National Institute for Health and Care Excellence

Health Technology Evaluation

Belantamab mafodotin with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma after 1 or more treatments (ID6211)
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	GlaxoSmithKline	Given the simultaneous occurrence of NICE processes for belantamab mafodotin with bortezomib and dexamethasone, and belantamab mafodotin with pomalidomide and dexamethasone, GSK acknowledges the suitability of the proposed evaluation method at this point in the process. Nonetheless, GSK is willing to engage in discussions to streamline the simultaneous processes. GSK consider the possibility that a level of cost-effectiveness may be reached that would make NICE's proportionate approach to technology appraisals an appropriate evaluation route for this appraisal.	Comments noted. The decision about which is the preferred approach will be made by NICE. No action needed.
	Janssen-Cilag	The topic and evaluation route are appropriate.	Comment noted. No action needed.
	Myeloma UK	Yes, this topic would be appropriate for a NICE appraisal.	Comment noted. No action needed.

Section	Stakeholder	Comments [sic]	Action
	Takeda	The topic and evaluation route are appropriate.	Comment noted. No action needed.
	UK MYELOMA FORUM and on behalf of the Royal College of Physicians	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 relapsed myeloma, particularly at later stages of the disease. 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. Belantamab mafodotin with Pomalidomide and Dexamethasone shows a improved PFS compared to Pomalidomide in combination with Bortezomib and Dexamethasone in patients with relapsed myeloma (DREAMM-8 study).	Comments noted. No action needed.
Wording	GlaxoSmithKline	GSK agree that the current wording of the decision problem remit reflects the anticipated marketing authorisation.	Comment noted. No action needed.
	Janssen-Cilag	No changes suggested.	Comment noted. No action needed.
	Myeloma UK	The wording of the scope reflects the issues of clinical and cost effectiveness.	Comment noted. No action needed.
	Takeda	No changes suggested.	Comment noted. No action needed.

Section	Stakeholder	Comments [sic]	Action
	UK MYELOMA FORUM and on behalf of the Royal College of Physicians	Yes	Comment noted. No action needed.
Timing issues	GlaxoSmithKline	GSK believe there is considerable need in current NHS practice for an alternative triplet-based therapeutic option, with a novel mechanism of action (MoA) targeting B-cell maturation antigen (BCMA), that can achieve durable responses in patients with relapsed or refractory multiple myeloma (RRMM), particularly in lenalidomide refractory patients that are difficult to treat earlier in the treatment pathway. Patients with MM will eventually relapse or become resistant to different classes of therapies as the disease progresses (1). Due to the extensive use of frontline lenalidomide-based therapies, most patients are refractory to lenalidomide at first relapse (2, 3). This presents a significant challenge in the treatment pathway, as there are limited triplet options available for patients who have had 1 prior line of therapy. Daratumumab plus bortezomib and dexamethasone, and selinexor plus bortezomib and dexamethasone (which has received preliminary NICE approval and subject to final NICE guidance) are alternative options in lenalidomide refractory patients (4). However, outcomes for these two triplets in lenalidomide refractory patients are poor, with a median progression-free survival (PFS) of 7.8 months reported for the lenalidomide-refractory subgroup in the CASTOR trial, and 10.2 months reported in the BOSTON trial (5-7). This highlights a significant unmet need for more effective and manageable triplet therapies in the lenalidomide-refractory setting, a need that is expected to grow as more patients become refractory to daratumumab following	Comments noted. NICE has scheduled this topic into its work programme. For further details, see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta11201. No action needed.

