National Institute for Health and Care Excellence

Single Technology Appraisal

Belantamab mafodotin for treating relapsed or refractory multiple myeloma after 4 or more therapies [ID2701]
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	GSK UK Ltd	The Company considers the evaluation and route of evaluation appropriate.	Thank you for your comment. No action needed.
	Janssen-Cilag Limited	The topic and evaluation route are appropriate.	Thank you for your comment. No action needed.
	Myeloma UK	This is the first NICE appraisal for a B cell maturation antigen (BCMA) treatment to be introduced into the pathway for myeloma patients and Myeloma UK considers it appropriate to refer this topic to NICE.	Thank you for your comment. No action needed.
	UK MYELOMA FORUM	This is a timely appraisal. This should be a single technology appraisal.	Thank you for your comment.

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		Belantamab is an innovative technology and is a step change in myeloma treatment. Firstly it is the first non-cellular technology appraised by NICE that targets B Cell Maturation Antigen (BCMA). BCMA is a novel treatment target for myeloma due to its highly selective expression in malignant plasma cells. Secondly it involves a novel mechanism of action, namely an antibody-drug conjugate that contains belantamab linked to mcMMAF, a cytotoxic microtubule disrupting agent. Finally this treatment demonstrates meaningful clinical benefit in patients who have exhausted all conventional treatment (proteasome inhibitor, immunomodulatory drug and anti-CD38 directed therapy). As monotherapy 32% patients respond with a median duration of 11 months in responders (Lonial et al Cancer 2021). It is easy to deliver on an outpatient basis and has a manageable toxicity profile. This is the first therapy that does not require ongoing steroid use for clinical benefit, which is often poorly tolerated by patients. There has been considerable use of this technology in the UK across both teaching and district general hospitals through a compassionate use programme supported by GSK.	The appraisal committee will consider the innovative nature of the technology. No action needed.
Wording	GSK UK Ltd	The company suggests the following change to the remit to accurately reflect the technology's licensed population[1]: *To appraise the clinical and cost effectiveness of belantamab mafodotin monotherapy within its marketing authorisation for the treatment of multiple myeloma in adult patients, who have received at least four prior therapies and*	Thank you for your comment. The remit has been left broad. The technology's licensed population is

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		whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. References: 1. EMA. (2020) Belantamab mafodotin summary of product characterstics. Available online: https://www.ema.europa.eu/en/documents/product-information/blenrep-epar-product-information_en.pdf [Accessed 29 June 2022]	stated in the 'The technology' section of the scope.
	Janssen-Cilag Limited	No changes suggested.	Thank you for your comment. No action needed.
	Myeloma UK	Myeloma UK considers the remit to reflect the issues of clinical and cost effectiveness.	Thank you for your comment. No action needed.
	UK MYELOMA FORUM	Belantamab mafodotin is the first licensed technology that targets BCMA using a novel immunotherapy approach using an antibody-drug conjugate. It is therefore a step change in treatment. Myeloma remains incurable. This appraisal addresses an unmet need with important new technology to extend survival.	Thank you for your comment. No action needed.
Timing issues	GSK UK Ltd	Myeloma is an incurable, rare, progressive, malignant plasma cell disorder. Despite improvements attributed to advances in both diagnostics and treatment, only 52% of UK myeloma patients survive for 5 or more years with an estimated 3,100 deaths/year.[1] The majority of patients will require further therapy for relapsed disease or where they have become refractory to existing regimens. Effective therapy in heavily pre-treated disease remains an ongoing challenge. Median overall survival (OS) declines from 11.2 months (non-triple refractory myeloma) to 5.6 months (penta-refractory myeloma).[2]	Thank you for your comment. No action needed.

