NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Teclistamab 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 Teclistamab 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: July 2024

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- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using Teclistamab in the NHS in England.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: 13 August 2024
- Second evaluation committee meeting: To be confirmed
- Details of membership of the evaluation committee are given in section 5

1 Recommendations

1.1 Teclistamab is recommended as an option for treating relapsed and refractory multiple myeloma in adults after 3 or more treatments (including an immunomodulatory drug, a proteasome inhibitor and an anti-CD38 antibody) when the myeloma has progressed on their last treatment. It is only recommended if:

- pomalidomide plus dexamethasone would otherwise be offered
- the company provides teclistamab according to the commercial arrangement (see section 2).

1.2 This recommendation is not intended to affect treatment with teclistamab 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.

Why the committee made these recommendations

The only treatment that is routinely used for relapsed and refractory multiple myeloma after 3 or more treatments is pomalidomide plus dexamethasone.

Teclistamab has not been directly compared in a clinical trial with pomalidomide plus dexamethasone. An indirect comparison suggests that teclistamab could increase how long people have before their cancer gets worse and how long they live compared with pomalidomide plus dexamethasone.

When considering the condition's severity, and its effect on quality and length of life, the most likely estimates are within the range that NICE considers an acceptable use of NHS resources. So, teclistamab is recommended if it is used only as an alternative to pomalidomide plus dexamethasone.

2 Information about teclistamab

Marketing authorisation indication

2.1 Teclistamab (Tecvayli, 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 three 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 teclistamab.

Price

2.3 The list price for teclistamab is £775.14 per 10-mg vial and £3,952.78 per 90-mg vial (excluding VAT, BNF online accessed June 2024)

2.4 The company has a commercial arrangement (simple discount patient access scheme). This makes teclistamab available to the NHS with a discount. The size of the discount is commercial in confidence.

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 organisation submission stated that there is a clear need for innovative treatments that deliver deep, durable responses for people with relapsed and refractory multiple myeloma. One patient expert explained how myeloma symptoms affected her physical health and made her feel very tired. She needs care from her husband and had to stop working as a nurse. The committee recognised the substantial impact multiple myeloma has on survival and quality of life. It acknowledged the unmet need for effective treatments for people with multiple myeloma who have already had several treatments.

Teclistamab

3.2 Teclistamab is a bispecific monoclonal antibody that binds to B-cell maturation antigen on plasma cells, plasmablasts and multiple myeloma cells, as well as to the CD3 receptor on T-cells. The patient organisation submission highlighted that because teclistamab has a newer mechanism of action, it may overcome treatment resistance. The patient expert at the committee meeting explained that they had exhausted all treatment options offered on the NHS, having had myeloma for almost 24 years. They stated that since starting teclistamab they have had a huge improvement in their physical health and quality of life compared with how they felt while having previous treatments. Both patient and clinical experts highlighted that teclistamab does not have to be used in combination with corticosteroids, unlike other treatments for multiple myeloma, including pomalidomide. This is a distinct advantage of teclistamab because of the side effects associated with corticosteroids. The patient organisation submission also explained that prolonged corticosteroid treatment can be physically and mentally tough on people with multiple myeloma and their families, and has a huge impact on their quality of life. The committee concluded that teclistamab is an innovative

medicine that could provide a novel treatment option for people with relapsed and refractory multiple myeloma.

Clinical management

Treatment pathway, positioning and comparators

3.3 According to the marketing authorisation, people having teclistamab 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 pomalidomide plus dexamethasone, a fourth-line treatment. The EAG had clinical advice that pomalidomide plus dexamethasone is the most relevant comparator for this evaluation. Clinical experts at the committee meeting agreed that pomalidomide plus dexamethasone is the most frequently used fourth-line treatment option for relapsed and refractory multiple myeloma. They explained that panobinostat with bortezomib plus dexamethasone is rarely used in NHS clinical practice. The committee concluded that pomalidomide plus dexamethasone is the most appropriate comparator for this evaluation.