Section	Stakeholder	Comments [sic]	Action
		treatment with daratumumab plus lenalidomide and dexamethasone in the frontline setting (TA917, approved Oct 2023) (8). Consequently, there is a pressing need at 2L for new, more efficacious triplet regimens for lenalidomide-refractory patients, especially those targeting B-cell maturation antigen (BCMA), a well-established therapeutic target for MM due to its high expression on malignant plasma cells (9-11). Given these challenges, there is a substantial need in the current NHS practice for alternative BCMA-targeting triplet therapy that can provide durable responses in relapsed or refractory MM patients. This underscores the urgent and significant need for the DREAMM-8 triplet early in the treatment pathway. **References** 1. Rajkumar SV. Treatment of multiple myeloma. Nat Rev Clin Oncol. 2011;8(8):479-91. 2. Moreau P, San Miguel J, Sonneveld P, Mateos MV, Zamagni E, Avet-Loiseau H, et al. Multiple myeloma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2017;28(suppl_4):iv52-iv61. 3. Botta C, Martino EA, Conticello C, Mendicino F, Vigna E, Romano A, et al. Treatment of Lenalidomide Exposed or Refractory Multiple Myeloma: Network Meta-Analysis of Lenalidomide-Sparing Regimens. Front Oncol. 2021;11:643490. 4. National Institute for Health and Care Excellence (NICE). Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma [ID3797] 2024 [updated 02 Feb 2024. Available from:https://www.nice.org.uk/guidance/gid-ta10646/documents/129]. 5. Touzeau C, Quignot N, Meng J, Jiang H, Khachatryan A, Singh M, et al. Survival and treatment patterns of patients with relapsed or refractory multiple myeloma in France - a cohort study using the French National Healthcare database (SNDS). Ann Hematol. 2021;100(7):1825-36.	

Section	Stakeholder	Comments [sic]	Action
		6. Mateos MV, Sonneveld P, Hungria V, Nooka AK, Estell JA, Barreto W, et al. Daratumumab, Bortezomib, and Dexamethasone Versus Bortezomib and Dexamethasone in Patients With Previously Treated Multiple Myeloma: Three-year Follow-up of CASTOR. Clin Lymphoma Myeloma Leuk. 2020;20(8):509-18. 7. Mateos M-V, Engelhardt M, Leleu X, Mesa MG, Auner HW, Cavo M, et al. P886: Efficacy, survival and safety of selinexor, bortezomib and dexamethasone (SYD) in patients with lenalidomide-refractory multiple myeloma: subgroup data from the BOSTON trial. HemaSphere. 2023;7(S3):e1470834. 8. National Institute for Health and Care Excellence (NICE). Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (TA783) 2022 [updated 13 Apr 2022. Available from:https://www.nice.org.uk/guidance/ta783]. 9. Cho SF, Anderson KC, Tai YT. Targeting B Cell Maturation Antigen (BCMA) in Multiple Myeloma: Potential Uses of BCMA-Based Immunotherapy. Front Immunol. 2018;9:1821. 10. Tai YT, Anderson KC. Targeting B-cell maturation antigen in multiple myeloma. Immunotherapy. 2015;7(11):1187-99. 11. Montes de Oca R, Alavi AS, Vitali N, Bhattacharya S, Blackwell C, Patel K, et al. Belantamab mafodotin (GSK2857916) drives immunogenic cell death and immune-mediated antitumor responses in vivo. Molecular Cancer Therapeutics. 2021;20(10):1941-55.	
	Janssen-Cilag	There is a high unmet need and urgency for new treatment options for patients with relapsed or refractory multiple myeloma after 1 or more treatments. Belantamab madodotin is a new class of drug versus existing NHS therapies. New classes of treatment are urgently required in a relapsed and refractory population with multiple drug resistance, as with each, subsequent relapse, there is a greater risk of additional clones arising due to genetic mutations within the myeloma cells.	Comments noted. NICE has scheduled this topic into its work programme. For further details, see the NICE website: https://www.nice.org.uk/guidance/indevelopmen

Section	Stakeholder	Comments [sic]	Action
			t/gid-ta11201. No action needed.
	Myeloma UK	Myeloma is a relapsing and remitting, incurable cancer, and even after successful treatment, almost all patients eventually become resistant to available drugs. New drugs and treatment combinations are urgently needed to overcome treatment resistance.	Comments noted. NICE has scheduled this topic into its work programme. For further details, see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta11201. No action needed.
	Takeda	No comments.	Comment noted. No action needed.
	UK MYELOMA FORUM and on behalf of the Royal College of Physicians	This is a timely appraisal for reasons listed above.	Comment noted. No action needed.
Additional comments on the draft remit	GlaxoSmithKline	None	Comment noted. No action needed.
	Janssen-Cilag	Janssen note that the draft scope currently states that belantamab mafodotin has an existing marketing authorisation as monotherapy for the treatment of multiple myeloma in adults who have received at least 4 prior therapies and whose condition is refractory to at least 1 proteasome inhibitor, 1 immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who	Comments noted. NICE is aware that the conditional marketing authorisation for belantamab mafodotin

