National Institute for Health and Care Excellence

Health Technology Evaluation

Belantamab mafodotin with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma after 1 or more treatments ID6212

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	GSK (company)	GSK agree with the proposed evaluation route.	Thank you for your comment.
	Myeloma UK	Yes, this topic would be appropriate for a NICE appraisal.	Thank you for your comment.
	UK MYELOMA SOCIETY	This is a relevant and timely appraisal. Whilst treatments for myeloma have clearly improved, patients will die as a result of this condition. There are limited treatment options for patients who have received at least 4 prior lines of therapy. There is, therefore, a clear unmet need to provide better treatments to induce a longer and more durable period of remission and limit, or prevent, myeloma associated complications.	Thank you for your comment.

Section	Stakeholder	Comments [sic]	Action
		Belantamab mafadotin with Bortezomib Dex shows a significant improvement in PFS compared to an established treatment (Daratumumab Bortezomib Dex, available at 1st relapse) https://ascopubs.org/doi/10.1200/JCO.2024.42.36_suppl.439572	
Wording	GSK (company)	GSK agree that the current wording of the decision problem remit reflects the anticipated marketing authorisation.	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 [the wording is appropriate].	Thank you for your comment.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	GSK (company)	**Current wording:** "Belantamab mafodotin, (BLENREP, GlaxoSmithKline) does not currently have a marketing authorisation in the UK for relapsed or refractory multiple myeloma after 1 or more treatments. It has been studied in combination with bortezomib and dexamethasone compared with daratumumab in combination with bortezomib and dexamethasone in adults with relapsed recurrent multiple myeloma who have received at least one prior treatment. It currently has a marketing authorisation as monotherapy for the treatment of multiple myeloma in adult patients who have received at least four prior therapies." **Suggested new wording:**	Thank you for your comment. The background section of the scope is intended to be a brief overview of the condition and the technology, and uses a standard format to ensure consistency across different scopes. No change to scope required.

Section	Consultee/ Commentator	Comments [sic]	Action
		"Belantamab mafodotin (BLENREP, GlaxoSmithKline) is a first in class anti-BCMA therapy. It currently has a GB marketing authorisation as monotherapy for the treatment of multiple myeloma in adult patients who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an antiCD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. BLENREP has been awarded a UK Medicines Health and Regulatory Agency (MHRA) Innovation Passport. Belantamab mafodotin in combination with bortezomib and dexamethasone does not currently have a marketing authorisation in the UK for relapsed or refractory multiple myeloma after 1 or more treatments. The randomised phase 3 DREAMM-7 study evaluated belantamab mafodotin plus bortezomib and dexamethasone vs daratumumab, bortezomib and dexamethasone in relapsed/refractory multiple myeloma for patients with ≥1 prior line of therapy." **Rationale** To include a complete description of the intervention and regulatory status.	
	Myeloma UK	We consider this information to be sufficient and accurate.	Thank you for your comment.
	UK MYELOMA SOCIETY	Yes [the information is accurate and complete].	Thank you for your comment.
Population	GSK (company)	No change is needed.	Thank you for your comment.

Section	Consultee/ Commentator	Comments [sic]	Action
	Myeloma UK	The description is accurate.	Thank you for your comment.
	UK MYELOMA SOCIETY	Yes [the description is accurate].	Thank you for your comment.
Subgroups	GSK (company)	No change is needed.	Thank you for your comment.
	Myeloma UK	We consider the population to be appropriately defined.	Thank you for your comment.
Comparators	GSK (company)	The current proposed comparators do not reflect the full complexity of the MM pathway as most patients in the frontline setting will be refractory to lenalidomide and many of the current proposed comparators are not clinically relevant. This could lead to spurious sequencing of options within the NICE pathway. We outline below what we regard as the complete set of relevant comparators at each line of treatment. **Current wording:** "For people who have had 1 prior therapy: • bortezomib monotherapy • lenalidomide plus dexamethasone • carfilzomib plus lenalidomide and dexamethasone • carfilzomib plus dexamethasone	Thank you for your comments. The comparators section of the scope is intended to be broad and inclusive, based on the treatments that are recommended at each point in the treatment pathway. The company will have the opportunity during the evaluation to outline which comparators it considers are relevant to the decision problem and will be included in the evidence

