NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Daratumumab with bortezomib for previously treated multiple myeloma

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

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

The appraisal committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

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Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

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

For further details, see NICE's guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 2 August 2018

Second appraisal committee meeting: TBC

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

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1 Recommendations

1.1 Daratumumab plus bortezomib and dexamethasone is not recommended, within its marketing authorisation, for previously treated multiple myeloma in adults.

1.2 This recommendation is not intended to affect treatment with daratumumab plus bortezomib 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 clinician consider it appropriate to stop.

Why the committee made these recommendations

Currently, second treatment options for multiple myeloma include bortezomib or carfilzomib (both plus dexamethasone) if thalidomide has been used first. For those who have had bortezomib first, retreatment with bortezomib is soon likely to become routine.

Clinical trial results show that, as a second treatment, daratumumab plus bortezomib and dexamethasone greatly improves how long people live for before the disease gets worse compared with bortezomib plus dexamethasone. The results also suggests that people having daratumumab plus bortezomib and dexamethasone live longer. However, the size of this benefit over the long term is unclear because the currently available trial data were collected over a short time. The benefits of daratumumab plus bortezomib and dexamethasone compared with carfilzomib plus dexamethasone are less clear because they haven't been compared directly in a trial.

The most plausible cost-effectiveness estimates for daratumumab plus bortezomib and dexamethasone are likely to be much higher than what NICE usually considers to be a cost-effective use of NHS resources. So,

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the treatment cannot be recommended for previously treated multiple myeloma.

2 Information about daratumumab

Marketing authorisation indication	Daratumumab (Darzalex, Janssen-Cilag) has a marketing authorisation 'in combination with… bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy'.
Dosage in the marketing authorisation	Daratumumab 16 mg/kg body weight is administered by intravenous infusion every week for weeks 1 to 9, every 3 weeks for weeks 10 to 24 and every 4 weeks from week 25 onwards. Bortezomib is administered by subcutaneous injection at a dose of 1.3 mg/m^2 twice weekly on days 1, 4, 8 and 11 for 8x21-day cycles. Dexamethasone is administered orally at a dose of 80 mg weekly.
Price	The company has a commercial arrangement (simple discount) for daratumumab which would apply if the technology had been recommended. There is also a commercial arrangement for bortezomib in which the company rebates the full cost of bortezomib for people whose disease response is less than partial after a maximum of 4 cycles of treatment.

3 Committee discussion

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

Treatment pathway

The appraisal focuses on daratumumab plus bortezomib and dexamethasone as a second-line treatment

3.1 The company presented evidence for daratumumab plus bortezomib and dexamethasone as a second-line treatment only. It stated that this was because offering this combination after only 1 previous treatment optimised its clinical- and cost effectiveness, and because there is a

clinical need for triple therapies at this point in treatment. The committee recognised that limiting this combination treatment to second line was narrower than its marketing authorisation and the population defined in the final NICE scope. However, the committee concluded that it would appraise daratumumab plus bortezomib and dexamethasone after 1 previous treatment, having only been presented with evidence for its use as a second-line therapy.

The treatment pathway for multiple myeloma is changing to allow retreatment with bortezomib

3.2 The treatment pathway for multiple myeloma depends on whether or not a stem cell transplant is suitable. If it is, people have bortezomib as induction treatment before a transplant. If it is not, people have either thalidomide or bortezomib as first-line therapy. The clinical experts stated that, in England, most people with multiple myeloma will have bortezomib as their first treatment. After initial therapy, current second-line treatment options include:

- chemotherapy, if bortezomib has been used first line
- bortezomib plus dexamethasone, or carfilzomib plus dexamethasone, if thalidomide has been used first line.