Clinical effectiveness

Teclistamab clinical trial data

3.4 The key clinical-effectiveness evidence for teclistamab in this evaluation came from the MajesTEC-1 trial. This is a phase 1/2, single-arm, open-label, multicentre study in people with triple-class exposed relapsed or 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, median

progression-free survival was 11.4 months and median time to next treatment was 12.6 months. The company also presented clinical evidence for teclistamab from 2 real-world retrospective studies (Dima et al. 2023 and Riedhammer et al. 2024), but it did not use these to inform the comparative effectiveness of teclistamab compared with pomalidomide plus dexamethasone. The committee noted that the median progression-free survival reported in these studies (5.4 months in Dima et al. and 8.7 months in Riedhammer et al.) was lower than in the MajesTEC-1 trial. It considered whether these studies may also have been appropriate to inform the comparative effectiveness of teclistamab. The clinical experts highlighted that the follow up in both Dima et al. and Riedhammer et al. is short but the overall response rate (66% in Dima et al. and 59.3% in Riedhammer et al.) was comparable to MajesTEC-1. The clinical experts also explained that 50% of the people in these studies would not have been eligible for MajesTEC-1 because they had more severe forms of myeloma, including plasma cell leukaemia and central nervous system involvement. So, the clinical experts considered that Dima et al. and Riedhammer et al. are less generalisable to UK clinical practice. The committee concluded the clinical-effectiveness evidence for teclistamab from MajesTEC-1 is appropriate.

Comparing teclistamab with pomalidomide plus dexamethasone

3.5 The clinical-effectiveness evidence for pomalidomide plus dexamethasone came from the UK real-world triple-class exposed relapsed or refractory multiple myeloma registry study. In this study, people with an Eastern Cooperative Oncology Group performance status of 0 or 1 (n=645) had follow up from starting their current line of treatment until either death, relocation outside of England, or the data cut off. The company presented data from the March 2023 data cut. The study had a median follow up of 26 months. Median overall survival was 9.78 months and median time to next treatment was 7.03 months. Because MajesTEC-1 did not include a control arm, the company did adjusted

indirect treatment comparisons to estimate the comparative effectiveness of teclistamab compared with pomalidomide plus dexamethasone for the relevant patient population. Because there was no progression-free survival data from the UK registry study, time to next treatment was used as a proxy for progression-free survival. This approach was validated by clinical expert advice to both the company and the EAG. There were 17 covariates identified, of which 5 were considered priority prognostic factors. Individual patient data from the UK registry study was available for only 6 of these variables, of which refractory status was the only priority prognostic factor. Autologous stem cell transplant was removed from the weighting process because there was no statistically significant difference in overall survival or time to next treatment found between people with or without previous autologous stem cell transplant. Adjustment for 5 covariates was made using the inverse probability of treatment weighting (IPTW) method and using the propensity score to derive weights for each person so that the baseline characteristics of people in the teclistamab arm and pomalidomide plus dexamethasone arm are balanced after adjustment. The results of the indirect treatment comparisons showed that teclistamab significantly improved both overall survival (hazard ratio 0.52, 95% confidence interval [CI] 0.36 to 0.74; p<0.0001) and time to next treatment (hazard ratio 0.56, 95% CI 0.40 to 0.79; p<0.0001), compared with pomalidomide plus dexamethasone. The EAG considered that the company's indirect treatment comparison methods had several limitations, including:

- Using the IPTW method to adjust the baseline characteristics may be unstable, and the estimated treatment effects may be biased.
- The company's base case did not use NICE Decision Support Unit guidance to perform trimming of the sample, or matching, to improve overlap.
- There were 4 priority prognostic factors (cytogenetic profile, International Staging System [ISS] stage, time to progress on last

regimen, and extramedullary plasmacytoma) that were not adjusted for. Clinical advice to the EAG is that cytogenetic profile is the most important factor.

- Violating the proportional hazard assumption introduces further uncertainty about the accuracy of reported treatment effects.

So, the EAG considered that the comparative effectiveness of teclistamab compared with pomalidomide plus dexamethasone is highly uncertain. The committee noted that the results of the indirect treatment comparisons looked promising for teclistamab compared with pomalidomide plus dexamethasone. But, because of the high level of uncertainty, particularly around the indirect treatment comparison methods, the committee questioned the reliability of these results. People in MajesTEC-1 had different characteristics to the in the UK registry study. So, the committee considered that the fact that the company's results were very similar before and after adjustment lacked face validity. There was also clinical-effectiveness evidence for pomalidomide plus dexamethasone available from another source, the ICARIA-MM trial. This was a phase 3 randomised controlled trial comparing isatuximab, pomalidomide, and dexamethasone with pomalidomide plus dexamethasone in people with refractory or relapsed and refractory multiple myeloma. The committee questioned whether clinical evidence for pomalidomide plus dexamethasone from ICARIA-MM could be used in an indirect treatment comparison. The company explained that it considered the UK registry study the best source of clinical evidence for pomalidomide plus dexamethasone, and used this to inform the indirect treatment comparison. The committee considered there was a lot of uncertainty in the indirect treatment comparisons' methods. It concluded that these methods are unreliable and the resulting point estimates for teclistamab compared with pomalidomide plus dexamethasone are highly uncertain and should be interpreted with caution, although it agreed that the trend favoured teclistamab.

