National Institute for Health and Care Excellence

Health Technology Evaluation

Daratumumab with bortezomib, lenalidomide and dexamethasone for untreated multiple myeloma when a stem cell transplant is unsuitable [ID3843]

Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Johnson & Johnson (for Janssen-Cilag)	Johnson & Johnson consider it important to evaluate daratumumab in combination with bortezomib, lenalidomide and dexamethasone (DBLd) for untreated multiple myeloma when a transplant is unsuitable to address the existing unmet need and to significantly improve clinical outcomes. Johnson & Johnson consider a single technology appraisal the most appropriate route rather than a cost comparison route, due to the expected improvement in clinical outcomes with DBLd compared to the current Standard of Care (SoC). This is further described in the “additional considerations” section.	Thank you for your comments. The route for this evaluation has been changed to Single Technology Appraisal.
	Myeloma UK	Yes, this topic is appropriate for a NICE appraisal.	Thank you for your comment.

Section	Stakeholder	Comments [sic]	Action
	UK Myeloma Society	It is appropriate to evaluate this regimen in light of its efficacy and published improved outcomes in this patient population.	Thank you for your comment.
Wording	Johnson & Johnson	The wording of the remit is appropriate.	Thank you for your comment.
	Myeloma UK	The wording of the scope reflects the issues of clinical and cost effectiveness.	Thank you for your comment.
	UK Myeloma Society	Yes, it does reflect the issues.	Thank you for your comment.
Additional comments on the draft remit	Johnson & Johnson	Johnson & Johnson welcome this appraisal and consider the timing appropriate. There is a growing body of evidence supporting the clinical benefit of quadruplet therapy over SoC triplet regimens for patients unsuitable for stem cell transplant including results from the Phase III CEPHEUS study investigating DBLd.	Thank you for your comment.
	Myeloma UK	Myeloma is a relapsing and remitting, incurable cancer, and even after successful treatment, it will come back. New drugs and treatment combinations are needed to extend remission times and ultimately life expectancy.	Thank you for your comments.
	UK Myeloma Society	There are effective treatment options for this patient population available currently, but the increase in response rates and progression free survival of this regimen would suggest that the sooner this regimen can be evaluated the better, to further optimise outcomes.	Thank you for your comments.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Johnson & Johnson	Johnson & Johnson currently note inconsistencies in the background sections between ID3843 and ID6249 (DBLd for untreated multiple myeloma when a transplant is suitable). Johnson & Johnson suggest updating the 5 year survival rate for adults with multiple myeloma to 55% with the reference: Cancer Research UK 'Survival for Myeloma'. This ensures consistencies between the two scopes.	Thank you for your comment. No update is needed. The source for survival data is up to date.
	Myeloma UK	We consider this information to be sufficient and accurate.	Thank you for your comment.
	UK Myeloma Society	This information is accurate.	Thank you for your comment.
Population	Johnson & Johnson	Yes, the population is appropriately defined.	Thank you for your comment.
	Myeloma UK	We consider the population to be appropriately defined.	Thank you for your comment.
	UK Myeloma Society	Yes.	Thank you for your comment.
Subgroups	Johnson & Johnson	No subgroups have been identified for which DBLd is expected to be more clinically or cost effective. Therefore, Johnson & Johnson do not consider any subgroups that should be considered separately.	Thank you for your comment. No changes needed.

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	Myeloma UK	We are not aware of any groups within this population that should be considered separately.	Thank you for your comment. No changes needed.
	UK Myeloma Society	A particular subgroup which is poorly served by the current first line transplant ineligible treatment options, that would be rectified if this regimen was funded, are those presenting with acute renal impairment. Evidence suggests that the daratumumab regimen, combined with lenalidomide (DRd) results in the most significant PFS of all the 1st line options currently available. However, patients with renal impairment, which is myeloma related, require bortezomib based therapies which results in the greatest chance of preserving or improving kidney function. Currently, such patients would be limited to a bortezomib and alkylator regimen (VCD) which has an inferior PFS when compared to DRd and are unable to gain the benefit of a daratumumab regimen at first line. Reimbursement of bortezomib, lenalidomide with daratumumab would overcome this discrepancy and would enable outcomes to be optimised for all patients, regardless of myeloma related renal impairment.	Thank you for your comments. No changes needed.
Comparators	Johnson & Johnson	Daratumumab in combination with lenalidomide and dexamethasone (DLd) represents the current SoC in transplant-ineligible patients and should be considered the main comparator for this appraisal. Johnson & Johnson internal market share estimates indicate that DLd is used in up to [redacted] of newly diagnosed transplant ineligible patients following its positive NICE recommendation (TA917). This is based on a comparison of [redacted].	Thank you for your comments. The comparators in the scope remain broad and no changes have been made. In its submission for NICE evaluation, the company should provide justification of