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		Remission durations also reduce with progression free survival (PFS) decreasing from 10 months with initial treatment to 4.5 months at fourth line therapy.[3] More frequent relapses in later lines cause patients to experience greater symptom and health related quality of life burden.[4] [redacted] . The unmet need and the benefit that belantamab mafodotin offers myeloma patients is supported by the observed increase in the uptake of [redacted]; in May 2022 alone, there were [redacted]. The total number of patients treated through [redacted] (as of May 2022). References: 1. Cancer Research UK. Myeloma statistics. 2022. Available online: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/myeloma/ [Accessed 16 June 2022] 2. Gandhi UH., Cornell R., Lakshman., et al. (2019) Outcomes of patients with multiple myeloma refractory to CD38-targeted monoclonal antibody therapy. Leukemia; 33(9):2266-2275 3. Kumar SK., Therneau TM., Gertz MA., et al (2004) Clinical course of patients with relapsed multiple myeloma. Mayo Clin Proc.; 79(7):867-874 4. Sparano F., Cavo M., Niscola P., et al (2018) Patient-reported outcomes in relapsed/refractory multiple myeloma: a systematic review. Support Care Cancer; 26(7): 2075-2090	
	Janssen-Cilag Limited	The timing of this appraisal is appropriate.	Thank you for your comment. No action needed.

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	Myeloma UK	None	Thank you for your comment. No action needed.
	UK MYELOMA FORUM	This is urgent – there is a need to rapidly introduce effective therapies to help prolong disease control and overall survival. Importantly this for a group of patients that have limited treatment options. This is evidenced by considerable uptake of the Belantamab compassionate use programme	Thank you for your comment. No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	GSK UK Ltd	For completeness, the Company suggests the addition of the following NICE guidance recommendations for people who have had at least 3 prior therapies: • Ixazomib with lenalidomide and dexamethasone (TA505, 2018; CDF) • Panobinostat in combination with bortezomib and dexamethasone (TA380, 2016) • Lenalidomide and dexamethasone (TA171, 2009) For completeness, the company suggests that the corresponding NICE guidance is also provided for the stated treatment options for people who have had at least 4 therapies: • Pomalidomide plus dexamethasone (TA427, 2017)	Thank you for your comment. Recommendations for people who have had at least 2 prior therapies has been added to the scope. The wording in the scope describes the minimum number of prior therapies someone should have had, so repeating these therapies for

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		• Panobinostat in combination with bortezomib and dexamethasone (TA380, 2016) • Lenalidomide and dexamethasone (TA171, 2009) To the statement '*Other drug combinations that people who have had at least 4 therapies can have include a combination of chemotherapy and a steroid with or without thalidomide'*, for completeness the Company suggests the addition of "as well as being enrolled into clinical trials and compassionate use schemes".	subsequent lines of treatments is not necessary.
	Janssen-Cilag Limited	No changes suggested.	Thank you for your comment. No action needed.
	Myeloma UK	We consider this information to be complete and accurate.	Thank you for your comment. No action needed.
	UK MYELOMA FORUM	The description of therapies available is correct.	Thank you for your comment. No action needed.
Population	GSK UK Ltd	The Company suggests the exact regulatory licence wording is replicated to describe the population more accurately, and to avoid any confusion[1]: Adult patients with multiple myeloma, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal	Thank you for your comment. The population has been updated to be consistent with the

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		antibody, and who have demonstrated disease progression on the last therapy. References: 1. EMA. (2020) Belantamab mafodotin summary of product characteristics. Available online: https://www.ema.europa.eu/en/documents/product-information/blenrep-epar-product-information_en.pdf [Accessed 29 June 2022]	summary of product characteristics.
	Janssen-Cilag Limited	As per the marketing authorisation, belantamab mafodotin is indicated 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 anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. In line with the SmPC, confirmed relapse on the last therapy should be considered when defining the population in the final scope.	Thank you for your comment. The population has been updated to be consistent with the summary of product characteristics.
	Myeloma UK	Yes	Thank you for your comment. No action needed.
	UK MYELOMA FORUM	Population is correctly defined as adults with relapsed/refractory myeloma, based upon the DREAMM2 trial.	Thank you for your comment. No action needed.
Subgroups	GSK UK Ltd	Given the high unmet need and poor outcomes observed in later lines of multiple myeloma treatment, the Company believes belantamab mafodotin should be made available to all eligible patients such that there are no subgroups which should be considered separately	Thank you for your comment. No action needed.