The clinical and patient experts expressed their frustration with this treatment pathway because retreating with bortezomib (that is, bortezomib at second line, having had bortezomib at first line) is not routinely commissioned by the NHS, and NICE guidance states that people also cannot have carfilzomib after bortezomib. This means that, currently, chemotherapy is the only second-line treatment option for people who had first-line bortezomib. The clinical experts did not consider that chemotherapy effectively treats multiple myeloma, nor did they consider it to be a relevant second-line treatment option because they offer it only as a transition to third-line treatment. The clinical experts prefer to offer bortezomib retreatment to people whose disease responded to their

previous (first-line) treatment with bortezomib but then relapsed. The Cancer Drugs Fund clinical lead stated that a treatment algorithm currently being developed by NHS England would allow retreatment with bortezomib second line, depending on disease response to the first course of bortezomib treatment. The committee agreed that the treatment pathway for multiple myeloma is changing and that retreating with bortezomib is likely to be routinely accessible in the near future to some people who have previously had bortezomib. It noted that changes to the treatment pathway are likely to be implemented in the near future. It therefore determined the relevant comparators based on the future treatment pathway.

Bortezomib and carfilzomib plus dexamethasone are both comparators for daratumumab plus bortezomib and dexamethasone

3.3 The committee noted that, for people who have not had bortezomib before, the relevant treatment options at second line are bortezomib and carfilzomib. It also heard that, for people who have had bortezomib before, bortezomib retreatment will be the main treatment option at second line when it becomes available, and will replace chemotherapy. The committee therefore concluded that the relevant comparators were bortezomib for everyone having second-line treatment, and carfilzomib only for people who have not had bortezomib (that is, had thalidomide) first line.

Clinical evidence

The clinical evidence for daratumumab plus bortezomib and dexamethasone compared with bortezomib plus dexamethasone is from CASTOR

3.4 The clinical evidence for daratumumab plus bortezomib and dexamethasone compared with bortezomib plus dexamethasone came from the open-label trial CASTOR, an international trial with no UK centres. Because the company chose to focus on daratumumab plus bortezomib and dexamethasone as a second-line treatment (see

section 3.1), it presented subgroup data from the trial for patients who had only had 1 previous treatment (122/251 [49%] in the daratumumab plus bortezomib and dexamethasone arm, and 113/247 [46%] in the bortezomib plus dexamethasone arm). The trial population was stratified by number of previous treatments, meaning that randomisation was maintained in this second-line subgroup. The primary outcome of the trial was progression-free survival. The company presented data for all trial outcomes from an interim analysis, which was pre-specified in the trial protocol based on adequate numbers for progression-free survival, but not overall survival.

The second-line subgroup is appropriate to assess clinical effectiveness but the effect of patient differences across treatment arms is unclear

3.5 There were imbalances in previous treatments between trial arms in CASTOR. Notably, more patients in the bortezomib plus dexamethasone arm (29%) had first-line lenalidomide (a treatment not routinely offered in the NHS) than in the daratumumab plus bortezomib and dexamethasone arm (12%). The Cancer Drugs Fund clinical lead suggested that this imbalance could have favoured daratumumab plus bortezomib and dexamethasone because patients in this trial arm may have had a better prognosis. The clinical experts stated that there was no evidence to suggest that previous lenalidomide therapy modifies the effect of subsequent treatments, but the committee did not see any evidence to the contrary either. The company suggested that other imbalances between the second-line subgroup arms, such as cytogenetic abnormality (17p deletion), are also important and would have biased the results against daratumumab plus bortezomib and dexamethasone. The committee concluded that there was some uncertainty associated with the differences between treatment arms in the second-line subgroup because there were imbalances in prognostic factors and treatment effect modifiers that could have acted in opposite directions.

Daratumumab plus bortezomib and dexamethasone improves progression-free survival compared with bortezomib plus dexamethasone

3.6 In the second-line subgroup, there was a statistically significant ($p<0.0001$) increase in progression-free survival with daratumumab plus bortezomib and dexamethasone (median survival 26 months) compared with bortezomib plus dexamethasone (median survival 8 months; hazard ratio [HR] 0.23, 95% confidence interval [CI] 0.16 to 0.33), after a median follow-up of 27 months (pre-specified interim analysis). The committee understood from patient and clinical experts, and the Cancer Drugs Fund clinical lead, that an 18-month improvement in median progression-free survival was considered a 'game-changing' treatment effect in the second-line treatment of multiple myeloma. It concluded that daratumumab plus bortezomib and dexamethasone had a statistically significant and clinically important effect on progression-free survival compared with bortezomib plus dexamethasone.