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		Bortezomib combination treatments are less relevant comparators for this population based on their decline since the introduction of DLd. In TA917, clinical experts highlighted bortezomib combination treatments would only sometimes be considered and estimated only 30% of patients may have bortezomib combination treatments. With the introduction of DLd this is expected to have reduced, and this is supported by internal market research conducted by Johnson & Johnson indicating the market shares of new patients on bortezomib combination treatments have continuously dropped from [redacted]% in Q4 2023, down to [redacted]% in Q1 of 2025. Lenalidomide with dexamethasone is also considered a less relevant comparator as its use has declined since the introduction of DLd. Lenalidomide with dexamethasone would typically only be offered to a small group of patients due to logistical/ practical issues travelling to hospital or patient choice for an oral option. Johnson & Johnson does not consider isatuximab with bortezomib, lenalidomide and dexamethasone a relevant comparator as it is subject to an ongoing NICE evaluation and is not a standard treatment used in the NHS.	the comparators it considers are relevant, including with input from clinical experts.
	Myeloma UK	We agree that the treatments listed are approved/available for use as an initial treatment for myeloma patients when a stem cell transplant isn't suitable. However, this list does not reflect the treatments patients receive in clinical practice. The main treatment used to treat this group of patients is daratumumab in combination with lenalidomide and dexamethasone. Some patients, particularly those with severely reduced kidney function, may get bortezomib in combination with cyclophosphamide and dexamethasone.	Thank you for your comments. No changes needed. The comparators in the scope remain broad.

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		Although a small number of very frail patients still get lenalidomide and dexamethasone we don't believe it is a relevant comparator for this appraisal due to the frailty of the patient population getting this treatment. Thalidomide based combinations are not typically used to treat this patient population.	
	UK Myeloma Society	Yes, all relevant comparators are included.	Thank you for your comment.
Outcomes	Johnson & Johnson	The outcomes listed are appropriate. Johnson & Johnson propose adding sustained MRD negativity as an additional response-based outcome measure based on the endpoints in the clinical trial that capture the most important health benefits.	Thank you for your comment. The MRD outcome has been reworded to be broader as follows: 'minimal residual disease negativity'.
	Myeloma UK	Yes.	Thank you for your comment.
	UK Myeloma Society	Yes.	Thank you for your comment.
Equality	Johnson & Johnson	Johnson & Johnson do not consider that any changes need to be made to the scope regarding equality.	Thank you for your comment.
	Myeloma UK	We don't anticipate that a positive recommendation would impact people protected by the equality legislation differently to the wider population.	Thank you for your comments. These have been recorded for

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		As with all treatments the costs incurred by hospital visits and time off work will have a more significant impact on people with lower incomes.	committee consideration in the Equality Impact Assessment for scoping.
	UK Myeloma Society	There are no issues of note in terms of equality that are unaddressed in this remit.	
Other considerations	Johnson & Johnson	N/A	N/A
	Myeloma UK	N/A	N/A
	UK Myeloma Society	N/A	N/A
Questions for consultation	Johnson & Johnson	*Have all the relevant comparators been included in the scope?* See response in “Comparators” section. *Are thalidomide combination treatments still commonly used in NHS practice in England for multiple myeloma when stem cell transplant is unsuitable? Would bortezomib with an alkylating agent and corticosteroid or lenalidomide with dexamethasone ever be used as a first line treatment where thalidomide combination treatments could be tolerated or was not contraindicated?* Thalidomide combination treatments are no longer used in NHS practice and are not considered relevant comparators for this appraisal. This is consistent	Thank you for your comment. Please see NICE response under Comparators section.

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		with the final scope for NICE ID3981, which does not list thalidomide combination treatments, and aligns with TA917, where thalidomide combination treatments were not deemed relevant comparators.	Thank you for your comment. No changes needed.
		Which factors drive treatment decisions when deciding between offering bortezomib with an alkylating agent and corticosteroid or lenalidomide with dexamethasone as alternatives to daratumumab with lenalidomide and dexamethasone? As discussed in the "Comparators" section, DLd represents current SoC with a high market share of ~[redacted] and only a very small minority of patients are treated with bortezomib with an alkylating agent and corticosteroid or lenalidomide with dexamethasone. Johnson & Johnson understand that it would only be patients with severe renal impairment/ require dialysis that may be considered for bortezomib-based treatments. Lenalidomide with dexamethasone would typically only be offered to a small proportion of patients due to logistical/ practical issues travelling to hospital or patient choice for an oral option.	Thank you for your comments. As per the previous response on Comparators, these remain broad in the scope.
		Where do you consider daratumumab with bortezomib, lenalidomide and dexamethasone will fit into the existing care pathway for multiple myeloma? DBLd is expected to be indicated [redacted]. If recommended by NICE, this will allow patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant to have access to this quadruplet therapy as	Thank you for your comment.