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	Janssen-Cilag Limited	No subgroups suggested.	Thank you for your comment. No action needed.
	Myeloma UK	No comment	Thank you for your comment. No action needed.
	UK MYELOMA FORUM	There are no subgroups that should be considered separately. Importantly this technology can be used in a widest range of patients, namely younger and frailer/elderly patients to provide disease control.	Thank you for your comment. No action needed.
Comparators	GSK UK Ltd	For the population under assessment, the Company considers pomalidomide plus dexamethasone to be the most relevant comparator, representing well established practice in the NHS. The Company acknowledges that there is some use of panobinostat with bortezomib and dexamethasone however, it is very limited such that it cannot be considered established practice. The Company does not consider chemotherapy and a steroid (with or without thalidomide) as an appropriate comparator for the appraisal of belantamab mafodotin in a fifth line and onwards triple class refractory myeloma population. The evidence and rationale to support the Company's view is provided in the responses to 'Questions for consultation' section below.	Thank you for your comment. The comparators have been updated to clarify chemotherapy can be had with or without a steroid and with or without thalidomide. The scope aims to be inclusive, so comparators are included even if only applicable to a small number of people. A rationale should be provided for adding or removing any

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			comparators in the evidence submission, which can be considered by the appraisal committee.
	Janssen-Cilag Limited	There are currently no NICE guidelines for relapse or refractory multiple myeloma specifically for the 5th line setting. Established clinical management within UK clinical practice can and may include a mix of treatment options dependent on what the patient had received prior. Given that these patients are refractory to proteasome inhibitor, immunomodulatory agent, and an anti-CD38 monoclonal, it is unclear whether re-treatment with any of these agents is allowed in the absence of alternative treatment options.	Thank you for your comment. Established clinical management has been added to the list of comparators in the scope.
	Myeloma UK	In current clinical practice it is our understanding that patients, after at least 4 prior therapies, will receive: • Pomalidomide and dexamethasone • Chemotherapy and a corticosteroid • Access to a clinical trial The combination of panobinostat with bortezomib and dexamethasone is not widely used in clinical practice and should not be used as a comparator in this NICE appraisal.	Thank you for your comment. The scope aims to be inclusive, so comparators are included even if only applicable to a small number of people. The committee can discuss the most appropriate comparators during the appraisal.

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		Myeloma UK believes that pomalidomide and dexamethasone should be the current standard comparator. In the current treatment pathway, some patients will receive the CDF approved combination of isatuximab, pomalidomide and dexamethasone (TA658) at 4th line of treatment. Therefore, they may be refractory to pomalidomide and dexamethasone at 5th line of treatment. These patients go onto receive standard chemotherapy or enter a clinical trial.	
	UK MYELOMA FORUM	There are limited treatment options for patients who have received 4 or more therapies (5th line and beyond). Patients will have been exposed to and be refractory to a proteosome inhibitor (Bortezomib or Carfilzomib), immunomodulatory drug (Lenalidomide) and an anti-CD38 monoclonal antibody (Daratumumab at 1st, 2nd or 4th line or Isatuximab at 4th line). There will be variation in clinical practice based upon response to prior therapies, performance status, ongoing toxicity from prior therapies (based on bone marrow reserve and non-haematological such as neuropathy) and of course disease related factors such as bone and renal disease. Some patients may prefer hospital delivered vs treatment given at home. There will be a group of patients that will receive palliative care alone. Comparators are correctly listed: 1. Pomalidomide Dexamethasone. This assumes patients did not receive this as 4th line treatment. 2. Panobinostat Bortezomib Dexamethasone. This assumes patients are not refractory to a proteasome inhibitor and do not have pre-existing neuropathy that would preclude its use.	Thank you for your comment. No action needed.