Daratumumab plus bortezomib and dexamethasone improves survival but by how much is unclear because there are no long-term trial data

3.7 Overall-survival data from CASTOR were immature because more than 50% of patients in both arms were still alive at the interim analysis. The committee noted that the available data showed that daratumumab plus bortezomib and dexamethasone reduced the risk of death by 50% compared with bortezomib plus dexamethasone (HR 0.50, 95% CI 0.30 to 0.84, $p=0.008$). It concluded that overall survival improved with daratumumab plus bortezomib and dexamethasone, but the absolute improvement in overall survival was unknown because the data were immature.

Daratumumab combination therapy improves minimal residual disease but there is no evidence on how this outcome correlates with overall survival

3.8 The company presented data on minimal residual disease (a measure of the residual tumour cells in bone marrow in people with disease that has had a complete response to treatment). The clinical experts stated that,

although minimal residual disease is not routinely measured in clinical practice, it is associated with better progression-free and overall survival. The committee discussed whether data on minimal residual disease could provide further insight into the survival benefit of daratumumab plus bortezomib and dexamethasone. In CASTOR (in the whole trial population), there was no residual disease in 12% of patients in the daratumumab plus bortezomib and dexamethasone arm compared with 2% of patients in the bortezomib plus dexamethasone arm. The clinical experts explained that observing no residual disease is unexpected at second line, and they considered the findings to confirm that daratumumab plus bortezomib and dexamethasone would confer a long-term survival benefit. The committee concluded that, although there may be an association between minimal residual disease and overall survival, the relationship between these outcomes over the long term had not been established. Therefore, it did not consider minimal residual disease could not be used as a proxy for overall survival because it had not seen evidence of a non-confounded association between them over a period longer than the CASTOR trial.

It is appropriate to adjust trial data for follow-on treatments not used in the NHS, but more information is needed on adjustment methods

3.9 The committee appreciated that the relative effects of daratumumab plus bortezomib and dexamethasone compared with bortezomib plus dexamethasone would likely have been biased by a different proportion of patients in the 2 arms of CASTOR having treatments at third line and beyond not available in the NHS and likely to prolong survival. The company adjusted the overall-survival results from CASTOR for treatments used third line and beyond that are not used in the NHS and are likely to prolong life, which the committee agreed was appropriate. The ERG explained that it could not validate the company's adjustment (which used the Inverse Probability of Censoring Weights method) because the company had not provided details of its analysis, particularly the censoring weights used. The committee concluded that adjusting for

subsequent therapies was appropriate in principle, but that it needed information for the ERG to review about how the company had arrived at its adjusted estimates associating treatment with daratumumab and length of life.

The clinical effectiveness of daratumumab plus bortezomib and dexamethasone compared with carfilzomib plus dexamethasone is unclear

3.10 In the absence of a trial directly comparing daratumumab plus bortezomib and dexamethasone with carfilzomib plus dexamethasone, the company carried out a network meta-analysis using data from the second-line subgroup of CASTOR and ENDEAVOR (which compared carfilzomib plus dexamethasone with bortezomib plus dexamethasone). The results of this meta-analysis favoured daratumumab plus bortezomib and dexamethasone for both progression-free survival and overall survival compared with carfilzomib plus dexamethasone. However, the committee noted that the duration of bortezomib treatment differed in CASTOR and ENDEAVOR. In CASTOR, it was capped at 24 weeks, which is consistent with the marketing authorisation for bortezomib. In ENDEAVOR, however, patients could take bortezomib until disease progression. Because longer treatment with bortezomib would be expected to increase its clinical effectiveness, the ERG took the view that not correcting for bortezomib treatment duration in ENDEAVOR may have underestimated the effectiveness of carfilzomib plus dexamethasone in that trial. This may therefore have overestimated the relative effectiveness of daratumumab plus bortezomib and dexamethasone compared with carfilzomib plus dexamethasone from the network meta-analysis. The committee noted that, in the appraisal of carfilzomib for previously treated multiple myeloma, the committee for that appraisal had preferred an adjustment for the length of time a person could have bortezomib. However, the company in the current appraisal stated that, although the planned number of doses of bortezomib was greater in ENDEAVOR, the actual cumulative dose patients had was similar between the 2 trials. The committee agreed that this was a relevant point in considering whether