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		• daratumumab plus bortezomib and dexamethasone • selinexor plus bortezomib and low-dose dexamethasone (subject to NICE evaluation) • ciltacabtagene autoleucel (subject to NICE evaluation)" **Suggested new wording:** "For people who have had 1 prior therapy: • carfilzomib plus dexamethasone • daratumumab plus bortezomib and dexamethasone • selinexor plus bortezomib and low-dose dexamethasone (for a subgroup of patients who are refractory to daratumumab and lenalidomide; subject to NICE consultation)" **Rationale** GSK do not consider bortezomib monotherapy to be a relevant comparator, as it is rarely used in the treatment of MM in clinical practice in the UK (12). Clinical experts have highlighted that this treatment is rarely used and bortezomib plus dexamethasone would instead be used in NHS clinical practice, although use of this doublet is very limited in clinical practice (4). GSK do not consider lenalidomide plus dexamethasone to be a relevant comparator after one prior line of therapy, as most patients at 1st relapse will be refractory to lenalidomide.	submission, with appropriate justifications. The committee will consider the most appropriate comparators during the evaluation. No change to scope required.

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		GSK do not consider carfilzomib plus lenalidomide and dexamethasone to be a relevant comparator after one prior line of therapy, as most patients at 1st relapse will be refractory to lenalidomide. Blueteq approval criteria also specifies that in order to be eligible for treatment with this triplet, patients must not have been previously treated with lenalidomide unless lenalidomide was received as part of induction therapy prior to a stem cell transplant (13). GSK do not consider ciltacabtagene autoleucel to be relevant comparator, as it is not yet approved for routine commissioning in the UK and is not part of established practice in the NHS. While GSK agrees that carfilzomib plus dexamethasone is a relevant comparator, doublet therapy is universally not recommended where there is a suitable triplet regimen available (e.g., daratumumab plus bortezomib and dexamethasone), with numerous studies demonstrating improved outcomes with triplets compared to doublets. Therefore, carfilzomib plus dexamethasone would only be a relevant comparator for patients for whom triplet therapy is not suitable or contraindicated due to comorbidities. Furthermore, carfilzomib plus dexamethasone is challenging to administer, requiring IV twice weekly, and it is generally not suitable for patients with existing cardiac comorbidities (14). **Current wording:** "For people who have had 2 prior therapies: • lenalidomide plus dexamethasone • ixazomib plus lenalidomide and dexamethasone • panobinostat plus bortezomib and dexamethasone	

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		• selinexor plus bortezomib and low-dose dexamethasone (subject to NICE evaluation) • ciltacabtagene autoleucel (subject to NICE evaluation)" **Suggested new wording:** GSK do not consider that any wording should be written in this section, as there are no relevant treatment alternatives in the target population for patients who are refractory to lenalidomide at 2nd relapse. **Rationale:** GSK do not consider therapies indicated for patients after 2 prior lines to be relevant comparators for patients who are refractory to lenalidomide. GSK do not consider lenalidomide-based regimens to be relevant comparators after 2 prior lines of therapy for reasons stated above. Most patients at this stage will be lenalidomide refractory, so the lenalidomide-dexamethasone doublet treatment will not be used for these patients. Similarly, ixazomib plus lenalidomide and dexamethasone is not suitable for lenalidomide refractory patients. GSK do not consider panobinostat plus bortezomib and dexamethasone to be a relevant comparator. This combination is primarily used at 4L+ (8, 15, 16), whereas GSK see belantamab mafodotin plus bortezomib and dexamethasone positioned earlier in the treatment pathway.	

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		GSK do not consider selinexor plus bortezomib and low-dose dexamethasone to be a relevant comparator. While this treatment regimen has received preliminary NICE approval and is under consultation (4), the approval is for patients with one prior line of therapy only. GSK therefore do not consider it to be a relevant comparator for later lines of therapy. GSK do not consider ciltacabtagene autoleucel to be a relevant comparator as it is not yet approved for routine commissioning in the UK and is not part of established practice in the NHS. **Current wording:** "For people who have had 3 or more prior therapies: • pomalidomide plus low-dose dexamethasone • daratumumab monotherapy • ixazomib plus lenalidomide and dexamethasone • lenalidomide plus dexamethasone • panobinostat plus bortezomib and dexamethasone • isatuximab plus pomalidomide and dexamethasone (subject to NICE evaluation) • selinexor plus bortezomib and low-dose dexamethasone (subject to NICE evaluation) • ciltacabtagene autoleucel (subject to NICE evaluation) • elranatamab (subject to NICE evaluation)"	