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		3. Combination chemotherapy and steroid. This is likely to be Cyclophosphamide, rather than Melphalan with a palliative intent. This will depend upon bone marrow reserve. Thalidomide is often not used in this setting Patient may access clinical trials or receive novel drugs as part of a compassionate use programme.	
Outcomes	GSK UK Ltd	The outcomes listed are appropriate apart from time to next treatment, which is not collected in the DREAMM-2 clinical trial.	Thank you for your comment. A rationale should be provided for excluding any outcomes from the evidence submission, which can be considered by the appraisal committee.
	Janssen-Cilag Limited	The outcomes in the final scope should also include median duration of response, time to progression, and duration of treatment.	The list of outcomes in the scope is not intended to be exhaustive, and the appraisal committee can consider other outcomes if appropriate. Median duration of response should be included as part of response rates. Time to progression should be included as part of

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			progression-free survival. Duration of treatment should be included in time to next treatment.
	Myeloma UK	Yes	Thank you for your comment. No action needed.
	UK MYELOMA FORUM	Yes	Thank you for your comment. No action needed.
Equality	GSK UK Ltd	No further considerations have been identified by the Company.	Thank you for your comment. No action needed.
	Janssen-Cilag Limited	No equality issues identified.	Thank you for your comment. No action needed.
	Myeloma UK	No comments	Thank you for your comment. No action needed.
	UK MYELOMA FORUM	No equality issues	Thank you for your comment. No action needed.

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Other considerations	GSK UK Ltd	No additional comments.	Thank you for your comment. No action needed.
	Janssen-Cilag Limited	The service impact arising from the time to oversee ocular toxicity by an ophthalmologist should be considered.	Thank you for your comment. The appraisal committee will consider the impact of any resource use. No action needed.
	Myeloma UK	No other considerations	Thank you for your comment. No action needed.
	UK MYELOMA FORUM	Belantamab is an innovative technology and is a step change in myeloma treatment involving a novel immunotherapy approach. It is easy to deliver, has a manageable technology profile and demonstrates impressive response rates in patients who have exhausted all other options. There has been widespread use of this technology through a compassionate use programme. This demonstrates both patients and clinicians are keen to utilise this novel therapy.	Thank you for your comment. The appraisal committee will consider the innovative nature of the technology. No action required.

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Questions for consultation	GSK UK Ltd	**Where do you consider belantamab mafodotin will fit into the existing care pathway for multiple myeloma?** Belantamab mafodotin offers an alternative treatment option for adult patients with multiple myeloma, who have already received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.	Thank you for your response. No action needed.
		Which treatments are considered to be established clinical practice in the NHS for relapsed or refractory multiple myeloma after at least 4 prior therapies? In accordance with NICE guidance and specifically those technologies available to the NHS through routine commissioning, pomalidomide plus dexamethasone (TA427)[1] and panobinostat in combination with bortezomib and dexamethasone (TA380)[2] offer possible treatment options for relapsed or refractory myeloma adult patients who have had four previous lines of therapy. For the population under consideration, adult patients with multiple myeloma, who have received at least four prior therapies **and** whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy, there is an exquisitely high unmet medical need, no established standard of care and limited clinical effectiveness evidence. As with treatment for other types of relapsed or refractory disease, a combination of treatments is commonly employed, as detailed in the following sections.	Thank you for your comment. No action needed.

