NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Daratumumab with bortezomib, lenalidomide and dexamethasone for untreated multiple myeloma when a stem cell transplant is unsuitable

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using daratumumab 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: January 2026

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- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using daratumumab with bortezomib, lenalidomide and dexamethasone in the NHS in England.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: 30 January 2026
- Second evaluation committee meeting: 12 March 2026
- Details of the evaluation committee are given in section 4

1 Recommendations

1.1 Daratumumab with bortezomib, lenalidomide and dexamethasone should not be used for untreated multiple myeloma in adults when an autologous stem cell transplant (ASCT) is unsuitable.

1.2 This recommendation is not intended to affect treatment with daratumumab with bortezomib, lenalidomide and dexamethasone 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

Daratumumab with bortezomib, lenalidomide and dexamethasone 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 daratumumab with bortezomib, lenalidomide and dexamethasone is value for money in this population.

Why the committee made these recommendations

NICE is evaluating daratumumab with bortezomib, lenalidomide and dexamethasone for untreated multiple myeloma when an autologous stem cell transplant is suitable separately.

Usual treatment for adults with untreated multiple myeloma when an ASCT is unsuitable includes:

- daratumumab plus lenalidomide and dexamethasone

- isatuximab plus bortezomib, lenalidomide and dexamethasone.

Daratumumab plus bortezomib, lenalidomide and dexamethasone has not been directly compared in a clinical trial with the usual treatments, but indirect comparisons suggest that it is likely to work as well as these.

Clinical trial evidence shows that daratumumab plus bortezomib, lenalidomide and dexamethasone increases how long people have before their condition gets worse and how long they live compared with bortezomib, lenalidomide and dexamethasone.

There are uncertainties in the economic model, including:

- the estimates of how long people live and how long they have before their condition gets worse, because the trial data is immature
- how the indirect comparisons with usual treatment have been undertaken
- the proportion of subsequent treatments offered in the NHS.

Also, the cost-effectiveness estimates are above the range that NICE considers an acceptable use of NHS resources. So, daratumumab with bortezomib, lenalidomide and dexamethasone should not be used.

2 Information about daratumumab

Marketing authorisation indication

2.1 Daratumumab (Darzalex, Johnson & Johnson) is indicated 'in combination with bortezomib, lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma'.

Dosage in the marketing authorisation

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

Price

2.3 The list price for daratumumab is £4,320 per 1,800 mg/15 ml vial (excluding VAT; BNF online accessed December 2025).

2.4 The company has a commercial arrangement. This makes daratumumab available to the NHS with a discount and it would have also applied to this indication if daratumumab with bortezomib, lenalidomide and dexamethasone had been recommended. The size of the discount is commercial in confidence.

Carbon Reduction Plan

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

3 Committee discussion

The evaluation committee considered evidence submitted by Johnson & Johnson, 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

Multiple myeloma

3.1 Multiple myeloma is an incurable, relapsing and remitting cancer that develops from bone marrow plasma cells. Patient experts emphasised that multiple myeloma is a highly individual and complex cancer that has a wide range of symptoms and varies in severity. They explained that the condition has a large psychological impact because of the constant possibility of relapse. With each relapse, the condition is more difficult to treat, and the number of future treatment options becomes more limited. The patient experts added that the condition can also have a large impact on quality of life, affecting all aspects of life for people with the condition, and their family and carers. The committee acknowledged that multiple myeloma is a chronic, incurable, highly individual condition that can have

a negative impact on quality of life for people with the condition, and their families and carers.

The treatment pathway

3.2 First-line treatment options for people with multiple myeloma depend on whether an autologous stem cell transplant (ASCT) is suitable. The committee recalled that the marketing authorisation for daratumumab is 'for the treatment of adult patients with newly diagnosed multiple myeloma'. The committee noted that this evaluation focuses on untreated multiple myeloma when an ASCT is unsuitable. The committee was aware of the ongoing NICE evaluation of daratumumab with bortezomib, lenalidomide and dexamethasone for untreated multiple myeloma when an autologous stem cell transplant is suitable, which includes the remaining population covered by the marketing authorisation. For untreated multiple myeloma when an ASCT is unsuitable, NICE recommends the following treatment options at first line:

- thalidomide, cyclophosphamide and dexamethasone (see NICE's technology appraisal guidance on bortezomib and thalidomide for the first-line treatment of multiple myeloma, from here TA228)
- bortezomib, cyclophosphamide and dexamethasone (Bor-Cyclo-Dex; see TA228)
- bortezomib, melphalan and prednisone (Bor-Mel-Dex; see TA228)
- lenalidomide and dexamethasone (Len-Dex; see NICE's technology appraisal guidance on lenalidomide plus dexamethasone for previously untreated multiple myeloma)
- daratumumab, lenalidomide and dexamethasone (Dar-Len-Dex; see NICE's technology appraisal guidance on daratumumab with lenalidomide and dexamethasone for untreated multiple myeloma when a stem cell transplant is unsuitable)
- isatuximab, bortezomib, lenalidomide and dexamethasone (Isa-Bor-Len-Dex; see NICE's technology appraisal guidance on isatuximab in combination for untreated multiple myeloma when a stem cell

transplant is unsuitable).

The patient experts explained that over time multiple myeloma becomes resistant to treatment. People with multiple myeloma should get the most effective treatment at first line because with each relapse subsequent treatments often become less effective and harder to tolerate. Patient experts also noted that people with myeloma are aware that ASCT is considered the most effective treatment. When an ASCT is unsuitable, alternative treatments that deliver comparable outcomes are needed. The company included the following comparators in its submission:

- Dar-Len-Dex
- Len-Dex
- bortezomib combinations (Bor-Mel-Dex and Bor-Cyclo-Dex).

The company stated that Dar-Len-Dex is the current NHS standard of care that most people with multiple myeloma have when an ASCT is unsuitable. It added that Len-Dex is mainly reserved for when a triplet regimen is not suitable, or if the patient lives far from hospital and would prefer an oral option. A small proportion of patients have bortezomib combinations. The company said it did not include Isa-Bor-Len-Dex as a comparator in its original submission because it would not be standard of care as it has only been recommended since September 2025. So, the company considered Dar-Len-Dex as the main comparator. At clarification, the EAG requested that the company provide a comparison with Isa-Bor-Len-Dex. In response, the company provided additional analyses with Isa-Bor-Len-Dex as a comparator. The clinical experts agreed that Dar-Len-Dex is the main first-line treatment for untreated multiple myeloma when an ASCT is unsuitable. They said that although they would like to offer Isa-Bor-Len-Dex, this combination is not yet widely used in NHS practice because at the time of the committee meeting it had only recently been recommended by

NICE. Isatuximab is also more difficult to provide because it is administered intravenously and more frequently than daratumumab, which is given subcutaneously. The clinical experts added that they hoped most NHS trusts would be able to offer Isa-Bor-Len-Dex within the next year. The NHS Cancer Drugs Fund clinical lead agreed that Isa-Bor-Len-Dex is not widely used, but it would be inappropriate to exclude it as a comparator. They also said that additional resource use associated with isatuximab treatment (such as increased nurse time) should be captured in the model. The committee accepted that Dar-Len-Dex was the current standard of care in the NHS, and therefore the main comparator for this appraisal. But it agreed that Isa-Bor-Len-Dex should also be considered a relevant comparator for this appraisal.

Clinical effectiveness

CEPHEUS

3.3 The clinical-effectiveness evidence for Dar-Bor-Len-Dex came from CEPHEUS, a phase 3, randomised, multicentre trial comparing Dar-Bor-Len-Dex with Bor-Len-Dex. The trial population included people with newly diagnosed, untreated multiple myeloma that was ineligible for an autologous stem cell transplant (ASCT-ineligible) or that was eligible for an ASCT, but the person declined or deferred (ASCT-declined or deferred). People were considered transplant ineligible if they were aged 18 to 70 with underlying comorbidities or over 70. Age and transplant eligibility were included as stratification factors at randomisation.