the duration of bortezomib treatment in ENDEAVOR should be adjusted. However, it was not presented with data about the cumulative dose of bortezomib, nor with data on whether cumulative dose was more closely associated with outcomes, and so could not appraise any potential effect of this at this time. The committee therefore concluded that the company's network meta-analysis could have overestimated the effectiveness of daratumumab plus bortezomib and dexamethasone compared with carfilzomib plus dexamethasone.

Data from the CASTOR second-line subgroup is appropriate for the main analyses but the effect of previous bortezomib treatment needs exploring

3.11 The committee noted that carfilzomib plus dexamethasone is only used by people who have not had previous bortezomib. The company's network meta-analysis used the second-line subgroups from CASTOR and ENDEAVOR and a subset of these subgroups, which included only patients who had not had previous bortezomib in a sensitivity analysis. The company stated that there was an interaction between previous bortezomib and progression-free survival in patients who had had 1 or more previous treatments. However, it did not state whether there was an interaction between previous bortezomib and progression-free survival in patients who had only had 1 previous treatment. The clinical experts advised that the available data suggested that the magnitude of benefit may have been slightly greater for patients who had not had bortezomib before. The company's sensitivity analysis using the second-line subgroup data, but only for patients who had not had previous bortezomib, resulted in a slightly smaller estimate of the clinical benefits of daratumumab plus bortezomib and dexamethasone relative to bortezomib plus dexamethasone and carfilzomib plus dexamethasone. The committee noted that the confidence interval around the hazard ratio from this analysis, and the confidence interval from the main analysis including all patients at second line, overlapped substantially. The committee noted the company's concerns that assessing a subset of the second-line subgroup resulted in uncertainty because it represented a post-hoc analysis of a

non-randomised group of patients. The committee considered that the subgroup of people having second-line treatments who had not had previous bortezomib was relevant for the comparison with carfilzomib plus dexamethasone, but that how previous treatments affected outcomes remained unclear. It concluded that, on balance, the data for the second-line subgroup was more robust because it was randomised. However, it also concluded that examining the sensitivity of the cost-effectiveness estimates to using the second-line, bortezomib-naive data was warranted.

The company's economic model

Long-term survival on daratumumab plus bortezomib and dexamethasone is overestimated and survival on current treatments is underestimated

3.12 To predict the long-term effectiveness of treatment, the company extrapolated overall survival using a Gompertz curve for bortezomib plus dexamethasone and a log-logistic curve for daratumumab plus bortezomib and dexamethasone. The ERG preferred the Weibull curve for both arms. The committee appreciated that any extrapolation would be associated with high uncertainty because it was based on a short-term trial, with immature data. Nevertheless, it considered the ERG's estimates to be more plausible than the company's because:

- The company assumed that no people would be alive at 10 years on bortezomib plus dexamethasone or carfilzomib. However, the clinical experts stated that around 5% to 10% of people currently having second-line treatment for multiple myeloma would be expected to be alive 10 years from now.
- The ERG estimated that 9% of people would be alive at 10 years on bortezomib plus dexamethasone, which was more in line with the clinical experts' opinion.
- The clinical experts considered that the company's prediction that 22% of people having daratumumab plus bortezomib and dexamethasone would be alive at 20 years to be overoptimistic, even taking into

account the benefits of this treatment on minimal residual disease and the potential for an association between minimal residual disease and overall survival (see section 3.8).

The committee concluded that the company had underestimated survival with bortezomib plus dexamethasone and with carfilzomib plus dexamethasone, and had overestimated survival with daratumumab plus bortezomib and dexamethasone.