Economic model

Company's modelling approach

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

- progression free
- progressed
- death.

The cycle length was 1 week and the time horizon was 40 years. Health-state occupancy of the cohort across model health states was as follows:

- Teclistamab arm: parametric distributions were fitted to the IPTW-adjusted MajesTEC-1 trial data for overall survival and time to next treatment (proxy for progression-free survival).
- Pomalidomide plus dexamethasone arm: parametric distributions were fitted to the UK registry study data for overall survival and time to next treatment.

The EAG was broadly satisfied with the company's model structure but had reservations about several assumptions and the parameter selections used to determine health-state occupancy (section 3.5 and section 3.6). The committee noted that the company's model was similar to previous models used for multiple myeloma and concluded that the model structure was appropriate for decision making.

Overall survival and progression-free survival extrapolations

3.7 To estimate long-term overall survival and progression-free survival beyond the trial follow-up period, the company fitted parametric distributions to MajecTEC-1 Kaplan–Meier data for the teclistamab arm and to the UK registry study Kaplan–Meier data for the pomalidomide plus dexamethasone arm. Data on time to next treatment was used as a proxy for progression-free survival (see section 3.5). The company selected the best fitting curve based on statistical fit using Akaike Information Criterion

(AIC) and Bayesian Information Criterion scores and validated it with clinical advice. The company selected log-normal and Gompertz distributions to model both long-term overall survival and progression-free survival in the economic model for the teclistamab arm and the pomalidomide plus dexamethasone arm, respectively. The company elicited a most likely range, most optimistic, and most pessimistic estimates of overall survival and progression-free survival at 5, 10, and 15 years for both the teclistamab arm and the pomalidomide plus dexamethasone arm at an advisory board with 3 clinical experts. In its base case, for the teclistamab arm only, the company fixed the long-term overall survival and progression-free survival to the midpoint of the range of the company's clinical experts' most likely estimates at 10 and 15 years. For the pomalidomide plus dexamethasone arm, it used the selected curves to extrapolate overall survival and progression-free survival without fixing these to the midpoint of the range of the company's clinical experts' most likely estimates at 10 and 15 years. The EAG considered that this approach was inconsistent between treatment arms. Instead, the EAG applied the same approach to both the teclistamab and pomalidomide plus dexamethasone treatment arms. The EAG also questioned the credibility of using clinical expert estimates to fix the selected overall survival and progression-free survival distribution. This is because these estimates are based on only 3 clinical experts and did not use the Delphi panel technique to elicit expert estimates. The EAG highlighted that these estimates do not provide exact values and the most optimistic and most pessimistic estimates are wider than the range for the clinical experts' most likely values. Because there is already a high level of uncertainty in the indirect treatment comparison results (see section 3.5), the committee explored a range of possible values provided by the company's clinical experts in its decision making. The committee agreed that it was appropriate to consider a more conservative approach to model long-term survival estimates to account for the uncertainty in the comparative effectiveness results. So, the committee concluded that it

would consider the long-term overall survival and progression-free survival modelled by fixing to the midpoint of the range of clinical experts' most likely values for both arms and a scenario fixed to the highest of the range of clinical experts' most likely values for the pomalidomide plus dexamethasone arm.

Time to stopping treatment extrapolation

3.8 The company estimated the proportion of people remaining on teclistamab treatment by fitting parametric distributions to time to stopping treatment data from the MajesTEC-1 Kaplan–Meier data. For the pomalidomide plus dexamethasone arm, because there was no time to stopping treatment data from the UK registry study, the company used the ratio of teclistamab progression-free survival (using time to next treatment as a proxy) to teclistamab time to stopping treatment data. It then applied this to the Gompertz distribution selected to model pomalidomide plus dexamethasone progression-free survival extrapolation. In the absence of relevant data, the EAG considered this a reasonable approach. For teclistamab time to stopping treatment the Gamma distribution was selected. The EAG considered that the curve selection for time to stopping teclistamab was not consistent with curve selection for teclistamab overall survival and progression-free survival. It noted that based on AIC scores, the log-normal distribution was the best fit to the MajesTEC-1 data. But, the company highlighted that this generated estimates of time to stopping treatment that were higher than the most likely values at 10 and 15 years estimated by the company's clinical experts. So, it selected the Gamma distribution with poorer statistical fit because it generated time to stopping treatment estimates at 10 and 15 years that were close to the estimated most likely values. The company did not fix the selected curves to the midpoint of the most likely range of clinical values at 10 and 15 years for both the teclistamab arm and the pomalidomide plus dexamethasone arm. The EAG considered that this was inconsistent with the approach used for curve selection for