3.4 The company's submission presented results from the latest data cut (May 2024) for the ASCT-ineligible subpopulation only (see section 3.6), that is excluding the ASCT-declined or deferred population. The primary outcome was overall minimal residual disease (MRD) negativity rate (a measure of residual tumour cells in bone marrow). At the latest data cutoff, the proportion of people who achieved MRD negativity was significantly higher with Dar-Bor-Len-Dex than with Bor-Len-Dex. Although MRD is not commonly used to inform treatment decisions in

practice, the EAG's clinical expert said that in terms of depth of response, these results translate into improved patient outcomes. Progression-free survival (PFS) and overall survival (OS) were included as secondary outcomes, but median survival for these outcomes had not yet been reached. In the ASCT-ineligible population, Dar-Bor-Len-Dex improved PFS compared with Bor-Len-Dex. But there was no significant difference in OS between the 2 groups. Because the study took place during the COVID-19 pandemic, the company provided results where deaths caused by COVID-19 were censored (see section 3.5). When adjusted for COVID-19, both PFS and OS were significantly improved with Dar-Bor-Len-Dex compared with Dar-Len-Dex. The committee concluded that Dar-Bor-Len-Dex may be an effective treatment option for untreated multiple myeloma when an ASCT is unsuitable. But it noted the data from the trial was immature and did not compare Dar-Bor-Len-Dex with the relevant comparators (see section 3.2), so the PFS and OS results were uncertain.

Population adjustment for COVID-19

3.5 In its submission, the company presented results for the ASCT-ineligible population, adjusted for COVID-19, as its preferred population. As CEPHEUS was done during the COVID-19 pandemic, a proportion of the participants died from COVID-19 (the numbers are confidential and cannot be reported here). The company preferred to adjust for these COVID-19 deaths in its analysis. The committee noted that although it may be appropriate to adjust for COVID-19 deaths, it had concerns with doing so. This is because adjusting for COVID-19 deaths removes a proportion of people from the results who are likely to be more at risk of mortality or adverse events from other causes, leaving a 'fitter' population that is likely to have a better response to treatment. The committee accepted that adjusting for COVID-19 was appropriate but acknowledged that it added uncertainty to the results and was a favourable assumption for Dar-Bor-Len-Dex.

ASCT-unsuitable population

3.6 The committee considered whether a population for whom an ASCT is not suitable would include people with multiple myeloma who decline or defer treatment. In its submission, the company stated that feedback from UK clinical experts confirmed that a 'transplant-deferred/refused transplant' group is not recognised as a distinct clinical subgroup for treatment. At the committee meeting, clinical experts said that relatively few patients would decline or defer treatment. They explained that someone could decline an ASCT for a variety of reasons, such as comorbidities or because of inconvenience (such as needing to take time off work for recovery). The committee considered the treatment pathway for people who defer or decline treatment. It noted that there was an ongoing NICE evaluation for Dar-Bor-Len-Dex for untreated multiple myeloma when an ASCT is suitable. Experts stated that when someone declines ASCT, they would not usually later revisit having an ASCT. They also said that if it were revisited later, an ASCT may no longer be a suitable option for that patient. The expert said that a deferral pathway is yet to be established in the UK and current funding does not cover a deferred population. So, they would expect people who decline or defer an ASCT to follow the same treatment pathway as the ASCT-ineligible population. The committee noted that people who defer or decline a transplant would not be able to follow the transplant pathway, so would not be included in the ongoing evaluation for the transplant-eligible population. It was satisfied by the clinical expert's comments that they would expect the ASCT-declined or -deferred population to follow the same pathway as the ASCT-ineligible population, and that they would be likely to experience similar outcomes. The committee was concerned that excluding people who decline or defer an ASCT from this appraisal would exclude a small number of people with untreated multiple myeloma who would be covered by the marketing authorisation. So, the committee concluded that it would like to see clinical evidence and economic analyses for the full CEPHEUS population alongside the ASCT-ineligible population.

Indirect treatment comparisons

3.7 No evidence directly compared Dar-Bor-Len-Dex with the relevant comparators, Dar-Len-Dex and Isa-Bor-Len-Dex. The company provided the following indirect comparisons in the ASCT-ineligible population:

- an inverse probability of treatment weighting (IPTW) indirect treatment comparison (ITC) for the comparison with Dar-Len-Dex
- a network meta-analysis (NMA) for the comparison with Dar-Len-Dex and Isa-Bor-Len-Dex
- a matching-adjusted indirect comparison (MAIC) for the comparison with Isa-Bor-Len-Dex.