Adjusting the survival estimates for carfilzomib plus dexamethasone in the model is appropriate, but there is uncertainty around plausibility of results

3.13 Because the treatment duration of bortezomib in ENDEAVOR was outside of its marketing authorisation (see section 3.10), the ERG adjusted the progression-free- and overall-survival estimates for carfilzomib plus dexamethasone. It did this in line with how they were adjusted in NICE's technology appraisal guidance on carfilzomib for previously treated multiple myeloma. This had a marked effect on the survival estimates, and meant that carfilzomib plus dexamethasone had near-identical modelled survival to daratumumab plus bortezomib and dexamethasone. The committee recognised that the daratumumab combination was a game-changing treatment (see section 3.6), and so it was expected to be better than carfilzomib plus dexamethasone. However, the committee maintained that it was appropriate to adjust for bortezomib's treatment duration in ENDEAVOR in the absence of evidence on the effect of the cumulative dose of bortezomib in that trial on outcomes (see section 3.10). However, this adjustment was uncertain because it resulted in a difference between the overall survival curves for daratumumab plus bortezomib and dexamethasone, and carfilzomib plus dexamethasone that was potentially underestimated. The committee concluded that the survival curve for carfilzomib plus dexamethasone was likely to lie between the company's and ERG's estimates.

The effect of disease progression on quality of life is underestimated and clarification of company's methodology is needed

3.14 Data used to derive utility values in the model came from EQ-5D data collected in CASTOR from the second-line population both before disease progression and shortly after disease progression. The ERG stated that the difference between the modelled utility of people before and after disease progression was small, which did not seem plausible because quality of life would be expected to decrease after disease progression. The committee heard the following reasons from the company and clinical experts as to why there might not be a noticeable difference between quality of life before and after disease progression:

- Quality of life after disease progression in CASTOR had been measured soon after progression.
- The measure of disease progression used in CASTOR was based on biological markers in a blood sample, and that noticeable symptoms might not have started to appear so soon after progression.

However, the committee considered that, in clinical practice, quality of life would be expected to decrease the more disease progresses. As such, the ERG's estimate of post-progression utility were more plausible, even though it came from ENDEAVOR and was not derived from EQ-5D data (the preferred quality-of-life measure in the NICE methods guide). The committee concluded that the company had underestimated the effect of disease progression on quality of life and that clarification on the company's methodology for collecting quality-of-life data in CASTOR was needed.

Cost-effectiveness estimate

The most plausible cost-effectiveness estimate is above the range usually considered a cost-effective use of NHS resources

3.15 The committee's preferred modelling assumptions were:

- using data from the second-line subgroup rather than the second-line bortezomib-naive subgroup. (see section 3.10)
- extrapolation of overall survival with bortezomib plus dexamethasone, and carfilzomib plus dexamethasone to reflected plausible 10-year survival estimates of between 5% to 10% (see section 3.11)
- extrapolation of overall-survival estimates on daratumumab plus bortezomib and dexamethasone to give 20-year survival estimates that were lower than the company's extrapolations using the log-logistic curve, and closer to the ERG's estimate using the Weibull curve (see section 3.11)
- assuming a greater decrease in utility after disease progression than that currently modelled by the company (see section 3.13)
- adjusting to account for people having bortezomib for longer than is stipulated in its marketing authorisation in ENDEAVOR (see section 3.12).

Because carfilzomib and some follow-on treatments in the model had confidential commercial access agreements, the incremental cost-effectiveness ratios (ICERs) for daratumumab plus bortezomib and dexamethasone compared with bortezomib or carfilzomib plus dexamethasone are confidential and cannot be reported here. Taking into account the committee's preferred assumptions, the ICERs for daratumumab plus bortezomib and dexamethasone were well over £30,000 per quality-adjusted life year gained. This meant that, at the current price of daratumumab, this treatment did not represent a cost-effective use of NHS resources.

There are outstanding uncertainties surrounding the economic modelling some of which have a large impact on the ICERs

3.16 The committee noted that the key outstanding uncertainties in the model were:

- whether the second-line subgroup data were generalisable for the comparison between daratumumab plus bortezomib and dexamethasone with carfilzomib plus dexamethasone because people having carfilzomib in clinical practice in England would not have had previous bortezomib (see section 3.11)
- the long-term survival on daratumumab plus bortezomib and dexamethasone, and the comparator treatments (see section 3.12)
- adusting for the duration of bortezomib treatment in ENDEAVOR (see section 3.13).