teclistamab overall survival and progression-free survival (see section 3.7). So, the EAG selected the log-normal distribution to model teclistamab time to stopping treatment in its base case. It also fixed the time to stopping treatment curves to the midpoint of the range of the company's clinical experts' most likely values at 10 and 15 years. The committee recalled its preference for a more conservative approach to model long-term survival estimates, to account for the uncertainty in the comparative effectiveness results (see section 3.7). It applied a similar approach to modelling long-term time to stopping treatment. The committee concluded that the log-normal distribution is more appropriate to model time to stopping teclistamab. It also concluded that the long-term time to stopping treatment should be modelled by fixing selected curves to midpoint of the range of the clinical expert's most likely values for both arms, and the committee would consider a scenario fixing to the lowest of the range of the clinical expert's most likely values for the pomalidomide plus dexamethasone arm.

Utility values

Source of utility values

3.9 For the teclistamab arm, the company used progression-free health state time-dependent utility values for people having treatment with teclistamab, based on EQ-5D data from MajesTEC-1 and validated by the company's clinical expert opinion. But the company did not implement time-dependent utilities for the teclistamab arm in the progressed disease health state, because of insufficient MajesTEC-1 data. The utility values are considered confidential by the company and cannot be reported here. For the pomalidomide plus dexamethasone arm, the company did not implement progression-free and progressed disease health state time-dependent utility values using EQ-5D data from MajesTEC-1. Instead, it used pomalidomide plus dexamethasone utility values based on the MM-003 trial and accepted by the committee in NICE's technology appraisal guidance on daratumumab monotherapy for treating relapsed and

refractory multiple myeloma (0.61 in the progression-free health state and 0.57 in the progressed disease health state). The EAG considered the company's approach to using treatment-specific utility values for the teclistamab arm and the pomalidomide plus dexamethasone arm inconsistent. It noted that clinical advice to the company suggested that it is appropriate to use utility values derived from MajesTEC-1 data for the pomalidomide plus dexamethasone arm. So the EAG used utility values generated from MajesTEC-1 data for people having treatment with both teclistamab and pomalidomide plus dexamethasone. The EAG also highlighted that the utility values used in the company's base-case model resulted in lower baseline progression-free health-state utility values for the pomalidomide plus dexamethasone arm compared with the teclistamab arm. But the company did not provide any reasoning for this. The committee recalled the negative impact of corticosteroids on people with myeloma (see section 3.3). Because of the distinct advantage of teclistamab being a corticosteroid-free treatment, utility values for people with myeloma having teclistamab are likely to differ from people having pomalidomide plus dexamethasone. The committee concluded that the treatment-specific utility values for the teclistamab arm and the pomalidomide plus dexamethasone arm are considered more appropriate.

Costs

Switching teclistamab regimen

3.10 The summary of product characteristics (SmPC) for teclistamab states that the proportion of people who have teclistamab and have a complete response or better for at least 6 months can be considered for reduced dosing frequency from once weekly to once every 2 weeks. The company assumed that people switch to the reduced dose frequency at the same rate as in the MajesTEC-1 trial. It modelled this by fitting parametric distributions to the MajesTEC-1 data. The EAG considered this implausible because the company's approach resulted in people in the model switching to reduced dosing frequency much earlier than allowed in

the SmPC. The exact figure is considered confidential by the company and cannot be reported here. Considering the mean time to complete response in MajesTEC-1, the EAG assumed that switching to reduced dose frequency would start at 52 weeks. From that point onwards, the EAG modelled switching to reflect the proportion of people in MajesTEC-1 who switched to the reduced dose frequency at different time points. The committee considered the company's approach to model switching to reduced teclistamab dose frequency was inconsistent with the SmPC and MajesTEC-1 data, and was highly implausible. It considered the EAG's approach more plausible. So, it concluded that it was more appropriate to switch to a reduced dose frequency of teclistamab starting from 52 weeks, followed by using MajesTEC-1 data to switch to reduced dose frequency at different time points from 52 weeks onwards.