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		a first-line treatment option. There is a separate, ongoing, NICE evaluation of DBLd for patients who are eligible for transplant (ID6249).	
		Please select from the following, will daratumumab with bortezomib, lenalidomide and dexamethasone be: C. Prescribed in secondary care with routine follow-up in secondary care Comparators and subsequent treatments are prescribed in secondary care with routine follow-up in secondary care.	Thank you for your comments.
		Would daratumumab with bortezomib, lenalidomide and dexamethasone be a candidate for managed access? Johnson & Johnson expect DBLd will be available via routine commission and therefore do not consider managed access to be appropriate.	Thank you for your comment.
		Do you consider that the use of daratumumab with bortezomib, lenalidomide and dexamethasone can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? The use of daratumumab in combination can result in potential substantial health-related benefits that are unlikely to be included in the QALY calculation. Such health-related benefits include: • Achieving increased rates of MRD negativity and sustaining those responses for longer are expected to translate to improvements in survival and result in: ○ Reduced demand for informal care, i.e., reduced carer burden	Thank you for your comments. As per the previous response on Outcomes, 'minimal residual disease

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		○ Positive social and economic impact associated with patients being able to get back to work, helping to reduce financial stress and anxiety • The sense of hope associated with long-term disease control and the prospect of a functional cure is also expected to positively impact the emotional and psychological well-being of patients with multiple myeloma. • The value of innovation in the frontline treatments as it marks a significant advancement in the treatment landscape. It aligns with the priorities of NICE and NHS, which focus on treatments that are effective, patient-friendly, and resource-efficient. *Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.* In addition to feedback from clinicians and patients, supporting evidence for uncaptured health benefits may include: • Result from literature searches • Patient preference market research *NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:* • *could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which*	negativity' has been included. Thank you for your comments.

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		daratumumab with bortezomib, lenalidomide and dexamethasone will be licensed; • *could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;* • *could have any adverse impact on people with a particular disability or disabilities.* *Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.* Please see response in the "Equality" section. *Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.* *NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.* • *Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?*	Thank you for your comment.

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		• *Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.* • *Will the intervention be used to treat the same population as the comparator(s)?* • *Overall is the technology likely to offer similar or improved health benefits compared with the comparators?* • *Would it be appropriate to use the cost-comparison methodology for this topic?* A cost comparison route is not appropriate for this appraisal. Cost comparisons require "similar or greater health benefits" whereas results from an indirect treatment comparison demonstrate DBLd results in [redacted] when compared to the current SoC (DLd). This will be further described in the company submission. Therefore, a full cost-utility analysis is required.	Thank you for your comments. The route for this evaluation has been changed to Single Technology Appraisal.
	Myeloma UK	*Where do you consider daratumumab with bortezomib, lenalidomide and dexamethasone will fit into the existing care pathway for multiple myeloma?* If approved, we believe that daratumumab with bortezomib, lenalidomide and dexamethasone would become the standard of care for stem cell transplant ineligible myeloma patients. Displacing both daratumumab with lenalidomide and dexamethasone and bortezomib with cyclophosphamide and dexamethasone. There will be some frailer patients or patients with other health conditions from whom daratumumab with bortezomib, lenalidomide and dexamethasone may not be suitable.	Thank you for your comment. No changes needed.

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		Would daratumumab with bortezomib, lenalidomide and dexamethasone be a candidate for managed access? Yes- the trial is ongoing *Do you consider that the use of daratumumab with bortezomib, lenalidomide and dexamethasone can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?* Improving remission times and life expectancy will positively impact carers and family members. It is a treatment for newly diagnosed patients. The first remission is often the deepest, longest remission and the period when a patient's quality of life is highest. It is widely held as the best opportunity to gain the best response with the longest time until disease progression. It is also the point in their disease where many patients will have the best quality of life post-diagnosis because their burden of treatment and illness is less than patients who are multiply relapsed.	Thank you for your comment. Thank you for your comments.
	UK Myeloma Society	N/A	N/A
Additional comments on the draft scope	Johnson & Johnson	N/A	N/A
	Myeloma UK	N/A	N/A
	UK Myeloma Society	N/A	N/A

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

Sanofi