Section	Consultee/ Commentator	Comments [sic]	Action
		Suggested new wording: GSK do not consider that any wording should be written in this section. **Rationale:** GSK consider belantamab mafodotin plus bortezomib and dexamethasone to be positioned earlier in the treatment pathway and is not seeking to gain reimbursement in later lines and GSK do not consider therapies for people who have had 3 or more prior therapies to be relevant comparators for reasons stated above. GSK do not consider isatuximab plus pomalidomide and dexamethasone to be a relevant comparator. While this treatment regimen has been approved for use within the Cancer Drugs Fund (CDF) (17), it is not established practice in the NHS and is not approved for routine commissioning. GSK do not consider selinexor plus bortezomib and low-dose dexamethasone to be a relevant comparator, for reasons stated above. GSK do not consider ciltacabtagene autoleucel to be relevant comparators, for reasons stated above. GSK do not consider elranatamab to be a relevant comparator, as it is not yet approved for routine commissioning in the UK and is therefore not established practice in the NHS.	

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		Current wording: "For people who have had any number of prior therapies: • conventional chemotherapy regimens • best supportive care" **Suggested new wording:** GSK do not consider that any wording should be written in this section. **Rationale** GSK do not consider conventional chemotherapy regimens and best supportive care to be relevant comparators to active treatments like belantamab mafodotin. Conventional chemotherapy regimens and best supportive care are used as palliative treatment options at later lines in the treatment pathway after all active agents have been tried, and therefore do not compare to an active treatment, where the intention is to achieve a period of progression free survival, as opposed to a symptom-controlled death with palliative care. A patient eligible for belantamab mafodotin would never be offered palliation as an alternative, and similarly a patient for whom palliation was the most appropriate treatment option would never be offered an active treatment like belantamab mafodotin. Including irrelevant alternatives is not appropriate under the NICE methods.	

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	Myeloma UK	We agree that the treatments listed are approved/available for use from 2nd line. However, this list does not reflect the treatments patients receive in clinical practice. Some treatments are not used well used and others are no longer options for a significant proportion of patients due to prior exposure. For example: Bortezomib monotherapy is no longer used at second line. Combination treatments such as daratumumab, bortezomib and dexamethasone are preferred over monotherapy. The lenalidomide containing combinations are not widely used at later lines as most patients will be refractory to lenalidomide have received lenalidomide at previous lines of treatment. Most stem cell transplant eligible patients receive lenalidomide maintenance at first line and most stem cell transplant ineligible patient get lenalidomide containing combinations at diagnosis.	Thank you for your comments. The comparators section of the scope is intended to be broad and inclusive, based on the treatments that are recommended at each point in the treatment pathway. No change to scope required.
	UK MYELOMA SOCIETY	This scope is very broad and identifies many potential comparators. Belantamab mafadotin with Bortezomib Dex would be suitable for those patients with relapsed myeloma where treatment with a proteosome inhibitor is appropriate. Appropriate comparators at 2nd line include Carfilzomib Dex, Daratumumab Bortezomib Dex. Carfilzomib Lenalidomide Dex or Lenalidomide Dex are appropriate comparators assuming the patient is not refractory to Lenalidomide. Bortezomib Dex is not given due to other treatment options being available.	Thank you for your comments. The comparators section of the scope is intended to be broad and inclusive, based on the treatments that are recommended at each point in the treatment pathway. No change to scope required.

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		Appropriate comparators at 3rd line include Panobinostat with Bortezomib Dex and Ixazomib Lenalidomide Dex (assuming the patient is not refractory to Lenalidomide). At 4th line and beyond, comparators are correctly listed. The only proteosome inhibitor used at this stage is Panobinostat with Bortezomib Dex. This is rarely given.	
Outcomes	GSK (company)	GSK is aligned with the outcomes listed.	Thank you for your comment.
	Myeloma UK	Yes [the outcomes listed are appropriate]	Thank you for your comment.
	UK MYELOMA SOCIETY	Yes [the outcomes listed are appropriate]	Thank you for your comment.
Equality	GSK (company)	GSK is not aware of any equality issues relating to the proposed remit and scope.	Thank you for your comment.
	Myeloma UK	The scope includes all myeloma patients who have had one or more treatments and therefore doesn't exclude any people protected by the equality legislation. We don't anticipate that a positive recommendation would impact people protected by the equality legislation differently to the wider population. 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.	Thank you for your comment.
Other considerations	GSK (company)	For reasons stated above, GSK believe there is considerable need in current NHS practice for a BCMA triplet-based therapeutic option that can achieve	Thank you for your comment.