Section	Stakeholder	Comments [sic]	Action
		have demonstrated disease progression on the last therapy. As stated on the NICE website for ID2701 (https://www.nice.org.uk/guidance/indevelopment/gid-ta10568), the MHRA is currently assessing the annual renewal of the GB marketing authorisation for belantamab mafodotin, as per the national procedure, and will make the decision on whether the licence is renewed in this country.	is under review. This information has been removed from the background information of the technology in the scope.
	Takeda	None	Comment noted. No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	GlaxoSmithKline	**Current wording:** "Belantamab mafodotin, (BLENREP, GlaxoSmithKline) with pomalidomide and dexamethasone, does not currently have a marketing authorisation in the UK for relapsed or refractory multiple myeloma after 1 or more treatments. Belantamab mafodotin has been studied in combination with pomalidomide and dexamethasone compared to pomalidomide in combination with bortezomib and dexamethasone in adults with relapsed refractory multiple myeloma who have received at least 1 prior line of treatment including a lenalidomide-containing regimen. Belantamab mafodotin currently has a marketing authorisation as monotherapy for the treatment of multiple myeloma in adults who have received at least 4 prior therapies and whose condition is refractory to at least 1 proteasome inhibitor, 1 immunomodulatory agent, and an anti-CD38	Comments noted. Minor differences in wording. The information about the marketing authorisation of belantamab mafodotin monotherapy has been removed from the background information of the technology in the scope.

Section	Consultee/ Commentator	Comments [sic]	Action
		monoclonal antibody, and who have demonstrated disease progression on the last therapy." **Suggested new wording:** "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 pomalidomide 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-8 study evaluated belantamab mafodotin plus pomalidomide and dexamethasone vs pomalidomide, bortezomib and dexamethasone in relapsed/refractory multiple myeloma for patients with ≥1 prior line of therapy including a lenalidomide-containing regimen." **Rationale** To include a complete description of the intervention and regulatory status.	
	Janssen-Cilag	No additional comments	Comment noted. No action needed.
	Myeloma UK	We consider this information to be sufficient and accurate.	Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
	Takeda	No comments.	Comment noted. No action needed.
	UK MYELOMA FORUM and on behalf of the Royal College of Physicians	Yes	Comment noted. No action needed.
Population	GlaxoSmithKline	**Current wording:** Population(s): “People with relapsed or refractory multiple myeloma who have had at least 1 prior line of treatment” **Suggested new wording:** “People with relapsed or refractory multiple myeloma who have had at least 1 prior line of treatment including a lenalidomide-containing regimen”	Comment noted. Population has been amended as suggested.
	Janssen-Cilag	Janssen consider the population to be appraised by NICE should align with the population specified in the final summary of product characteristics. To align with the patient population studied for belantamab mafodotin in combination with pomalidomide and dexamethasone, Janssen suggest that the population is updated to: ‘*relapsed refractory multiple myeloma who have received at least 1 prior line of treatment including a lenalidomide-containing regimen*.’	Comment noted. Population has been amended as suggested.
	Myeloma UK	The description is accurate.	Comment noted. The population has been amended to specify people have had “at