3.8 The IPTW ITC was the company's preferred approach for a comparison with Dar-Len-Dex because it had individual patient data from both CEPHEUS (the trial used to inform the Dar-Bor-Len-Dex arm) and MAIA (the trial used to inform the Dar-Len-Dex arm), in line with NICE's decision support unit technical support document 18 on methods for population-adjusted indirect comparisons. Heterogeneity between CEPHEUS and MAIA populations was assessed and adjusted for in the IPTW methods. COVID-19 and 11 other covariates, including age, sex and Eastern Cooperative Oncology Group (ECOG) performance status, were adjusted for in the main analysis. Results from the IPTW ITC showed that Dar-Bor-Len-Dex improves PFS and OS compared with Dar-Len-Dex. The company also provided a fixed-effects network meta-analysis (NMA) to support the IPTW ITC results for comparison with Dar-Len-Dex, and as the primary analysis for comparing Dar-Bor-Len-Dex with Isa-Bor-Len-Dex. The company said that an IPTW ITC would not be possible for the comparison with Isa-Bor-Len-Dex because individual patient data was not available from the informing trial, IMROZ. Eleven studies were included in the network, but only 2 were used for the Isa-Bor-Len-Dex comparison: CEPHEUS for the Dar-Bor-Len-Dex arm and IMROZ for the Isa-Bor-Len-Dex arm. Both studies had Bor-Len-Dex as the comparator arm. The company did not adjust the comparison with Isa-Bor-Len-Dex for COVID-

19. This is because, although both trials took place during the pandemic, the company was not able to adjust the IMROZ trial data for COVID-19, because it did not have individual patient data. The company thought it would be inappropriate to censor data in the Dar-Bor-Len-Dex arm but not in the Isa-Bor-Len-Dex arm. The company said that the unadjusted analysis was conservative because of the higher proportion of COVID-19 deaths in the CEPHEUS trial. The EAG noted that, overall, the statistical methods of the NMA were appropriate, and agreed that it was appropriate to use results unadjusted for COVID-19 for the Isa-Bor-Len-Dex comparison. The committee noted that the IPTW ITC and NMA showed the same direction of effect for OS, but had different magnitudes for the comparison of Dar-Bor-Len-Dex with Dar-Len-Dex. It was also concerned that, although an IPTW approach balances effect modifiers, it does not retain the original trial randomisation, whereas an NMA would retain randomisation. One of the studies included in the NMA (SWOG S077) did not report results for an ASCT-ineligible subgroup, so a no-intent-to-transplant subgroup was used as a proxy population. The committee noted that a no-intent-to-transplant proxy population from SWOG S0777 was also included in the NMA for NICE's evaluation of isatuximab in combination for untreated multiple myeloma when a stem cell transplant is unsuitable (from here, TA1098). The committee noted that SWOG S0777 was an older study with several generalisability issues, including:

- different baseline population characteristics from the current NHS population
- changes in the delivery of bortezomib (which can now be given subcutaneously and is more tolerated)
- there are now more treatment options available for people who are older or whose myeloma has progressed
- the no-intent-to-transplant group would include people who were eligible but chose not to have an ASCT, which is not fully representative of the ASCT-ineligible population.

The committee noted that it would usually have a methodological preference for maintaining randomisation, which is the case with the NMA. It recalled the IPTW ITC does not retain the trial original randomisation, which increased uncertainty. But the committee concluded that the IPTW ITC was more appropriate for the Dar-Bor-Len-Dex comparison with Dar-Len-Dex, because SWOG S0777 was a key connecting point for this comparison in the NMA, and this study introduced high uncertainty because of a likely imbalance of important effect modifiers that could not be adjusted for in the analysis. The committee also said that the IPTW ITC was more reliable than MAICs because it used individual patient data. It concluded that the NMA for the Isa-Bor-Len-Dex comparison was acceptable, noting that this comparison did not use the SWOG S0777 study in the NMA network. The committee recalled the indirect comparisons focused on the ASCT-ineligible population from CEPHEUS. It concluded that it would like to see results of all indirect comparisons using the whole CEPHEUS trial population. The committee also noted that it was not presented with evidence of the proportional hazards assumption in the NMA. Although this was not a deciding factor for the most appropriate ITC approach, the committee would like to see the proportional hazards data.