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		durable responses in lenalidomide-refractory patients with RRMM earlier in the treatment pathway.	
	UK MYELOMA SOCIETY	There is clearly an unmet clinical need for patients with relapsed myeloma. It has a manageable side effect profile, although consideration would have to be given to monitoring ocular side effects.	Thank you for your comment.
Questions for consultation	GSK (company)	**Where do you consider belantamab mafodotin with bortezomib and dexamethasone will fit into the existing care pathway for people with relapsed or refractory multiple myeloma who have had 1 to 3 prior lines of therapy?** GSK consider belantamab mafodotin in combination with bortezomib and dexamethasone to be positioned early in the treatment pathway for RRMM patients. **Are the listed comparators correct for each relevant subgroup (after 1, 2 or 3+ treatments)?** GSK consider belantamab mafodotin to be positioned earlier than 3 prior therapies in the treatment pathway. Please refer to the earlier section on comparators. **Would belantamab mafodotin with bortezomib and dexamethasone be a candidate for managed access?** GSK would consider managed access if this was an appropriate route to ensure patient access.	Thank you for your comments.

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		Do you consider that the use of belantamab mafodotin with bortezomib and dexamethasone can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Belantamab mafodotin with bortezomib and dexamethasone is an innovative combination with a novel MoA (BCMA). There is a whole system benefit of additional treatment modalities on a given line of therapy given the complexity of the MM treatment pathway with belantamab mafodotin plus bortezomib and dexamethasone used earlier in the treatment pathway. Due to the limited number of triplets available at 1st relapse for len- refractory patients, access to a BCMA-targeted triplet that has demonstrated a statistically significant and clinically meaningful PFS benefit compared directly to SoC, will potentially also help reduce relapse-associated anxiety in both patients and carers (DREAMM-7 interim analysis: 36.6 vs 13.4 months, HR, 0.41; P<0.00001) (18, 19). An additional benefit of offering belantamab mafodotin to patients with RRMM who have received one or more prior lines of therapy is the potential to increase therapeutic options for subsequent lines of therapy, as well as the number of UK patients eligible for recruitment into clinical trials. As future patients will be refractory to lenalidomide and daratumumab at 1st relapse due to treatment with daratumumab plus lenalidomide and dexamethasone in the frontline setting, belantamab mafodotin will offer an additional benefit to these patients.	
	Myeloma UK	***Where do you consider belantamab mafodotin with bortezomib and dexamethasone will fit into the existing care pathway for people with relapsed or refractory multiple myeloma who have had 1 to 3 prior lines of therapy?***	Thank you for your comments.

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		Myeloma is a very heterogenous cancer, and there is a need for flexibility to ensure patients have options if they do not respond to or tolerate standard treatments. *Patients should be given the best available treatment as early as possible in the pathway.* *We believe the use of belantamab mafodotin with bortezomib and dexamethasone will evolve as newly diagnosed patients and those already receiving treatment move through the pathway.* *There is an urgent need for new treatment options at 3rd line (2 prior treatments) due to the increasing use of lenalidomide at 1st and the restricted single-line use of other myeloma treatments.* *In the coming years, this gap will move further up the pathway to 2nd line as patients who had daratumumab, lenalidomide and dexamethasone at 1st line.* ***Would belantamab mafodotin with bortezomib and dexamethasone be a candidate for managed access?*** *Yes – the trial for this combination is still ongoing.* ***Do you consider that the use of belantamab mafodotin with bortezomib and dexamethasone can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?*** *Yes, due to treatment resistance and the heterogenous nature of myeloma, there is a need for treatments which kill myeloma cells in innovative ways.* *Belantamab mafodotin is an innovative treatment with a novel mechanism of action.*	

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Additional comments on the draft scope	UK MYELOMA SOCIETY	The technology will the first BCMA targeted therapy to be approved at this early stage in the myeloma treatment pathway. This is a step change in the management of myeloma patients. Results from the DREAMM-7 show a really impressive improvement in PFS (compared to Daratumumab Bortezomib Dexamethasone). NICE is considering BCMA targeted at later lines of treatment.	Thank you for your comment.

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

Leukaemia Care