The committee noted that using the second-line, bortezomib-naive data for the comparaison with carfilzomib plus dexamethasone had minimal impact on the ICER. By contrast, using the Weibull curve to model overall survival for daratumumab plus bortezomib and dexamethasone, and bortezomib plus dexamethasone, as per the ERG base case, increased the ICERs by more than £30,000 per QALY gained. Likewise, adjusting for bortezomib's treatment duration in ENDEAVOR had a substantial impact on the ICER for daratumumab plus bortezomib and dexamethasone compared with carfilzomib plus dexamethasone, increasing it by more than £400,000 per QALY gained. This was driven by a small QALY difference between the 2 treatments. The committee concluded that the uncertainties to which the model was most sensitive were the long-term effect of treatments on overall survival and the approprtiate duration of bortezomib treatment.

Daratumumab plus bortezomib and dexamethasone is an innovative treatment

3.17 The company and patient experts stated that they considered daratumumab plus bortezomib and dexamethasone to be innovative because it has a different mechanism of action to other available treatments for multiple myeloma. The committee agreed that the improvements in progression-free survival with daratumumab plus bortezomib and dexamethasone are large and that this combination is a step-change in the treatment of people with multiple myeloma. The patient

experts stated that the psychological benefit of delaying a second relapse had not been captured in the quality-of-life measure in the trial. The committee agreed that this had not been captured in the model, but that there were no methods to do so. It considered that daratumumab plus bortezomib and dexamethasone is an innovative treatment and that this should be taken into account in its decision-making. However, the committee concluded that, even taking into account the innovative nature of daratumumab plus bortezomib and dexamethasone, it did not consider the treatment to be a cost-effective use of NHS resources, so could not recommend it for the routine treatment of multiple myeloma.

Cancer Drugs Fund

Daratumumab plus bortezomib and dexamethasone is not a candidate for the Cancer Drugs Fund

3.18 Having concluded that it could not recommend daratumumab plus bortezomib and dexamethasone for routine use, the committee then considered if it could recommend the treatment within the Cancer Drugs Fund. It discussed the arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting the addendum to the NICE process and methods guides. It also noted that the company had not expressed an interest in providing the treatment through the Cancer Drugs Fund. The committee appreciated that the Cancer Drugs Fund is designed to resolve uncertainties, and that the key uncertainty in this appraisal was the long-term survival benefit of daratumumab plus bortezomib and dexamethasone. It acknowledged that, while further long-term data could be collected in the Cancer Drugs Fund, it could also be collected from the on-going CASTOR trial. Given the uncertainty around the long-term survival estimate of daratumumab plus bortezomib and carfilzomib, it was not possible to say whether this combination had a plausible potential to be cost effective without additional analyses to further characterise the clinical uncertainties and their impact on cost effectiveness. Nevertheless, the committee could not rule out the

possibility that daratumumab plus bortezomib and dexamethasone could be a candidate for the Cancer Drugs Fund.

Conclusion

Daratumumab plus bortezomib and dexamethasone is not recommended

3.19 Daratumumab plus bortezomib and dexamethasone is not recommended, within its marketing authorisation, for previously treated multiple myeloma in adults. Despite taking into account the innovative nature of this daratumumab combination, using the committee's most plausible assumptions on long-term survival, the ICERs for the comparisons with bortezomib plus dexamethasone and with carfilzomib plus dexamethasone were above the range considered to be a cost-effective use of NHS resources. Therefore, the committee could not recommend it for the routine treatment of previously treated multiple myeloma.

4 Proposed date for review of guidance

4.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Amanda Adler
Chair, Appraisal Committee
June 2018

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5 Appraisal committee members and NICE project team

Appraisal committee members

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

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

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

NICE project team

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

Mary Hughes, Marcela Haasova
Technical Leads

Ahmed Elsada
Technical Adviser

Jeremy Powell
Project Manager

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