Economic model

Company's modelling approach

3.9 The company provided a partitioned survival model with a time horizon of 28 years and cycle length of 4 weeks. The model included 3 health states: pre-progression, post-progression and death. The probability of being in each health state was calculated using extrapolated PFS and OS curves. The company fitted independent extrapolations to patient-level data for the Dar-Bor-Len-Dex and Dar-Len-Dex treatment arm. Extrapolations for Isa-Bor-Len-Dex were generated by applying the PFS and OS hazard ratio from the NMA to the Dar-Bor-Len-Dex extrapolations. For Dar-Bor-Len-Dex, COVID-19-adjusted OS, PFS and TTD average treatment

effect-weighted Kaplan–Meier data from the ASCT-ineligible population of CEPHEUS were used. For Dar-Len-Dex, COVID-19-adjusted OS, PFS and TTD average treatment effect-weighted Kaplan–Meier data from the MAIA trial (less than 80 years) were used. The committee concluded that, overall, the model was acceptable for decision making, but it recalled median OS and PFS were not reached in the CEPHUS trial, so it would like to see scenario analyses exploring the use of alternative baseline OS curves with relative treatment effects applied. For example, using Systemic Anti-Cancer Therapy (SACT) data for Dar-Len-Dex as the baseline OS curve and the relevant hazard ratio applied to that. It also noted that for independently fitted extrapolations, it would like to see the plot of the implied hazard ratio between the modelled arms over time. It also recalled its previous conclusion that it would like to see scenario analyses using data from the whole CEPHEUS trial population.

Generalisability of baseline characteristics

3.10 In the company's model, baseline characteristics were based on the CEPHEUS ASCT-ineligible population (this is considered confidential by the company and cannot be reported here). Clinical advice to the EAG said that people with untreated multiple myeloma in the NHS are likely to be slightly older than the CEPHEUS ASCT-ineligible population, and that a higher proportion of the population would be male. So, based on clinical advice, the EAG preferred to use a higher mean age of 75 years and a higher proportion of males (55%). The EAG also noted that its preferred figures closely reflected real-world data from England between 2015 and 2022 (this data is confidential and cannot be reported here). At the committee meeting, the company highlighted that it preferred to use data based on the trial characteristics for consistency with the trial outcome data used in the model. The committee concluded that it preferred to use the mean age of 75 years and 55% proportion of males because this was more reflective of the NHS population.

Subsequent treatment: the proportion of people who have second-line treatment

3.11 In the company's model, the proportion of people having Dar-Bor-Len-Dex who go on to have second-line treatment (sourced from CEPHEUS and considered confidential by the company so cannot be reported here) was lower than the proportion in the Dar-Len-Dex arm (81%, sourced from MAIA) and the Isa-Bor-Len-Dex arm (72%, sourced from IMROZ). The company stated this was because of the improved PFS benefit observed with Dar-Bor-Len-Dex. It also said that people having Dar-Bor-Len-Dex would be older at the point of disease progression and less likely to have subsequent treatments. The committee noted that the company applied a fixed proportion, when the number of people who have second-line treatment would vary over time. The EAG reported that its clinical expert said it was unlikely for the proportion of people having second-line treatment to be as low with Dar-Bor-Len-Dex as the company suggested. It also highlighted that the median OS and PFS for CEPHEUS has not yet been reached, and that the proportion of people needing second-line treatment would increase over time. The EAG preferred to assume a higher proportion of second-line treatment with Dar-Bor-Len-Dex and Isa-Bor-Len-Dex (75%) and noted that more mature data would provide more certainty. At the committee meeting, experts agreed that age would be a factor when considering long-term survival and fitness for second-line treatments. They also said that people who have a complete response would not need second-line treatment because the disease is controlled. They suggested this would be more likely to happen with Dar-Bor-Len-Dex than with Dar-Len-Dex, but it was uncertain if this would happen more than with Isa-Bor-Len-Dex. The committee noted the company's figure was likely to underestimate the proportion of people having Dar-Bor-Len-Dex who would go on to have second-line treatment. This is because it was based on an earlier data cut from CEPHEUS, and the committee would expect the proportion to increase with time (at a later data cut). It recalled there remained some uncertainty in applying a fixed

proportion to a time-dependent variable, but it concluded the EAG's assumption of 75% for Dar-Bor-Len-Dex and Isa-Bor-Len-Dex was appropriate for decision making.