Intravenous immunoglobulin use

3.11 People in MajesTEC-1 could have immunoglobulin to prevent or treat infections. In the company's base-case analysis, immunoglobulin use in people having teclistamab is modelled in line with the observed frequency and duration of intravenous immunoglobulin (IVIG) and subcutaneous immunoglobulin infusions in MajesTEC-1. The exact numbers are considered confidential by the company and cannot be reported here. The company considered this a conservative approach, given that the eligibility criteria for having immunoglobulin in MajesTEC-1 were less stringent compared with the criteria currently used in UK clinical practice. The NHS England submission noted that the overall response rate for teclistamab from MajecTEC-1 was high (63%) with a median duration of response of 24 months. It highlighted that clinical expert advice to NHS England is that most of the people whose myeloma responds to teclistamab will need secondary prophylaxis with immunoglobulin for substantial periods of time. So, it suggested that the committee should consider scenarios in which at least 50% of people have at least 6 and up to 10 doses of IVIG. The company and EAG agreed that without understanding the impact of

IVIG on patient outcomes, the full impact of increased IVIG use on the cost effectiveness of teclistamab is unclear. The patient expert explained that they have had IVIG for a long time since starting teclistamab. One clinical expert highlighted that while current IVIG use is low in people with myeloma, recent real-world evidence suggests an increase in IVIG use. They stated that, in line with recent publications, 50% of people with myeloma having IVIG is a reasonable estimate. The committee concluded that the company's scenario using the proportion of people having 9 doses of IVIG, informed by MajesTEC-1, is appropriate.

Drug wastage

3.12 The company submission considered that vial sharing occurs in NHS practice and 15% drug wastage for teclistamab is assumed, in line with NICE's technology appraisal guidance for belantamab mafodotin for treating relapsed or refractory multiple myeloma after 4 or more therapies. It considered that this is a conservative approach based on the shelf life for reconstituted teclistamab of 20 hours compared with 4 hours for belantamab mafodotin. The company also highlighted evidence from an early access programme for teclistamab. This supports the assumption of low drug wastage in the company's base case and has a plausible upper bound of about 25% wastage. The EAG advised that, given the evidence presented by the company, drug wastage is likely to be closer to 15% than 25%. The NHS England submission highlighted that drug wastage for teclistamab varies according to people's weight, and teclistamab vial sharing is unlikely in clinical practice. It calculated 28.8% wastage of teclistamab if there is no vial sharing, based on the overall weight distribution of people with fourth-line myeloma. In the meeting, the company agreed that NHS England's estimate of 28.8% drug wastage is acceptable. The committee concluded that 28.8% drug wastage with teclistamab should be used in the economic model.

Teclistamab skipped doses

3.13 In the company submission, a proportion of maintenance doses of teclistamab skipped was included in the base-case model, based on MajesTEC-1 data. The proportion of skipped doses is considered confidential by the company and cannot be reported here. Dose skipping was applied from cycle 2 onwards in the model because none of the people in MajesTEC-1 missed a step-up dose. During clarification, the company updated its base-case model by applying a higher proportion of teclistamab skipped doses. The proportion of missed doses in the company's updated base case after clarification was based on:

- doses formally recorded as 'skipped' in MajesTEC-1
- dose delays between or within cycles in MajesTEC-1
- missed doses between last drug exposure and decision to stop treatment in MajesTEC-1, and
- adjustment for monthly and bi-monthly regimens to align with the SmPC.

3.14 The EAG considered the company's updated approach acceptable, except for applying an adjustment for monthly and bi-monthly regimens to align with the SmPC. The EAG considered it inappropriate to model people moving to monthly and bi-monthly teclistamab treatment schedules, because this would be not permitted in NHS practice. So the EAG preferred company's updated proportion of teclistamab skipped doses without adjustment for monthly and bi-monthly regimens to align with the SmPC. The committee concluded that the company's updated approach to inform teclistamab skipped doses without adjustment for monthly and bi-monthly regimens to align with the SmPC was appropriate for decision making.

Severity

3.15 The committee considered the severity of the condition (the future health lost by people living with the condition and having standard care in the NHS). The committee may apply a greater weight to quality-adjusted life-

years ([QALYs] a severity modifier) if technologies are indicated for conditions with a high degree of severity. The company provided absolute and proportional QALY shortfall estimates in line with NICE's health technology evaluations manual. The company and the EAG agreed that it was appropriate to apply a severity weight of 1.2 to the QALYs. So, the committee concluded that the severity weight of 1.2 applied to the QALYs was appropriate.

