained.

Company and EAG cost-effectiveness estimates

3.14 Because of confidential commercial arrangements for talquetamab and some of the comparators, the exact cost-effectiveness results are confidential and cannot be reported here.

Committee's preferred assumptions and request for additional analyses

3.15 The committee's preferred assumptions included:

- including in the model the costs and benefits of using subsequent talquetamab and subsequent teclistamab after initial treatment (see section 3.10)
- the proportions having IVIg use in the talquetamab arm being based on MonumenTAL-1 data and in the teclistamab arm being based on MajesTEC-1 data (see section 3.11)
- IVIg use being modelled for subsequent talquetamab and teclistamab treatments (see section 3.11)
- discounting for costs and QALYs from the second year of the model (see section 3.8)
- the exclusion of half-cycle correction of costs and QALYs in the economic model (see section 3.8).

Because of the uncertainties in the clinical-effectiveness evidence and in the economic model the committee could not determine the most likely cost-effectiveness estimates for talquetamab compared with

teclistamab. So, the committee requested that the company provide the following:

- the clinical-effectiveness results for talquetamab using analyses of all data from cohort A and cohort C from MonumenTAL-1 pooled, and related economic analyses (see section 3.3)
- indirect treatment comparisons for the clinical effectiveness of talquetamab using all data from cohort A and cohort C from MonumenTAL-1 pooled (see sections 3.4 to 3.7)
- a survival analysis censoring for deaths related to COVID-19 (see section 3.7)
- long-term overall survival, progression-free survival and time to treatment discontinuation extrapolations modelled independently for each outcome for both the teclistamab and talquetamab arms without applying a calibration to clinical-expert estimates (see section 3.9)
- a more detailed explanation of overall methods used to adjust for subsequent treatments not available in the NHS (see section 3.10)
- analyses using parametric models other than the Weibull model when adjusting for subsequent treatments using the 2-stage adjustment approach (see section 3.10)
- inclusion of the impact of altered taste and associated weight loss in the adverse-event disutility for talquetamab (see section 3.12).

Other factors

Equality

3.16 A professional-organisation submission noted that there is an increased incidence of multiple myeloma and development of more severe disease in African and African-Caribbean people. People with more severe multiple myeloma are more likely to need further lines of treatment because it is associated with an increased risk of relapse with prior lines of treatment. Race is a protected characteristic under the Equality Act 2010. A patient organisation also said that as with all treatments the costs

incurred by hospital visits and time off work will have a more significant impact on people with lower incomes. The committee considered that its recommendations do not restrict access to treatment for some people over others. So, the committee agreed that these were not potential equality issues in this evaluation. The committee did not identify any other equality issues.

Conclusion

Recommendation

3.17 The clinical-effectiveness evidence for talquetamab is uncertain because of uncertainties in the indirect comparison results for overall survival compared with teclistamab. There are also uncertainties in the economic model. The committee considered that the cost-effectiveness estimates presented by the company and the EAG were highly uncertain. The committee decided that, given its preferred assumptions, and based on the analysis it had seen, it could not determine the most likely cost-effectiveness estimates for talquetamab. Given the uncertainty, the committee would like to see additional analyses (see section 3.15). So, talquetamab should not be used.

4 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee C.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Stephen O'Brien

Chair, technology appraisal committee C

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser, a project manager and an associate director.

Zain Hussain

Technical lead

Alexandra Filby

Technical adviser

Leena Issa and Louise Jafferally

Project managers

Ross Dent

Associate director

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