Subsequent treatment: the proportion of second- and third-line treatment offered in the NHS

3.12 The company's model incorporates a distribution of subsequent treatments from second to fourth line. The company assumed the same distribution at second and third line for Dar-Bor-Len-Dex, Dar-Len-Dex and Isa-Bor-Len-Dex. The EAG stated that it would prefer different distributions at second line and third line, based on input from clinical experts. At second line, the company assumed that 87.5% of people had Bel-Bor-Dex, whereas the EAG preferred a lower proportion (74%), based on clinical advice that Bel-Bor-Dex had been recommended in June 2025. The EAG also preferred a different distribution of Sel-Bor-Dex at third line based on clinical expert opinion, using 10% instead of the company's preferred 41.18%, following initial treatment with Dar-Bor-Len-Dex, Isa-Bor-Len-Dex and Dar-Len-Dex, because availability of Sel-Bor-Dex is limited. At the committee meeting, the clinical experts said that selinexor was still commonly used, particularly at third line. They also noted that uptake of Bel-Bor-Dex varies across the UK. The clinical experts explained that, looking at current usage, Bel-Bor-Dex would be used far less than the 87.5% assumed in the company's base case, but as availability increases and healthcare professionals become more familiar with managing toxicities associated with belantamab mafodotin, usage will probably increase. The experts said they would expect Bel-Bor-Dex to be the most popular option at second line. But the NHS England Cancer Drugs Fund lead added that a figure as high as 87.5% suggests that Bel-Bor-Dex is used universally across the NHS, which is unlikely at this time. The committee concluded that the distributions of subsequent treatments at second and third line were uncertain, so it requested more evidence to demonstrate what would be expected in NHS practice and validation of the distributions used. This may include using SACT data to inform the

proportion of subsequent treatments, particularly selinexor use at third line.

Cost-effectiveness estimates

Acceptable ICER

3.13 NICE's manual on health technology evaluations notes that, above a most plausible 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 trial is still ongoing and median PFS and OS have not been reached (see section 3.4 and section 3.9).
- uncertainties in the ITC approaches (see section 3.7)
- uncertainties in the distribution of second- and third-line treatments (see section 3.12)

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

3.14 The committee noted its preferred assumptions, which were:

- including Dar-Len-Dex and Isa-Bor-Len-Dex as relevant comparators (see section 3.2)
- using an IPTW ITC to inform the clinical effectiveness of the Dar-Len-Dex comparison, and an NMA to inform the clinical effectiveness of the Isa-Bor-Bel-Dex comparison (see section 3.7)

- baseline characteristics in the model of 75 years and 55% male (see section 3.10)
- 75% of people in the model go on to have subsequent treatment after Dar-Bor-Len-Dex and Isa-Bor-Len-Dex (see section 3.11).

Committee's requests for additional analyses

3.15 The committee requested the following additional analyses:

- analyses that include the full trial population from CEPHEUS, alongside analyses for the ASCT-ineligible subpopulation updated based on committee preferences (see section 3.6, section 3.7 and section 3.9)
- an exploration of different baseline OS curves used in the model (see section 3.9)
- more evidence to validate the distribution of second- and third-line treatments (see section 3.12).

Company and EAG cost-effectiveness estimates

3.16 The committee considered the cost effectiveness of Dar-Bor-Len-Dex compared with Dar-Len-Dex and the other relevant comparators. The exact ICERs cannot be reported here because some prices are confidential. The committee noted that there was a notable difference between the probabilistic and deterministic ICERs. Both the company and EAG base-case ICERs were above the range that NICE considers a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained).

Other factors

Equality

3.17 The committee did not identify any equality issues.

Uncaptured benefits

3.18 The committee considered whether there were any uncaptured benefits of daratumumab. It noted that there may be uncaptured benefits because daratumumab can be delivered subcutaneously, which may be more

convenient than some alternative treatments, such as isatuximab, that can only be delivered intravenously.

Conclusion

Recommendation

3.19 The committee has requested further information to inform the evaluation of Dar-Bor-Len-Dex for untreated multiple myeloma when an ASCT is unsuitable. Also, the current ICERs are above the range that NICE considers a cost-effective use of resources. So, Dar-Bor-Len-Dex is not recommended.

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 B.

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

Charles Crawley

Chair, technology appraisal committee B

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.

Lauren Elston
Technical lead

Nigel Gumbleton
Technical adviser

Jeremy Powell
Project manager

Emily Crowe
Associate director

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