Section	Consultee/ Commentator	Comments [sic]	Action
			least 1 prior line of treatment including a lenalidomide-containing regimen".
	Takeda	Yes	Comment noted. The population has been amended to specify people have had "at least 1 prior line of treatment including a lenalidomide-containing regimen".
	UK MYELOMA FORUM and on behalf of the Royal College of Physicians	Yes	Comment noted. The population has been amended to specify people have had "at least 1 prior line of treatment including a lenalidomide-containing regimen".
Subgroups	GlaxoSmithKline	No change is needed	Comment noted. No action needed.
	Janssen-Cilag	None	Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
	Myeloma UK	We consider the population to be appropriately defined.	Comment noted. No action needed.
	Takeda	No subgroups suggested.	Comment noted. No action needed.
Comparators	GlaxoSmithKline	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 in the context of this appraisal. 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 with dexamethasone • carfilzomib with dexamethasone • carfilzomib with lenalidomide and dexamethasone • daratumumab with bortezomib and dexamethasone • selinexor with bortezomib and low-dose dexamethasone (subject to NICE evaluation)" **Suggested new wording:** "For people who have had 1 prior therapy:	Comments noted. In line with the population that has been amended to specify that people have had "at least 1 prior line of treatment including a lenalidomide-containing regimen", therapies including lenalidomide have been removed from the comparator section. To keep the scope broad to ensure that NICE can appraise the technology within its marketing authorisation, other possible comparators including technologies subject to NICE evaluation have been retained.

Section	Consultee/ Commentator	Comments [sic]	Action
		• carfilzomib with dexamethasone • daratumumab with bortezomib and dexamethasone • selinexor with bortezomib and low-dose dexamethasone (for a subgroup of patients who are refractory to daratumumab and lenalidomide; subject to final NICE guidance)" **Rationale** GSK do not consider bortezomib monotherapy to be a relevant comparator for the treatment of MM in the UK, as it is rarely used in clinical practice, as indicated in ID3797 (4, 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 1 prior line of therapy, as most patients at first relapse will be refractory to lenalidomide. GSK do not consider carfilzomib plus lenalidomide and dexamethasone to be a relevant comparator after 1 prior line of therapy, as most patients at first 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).	The company will have the opportunity during the full appraisal to outline which comparators it considers to be most relevant.

Section	Consultee/ Commentator	Comments [sic]	Action
		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 and is generally not suitable for patients with existing cardiac comorbidities (14). **Current wording:** "For people who have had 2 prior therapies: • lenalidomide with dexamethasone • ixazomib with lenalidomide and dexamethasone • panobinostat with bortezomib and dexamethasone • selinexor with bortezomib and low-dose dexamethasone (subject to NICE final guidance)" **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 second relapse. **Rationale**	

Section	Consultee/ Commentator	Comments [sic]	Action
		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. Because of the common use of lenalidomide in the 1L setting, patients will likely be refractory to lenalidomide when they inevitably relapse (15). GSK do not consider panobinostat plus bortezomib and dexamethasone to be a relevant comparator, as it is rarely used in the UK due to its toxic effects (13). Additionally, this combination is primarily used at 4L+ (8, 16, 17), whereas GSK see belantamab mafodotin plus pomalidomide and dexamethasone positioned earlier in the treatment pathway. 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 subject to final NICE guidance (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. **Current wording:**	

Section	Consultee/ Commentator	Comments [sic]	Action
		"For people who have had 3 prior therapies: • daratumumab monotherapy • lenalidomide with dexamethasone • ixazomib with lenalidomide and dexamethasone • panobinostat with bortezomib and dexamethasone • pomalidomide with low-dose dexamethasone • isatuximab with pomalidomide and dexamethasone (subject to NICE evaluation) • elranatamab (subject to NICE evaluation)" **Suggested new wording:** GSK do not consider that any wording should be written in this section. **Rationale** GSK consider belantamab mafodotin with pomalidomide 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. **Current wording:** "For people who have had 4 prior therapies:	

Section	Consultee/ Commentator	Comments [sic]	Action
		• panobinostat with bortezomib and dexamethasone • pomalidomide with low-dose dexamethasone • selinexor with dexamethasone (18) • elranatamab (subject to NICE evaluation)” **Suggested new wording:** GSK do not consider that any wording should be written in this section. **Rationale** GSK consider belantamab mafodotin with pomalidomide 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 4 or more prior therapies to be relevant comparators for reasons stated above. **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.	

Section	Consultee/ Commentator	Comments [sic]	Action
		Rationale GSK do not consider conventional chemotherapy regimens and best supportive care to be relevant comparators to active treatments like belantamab mafodotin in combination with pomalidomide and dexamethasone. 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. **References** 4. National Institute for Health and Care Excellence (NICE). Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma [ID3797] 2024 [updated 02 Feb 2024. Available from:https://www.nice.org.uk/guidance/gid-ta10646/documents/129]. 8. National Institute for Health and Care Excellence (NICE). Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (TA783) 2022 [updated 13 Apr 2022. Available from:https://www.nice.org.uk/guidance/ta783].	