Cost-effectiveness estimates

Company and EAG cost-effectiveness estimates

3.16 The cost-effectiveness estimates used by the committee for decision making took into account all of the available confidential discounts, including those for comparators and follow-up treatments. These estimates are confidential and cannot be reported here. The company's base-case results were below the range normally considered a cost-effective use of NHS resources. The EAG updated the company's model using its preferred assumptions. The EAG's base-case results for teclistamab compared with pomalidomide plus dexamethasone were within the range normally considered a cost-effective use of NHS resources.

Acceptable ICER

3.17 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 recalled that there were benefits of teclistamab that may not have been captured in the economic modelling. Also, an advantage of teclistamab is that it does not have to be

used in combination with corticosteroids, but this was indirectly accounted for by using treatment-specific utility values (see section 3.9). The committee noted the high level of uncertainty, specifically the:

- lack of a direct comparison between teclistamab and pomalidomide plus dexamethasone (see section 3.5)
- limitations in the indirect treatment comparison and uncertainty of its results (see section 3.5)
- long-term overall survival and progression-free survival estimates for teclistamab and pomalidomide plus dexamethasone (see section 3.7).

So, the committee concluded that an acceptable ICER would be towards the lower end of the range NICE considers a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained).

Committee's preferred assumptions

3.18 Because of confidential discounts for teclistamab and pomalidomide plus dexamethasone, all cost-effectiveness results are commercial in confidence and cannot be reported here. The committee's preferred assumptions included:

- scenario 1: overall survival, progression-free survival and time to stopping treatment extrapolations modelled by fixing selected curves to midpoint of the range of the clinical expert's most likely values for both arms (see section 3.7 and section 3.8)
- scenario 2: as scenario 1 for teclistamab but overall survival, progression-free survival extrapolations modelled by fixing selected curves to highest of the range of the clinical expert's most likely values and time to stopping treatment modelled to lowest of the range of the clinical expert's most likely values for the pomalidomide plus dexamethasone arm (see section 3.7 and section 3.8)
- log-normal distribution to extrapolate time to stopping treatment for the teclistamab arm (see section 3.8)

- treatment-specific utility values (see section 3.9)
- switching teclistamab from once weekly to once every other week starting at 52 weeks, then using the MajesTEC-1 data (see section 3.10)
- the number of people having IVIG based on MajesTEC-1 data and 9 doses of IVIG (see section 3.11)
- teclistamab drug wastage of 28.8% estimated by NHS England (see section 3.12)
- company's updated approach to inform teclistamab skipped doses without adjustment for monthly and bi-monthly regimens to align with the SmPC (see section 3.13).

Using the committee's preferred assumptions resulted in ICERs in both scenarios are within the range considered a cost-effective use of NHS resources (see section 3.16). So, the committee concluded that teclistamab could be recommended for routine commissioning.

Other factors

Equality

3.19 The patient carer organisation stated that teclistamab may need to be delivered at better-equipped treatment centres with specifically trained healthcare professionals. This may pose challenges for people who live further from these treatment centres and cannot afford, for financial or logistical reasons, to travel longer distances. The patient carer organisation also highlighted that issues around capacity for day units and inpatient access may cause unequal access to teclistamab. The committee considered these equality issues, and agreed that its recommendations do not have a different impact on people protected by the equality legislation than on the wider population. The committee considered that there were no equalities issues that could be addressed by its recommendations.

Conclusion

Recommendation

3.20 The comparative evidence for teclistamab compared with pomalidomide plus dexamethasone is highly uncertain because of the unreliable methods used in the indirect treatment comparisons. The real-world evidence for teclistamab is also uncertain because of short follow up. This means the long-term estimates of overall survival and progression-free survival with teclistamab compared with pomalidomide plus dexamethasone are also uncertain. Despite the uncertainty, the ICERs that incorporate the committee's preferred assumptions are within the range considered a cost-effective use of NHS resources. So, teclistamab is recommended if it is used only as an alternative to pomalidomide plus dexamethasone.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication.

4.2 Chapter 2 Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for routine commissioning, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Interim funding will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early Access to Medicines Scheme designation or cost comparison evaluation),

at which point funding will switch to routine commissioning budgets. The NHS England Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final draft guidance.

4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has relapsed and refractory multiple myeloma and the healthcare professional responsible for their care thinks that teclistamab is the right treatment, it should be available for use, in line with NICE's recommendations.

5 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 and a project manager.

Zain Hussain

Technical lead

Sally Doss

Technical adviser

Louise Jafferally

Project manager

ISBN: [to be added at publication]