Section	Consultee/ Commentator	Comments [sic]	Action
		12. National Institute for Health and Care Excellence (NICE). Bortezomib monotherapy for relapsed multiple myeloma [TA129] 2007 [Available from:https://www.nice.org.uk/guidance/ta129]. 13. National Health Service (NHS). National Cancer Drugs Fund List 2024 [updated 19 Jan 2024. Available from:https://www.england.nhs.uk/wp-content/uploads/2017/04/National-Cancer-Drugs-Fund-list--version-1.287.pdf]. 14. Electronic Medicines Compendium. Kyprolis powder for solution for infusion 2022 [updated 28 Apr 2022. Available from:https://www.medicines.org.uk/emc/product/5061/smpc#about-medicine]. 15. Kortum KM, Nagar, S. P., Singh, E., Davis, K. L., & Lin, PL.,. A multinational chart review of real-world treatment patterns and clinical outcomes in patients with relapsed/refractory multiple myeloma. . HemaSphere,. 2021; 52(S2),: 466-7. 16. National institute for Health and Care Excellence (NICE). Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (TA427) 2017 [updated 11 Jan 2017. Available from:https://www.nice.org.uk/guidance/ta427]. 17. National Institute for Health and Care Excellence (NICE). Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (TA870) 2023 [updated 22 Feb 2023. Available from:https://www.nice.org.uk/guidance/ta870]. 18. National institute for Health and Care Excellence (NICE). Selinexor with dexamethasone for treating relapsed or refractory multiple myeloma after 4 or more treatments [ID6193] 2024 [Available from:https://www.nice.org.uk/guidance/gid-ta11223/documents/674-2].	
	Janssen-Cilag	• For people who have had 1 prior therapy and for people who had 2 prior therapies, Janssen understand that there is an ongoing appraisal for belantamab mafodotin with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma after 1 or more	Comments noted. The appraisal on teclistamab (ID6333) has been added to the

Section	Consultee/ Commentator	Comments [sic]	Action
		treatments (ID6212). This should be included as a potential comparator in this appraisal, subject to NICE evaluation. • Given the ongoing NICE evaluation, for people who have had 3 prior therapies, Janssen consider that teclistamab should be included as a potential comparator, subject to NICE evaluation. • For completeness, for patients who have had 4 prior therapies, belantamab mafodotin [ID2701] should be included as a potential comparator, subject to the outcome of the NICE pause in the appraisal.	scope because it is expected to publish in August 2024. The appraisal on belantamab mafodotin with bortezomib and dexamethasone (ID6212) has not been added because of overlapping development timelines with ID6211. The appraisal on belantamab mafodotin monotherapy (ID2701) has not been added because its conditional marketing authorisation has been withdrawn by the EMA and is under review with the MHRA.
	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.	Comments noted. In line with the population that has been amended to specify that people have had “at least 1 prior line of treatment including a lenalidomide-containing

Section	Consultee/ Commentator	Comments [sic]	Action
		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.	regimen", therapies including lenalidomide have been removed from the comparator section. To keep the scope broad to ensure that NICE can appraise the technology within its marketing authorisation, other possible comparators including technologies subject to NICE evaluation have been retained. The company will have the opportunity during the full appraisal to outline which comparators it considers to be most relevant.
	Takeda	Yes and Yes.	Comments noted. In line with the population that has been amended to specify that people have had "at least 1 prior line of treatment including a

Section	Consultee/ Commentator	Comments [sic]	Action
			lenalidomide-containing regimen", therapies including lenalidomide have been removed from the comparator section. To keep the scope broad to ensure that NICE can appraise the technology within its marketing authorisation, other possible comparators including technologies subject to NICE evaluation have been retained. The company will have the opportunity during the full appraisal to outline which comparators it considers to be most relevant.
	UK MYELOMA FORUM and on behalf of the Royal College of Physicians	This scope is very broad and identifies many potential comparators. Belantamab mafadotin with Pomaldiomide Dex would be suitable for those patients with relapsed myeloma that are exposed /refractory to Lenalidomide (a requirement for this trial). The comparator in the DREAMM8 trial	Comments noted. In line with the population that has been amended to specify that people have had "at least 1 prior line of treatment

Section	Consultee/ Commentator	Comments [sic]	Action
		(Pomalidomide Bortezomib and Dexamethasone) is not available in the current pathway. Most patients are likely to be Lenalidomide refractory after 1st line treatment., either receiving Lenalidomide maintenance for transplant eligible patients (TA680), or Daratumumab Lenalidomide Dexamethasone for non-transplant eligible patients (TA917). There will be a group of patients who will receive Lenalidomide at 2nd or 3rd line. Assuming the patient is Lenalidomide refractory at 2nd line, appropriate comparators include Carfilzomib Dex; Daratumumab Bortezomib Dex; Selinexor Bortezomib Dex (when Daratumumab and Lenalidomide refractory). Carfilzomib Lenalidomide Dex or Lenalidomide Dex are not appropriate comparators. Bortezomib Dex is not given due to other treatment options being available. Assuming the patient is Lenalidomide refractory at 3rd line, appropriate comparators include Selinexor Bortezomib Dex; Panobinostat with Bortezomib Dex. Ixazomib Lenalidomide Dex is not an appropriate comparator. At 4th line and beyond, comparators are correctly listed, other than Lenalidomide containing regimens that will have been given by this stage.	including a lenalidomide-containing regimen", therapies including lenalidomide have been removed from the comparator section. To keep the scope broad to ensure that NICE can appraise the technology within its marketing authorisation, other possible comparators including technologies subject to NICE evaluation have been retained. The company will have the opportunity during the full appraisal to outline which comparators it considers to be most relevant. As noted, pomalidomide with bortezomib and dexamethasone (TA602) is not available for use in the NHS

Section	Consultee/ Commentator	Comments [sic]	Action
			because the company did not provide an evidence submission.
Outcomes	GlaxoSmithKline	GSK is aligned with the outcomes listed.	Comment noted. No action needed.
	Janssen-Cilag	No additional comments	Comment noted. No action needed.
	Myeloma UK	Yes	Comment noted. No action needed.
	Takeda	Yes and Yes.	Comment noted. No action needed.
	UK MYELOMA FORUM and on behalf of the Royal College of Physicians	Yes	Comment noted. No action needed.
Equality	GlaxoSmithKline	GSK is not aware of any equality issues relating to the proposed remit and scope.	Comment noted. No action needed.
	Janssen-Cilag	No equality issues identified	Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
	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.	Comments noted. No action needed.
	Takeda	No equality issues identified.	Comment noted. No action needed.
	UK MYELOMA FORUM and on behalf of the Royal College of Physicians	Yes	Comment noted. No action needed.
Other considerations	GlaxoSmithKline	For reasons stated above, GSK believe there is considerable need in current NHS practice for a BCMA triplet-based therapeutic option that can achieve durable responses in lenalidomide-refractory patients with RRMM earlier in the treatment pathway. Please refer to the earlier section on timing issues.	Comments noted. No action needed.
	Janssen-Cilag	Current UK frontline standard of care treatment is a daratumumab containing regimen, in combination with lenalidomide and dexamethasone for patients unsuitable for transplant, or in combination with bortezomib, thalidomide and dexamethasone with lenalidomide maintenance for those eligible for transplant.	Comments noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		As patients are likely to be exposed to both daratumumab and lenalidomide in the frontline setting, more data is required to understand how belantamab mafodotin in combination with pomalidomide and dexamethasone performs specifically in a CD38 and lenalidomide-exposed population. It may be anticipated that outcomes are different in a double refractory versus a single refractory patient population.	
	Myeloma UK	No comments	Comment noted. No action needed.
	Takeda	No comments.	Comment noted. No action needed.
	UK MYELOMA FORUM and on behalf of the Royal College of Physicians	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.	Comments noted. No action needed.
Questions for consultation	GlaxoSmithKline	Please find below GSK's responses to the additional consultation questions. **Where do you consider belantamab mafodotin with pomalidomide and dexamethasone will fit into the existing care pathway for treating relapsed or refractory multiple myeloma after 1 or more treatments?** GSK consider belantamab mafodotin in combination with pomalidomide and dexamethasone to be positioned early in the treatment pathway for RRMM patients.	Comments noted. Innovation will be considered by the appraisal committee when formulating its recommendations. The company will have an opportunity to provide evidence on the innovative nature of its product in its

Section	Consultee/ Commentator	Comments [sic]	Action
		Are there any relevant subgroups that should be considered? There are no relevant subgroups that should be considered. **Would belantamab mafodotin with pomalidomide and dexamethasone be a candidate for managed access?** GSK would consider managed access if this was an appropriate route to ensure patient access. **Do you consider that the use of belantamab mafodotin with pomalidomide and dexamethasone can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Belantamab mafodotin combined with pomalidomide 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 pomalidomide and dexamethasone used earlier in the treatment pathway. Due to limited effective treatment options and the high unmet need in patients who first relapse on a lenalidomide-containing regimen, the availability of a treatment option at first relapse that has demonstrated significantly improved progression-free survival compared to the EHA-ESMO recommended triplet (pomalidomide with bortezomib and dexamethasone) will potentially also help reduce relapse-associated anxiety in both patients and carers (19, 20). 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	submission. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		number of UK patients eligible for recruitment into clinical trials and early access schemes. As future patients will be refractory to lenalidomide and daratumumab at first relapse due to treatment with daratumumab plus lenalidomide and dexamethasone in the frontline setting, belantamab mafodotin will offer additional benefit to these patients. **References** 19. GSK. [Press release] GSK announces positive results from DREAMM-8 phase III trial for Blenrep versus standard of care combination in relapsed/refractory multiple myeloma 2024 [Available from:https://www.gsk.com/en-gb/media/press-releases/gsk-announces-positive-results-from-dreamm-8-phase-iii-trial-for-blenrep-versus-standard-of-care-combination-in-relapsedrefractory-multiple-myeloma/]. 20. Dimopoulos MA, Moreau P, Terpos E, Mateos MV, Zweegman S, Cook G, et al. Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up(†). Ann Oncol. 2021;32(3):309-22.	
	Janssen-Cilag	No comments	Comment noted. No action needed.
	Myeloma UK	***Where do you consider belantamab mafodotin with pomalidomide and dexamethasone will fit into the existing care pathway for treating relapsed or refractory multiple myeloma after 1 or more treatments?*** *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.*	Comments noted. The appraisal committee will discuss the potentially innovative nature of this technology. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		We believe the use of belantamab mafodotin with pomalidomide 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 after 1 or more 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 pomalidomide and dexamethasone be a candidate for managed access?*** *Yes it would, as there are trials for this combination which are still recruiting / ongoing.* ***Do you consider that the use of belantamab mafodotin with pomalidomide 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.*	

Section	Consultee/ Commentator	Comments [sic]	Action
	Takeda	**Where do you consider belantamab mafodotin with pomalidomide and dexamethasone will fit into the existing care pathway for treating relapsed or refractory multiple myeloma after 1 or more treatments?** That will depend on the detailed clinical evidence from the DREAMM-8 trial, which is not yet in the public domain. It seems likely that it will be used in patients at later lines of therapy where there are less treatment options available. **Are there any relevant subgroups that should be considered?** This will depend on the detailed clinical evidence from the DREAMM-8 trial, which is not yet in the public domain. **Would belantamab mafodotin with pomalidomide and dexamethasone be a candidate for managed access?** No comment. **Do you consider that the use of belantamab mafodotin with pomalidomide and dexamethasone can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** No comment. **Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** N/A.	Comments noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Questions re potential equality issues/impacts: We see no equality issues/impacts. **Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.** N/A. **NICE intends to evaluate this technology through its Single Technology Appraisal process.** This seems appropriate to us.	
Additional comments on the draft scope	GlaxoSmithKline	None	Comment noted. No action needed.
	Janssen-Cilag	No comments	Comment noted. No action needed.
	Takeda	None.	Comment noted. No action needed.