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		References 1. NICE (2017) Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib; Technology appraisal guidance [TA427] Available online: Overview | Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib | Guidance | NICE [Accessed: 6 June 2022] 2. NICE (2016) Panobinostat for treating multiple myeloma after at least 2 previous treatments; Technology appraisal guidance [TA380] Available online: Overview | Panobinostat for treating multiple myeloma after at least 2 previous treatments | Guidance | NICE [Accessed: 6 June 2022] 3. NICE (2009) Lenalidomide for the treatment of multiple myeloma in people who have received at least 2 prior therapies; Technology appraisal guidance [TA171] Available online: Overview | Lenalidomide for the treatment of multiple myeloma in people who have received at least 2 prior therapies | Guidance | NICE [Accessed: 6 June 2022]	
		Are pomalidomide plus dexamethasone, or panobinostat with bortezomib and dexamethasone, considered established clinical practice in the NHS for relapsed or refractory multiple myeloma after at least 4 prior therapies? In line with the feedback from UK haematologists, the Company considers pomalidomide plus dexamethasone to be the primary clinically relevant comparator and established clinical practice for this heavily pre-treated triple class refractory population of interest. The Company's analysis of [redacted] shows that at fifth line [redacted]) most patients receive pomalidomide plus dexamethasone (approximately [redacted]%). The Company acknowledges some use of panobinostat with bortezomib and dexamethasone in the management of these patients across NHS England and Wales however, it is very limited and as such cannot be considered established practice. As stated in the recent NICE TA 783 (April 2022), 'the Cancer Drugs Fund clinical lead explained that […] few clinicians offer panobinostat plus bortezomib and dexamethasone after 3 previous lines of treatment'. The Company's analysis of [redacted] suggest that less than [redacted] of	Thank you for your comment. The scope aims to be inclusive, so comparators are included even if only applicable to a small number of people. A rationale should be provided for adding or removing any comparators in the evidence submission, which can be considered by the appraisal committee.

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		patients receive this combination at fifth line. To the best Company's knowledge there is no published evidence of panobinostat with bortezomib and dexamethasone in a fifth line plus triple class refractory population. While there is limited evidence in the fifth line plus setting, reported outcomes for patients who are proteasome inhibitor refractory are poor (e.g., median PFS: 1.5 months; OS: 7.6 months)[1]. References 1. Bird S., Pawlyn C., Nallamilli S., et al. (2020) A real-world study of panobinostat, weekly bortezomib and dexamethasone in a very heavily pre-treated population of multiple-myeloma patients. British Journal of Haematology; 191: 927–944	
		Are other combinations of chemotherapy and a steroid (with or without thalidomide) used to treat relapsed or refractory multiple myeloma after at least 4 prior therapies? If so, which combinations are used? It is unclear specifically which chemotherapies are considered within the comparator category listed as "*combinations of chemotherapy and a steroid (with or without thalidomide*)". Real-world evidence from [redacted] captures some use of chemotherapies such as cyclophosphamide and melphalan in this fifth line onwards triple class refractory setting however, usage is minimal ([redacted]) compared to pomalidomide in combination with dexamethasone. This suggests a palliative usage of chemotherapy combinations rather than an active treatment approach and this is consistent with UK clinical experts' opinion. Chemotherapies such as cyclophosphamide and melphalan have not robustly demonstrated efficacy in late lines of triple class refractory treatment (the Phase 3 open label study, FOCUS did not report outcomes for patients with triple class refractory disease;[1] the MUK8 trial included only 9 pts on	Thank you for your comment. The scope aims to be inclusive, so comparators are included even if only applicable to a small number of people. A rationale should be provided for adding or removing any comparators in the evidence submission, which can be considered by the appraisal committee.

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		cyclophosphamide with previous anti-CD38 exposure which is a very limited sample size to demonstrate efficacy and safety[2]). In addition, melphalan is generally considered to have an unacceptable safety profile in a fifth line plus population. Further, paucity of evidence for chemotherapies in triple class refractory disease at fifth line plus means that any attempt to compare belantamab mafodotin with chemotherapies will be challenging and will unlikely generate significant and interpretable results suitable for decision making. A very small use of bendamustine has also been observed within [redacted]. However, bendamustine is not commissioned by NHS England for the treatment of relapsed or refractory myeloma; therefore, it is not an appropriate comparator.[3] Finally, in a triple class refractory population, patients have already received and relapsed on an immunomodulatory agent. Feedback from UK clinical experts has indicated that treatment with the least efficacious IMiD (thalidomide) should be discouraged for these patients as corresponding outcomes are likely to be poor. Given the considerations listed above, the Company believes that the combination of chemotherapy and a steroid (with or without thalidomide) is not an appropriate comparator for the appraisal of belantamab mafodotin. References 1. Hájek R., Masszi T., Petrucci MT., et al. (2017) A randomized phase III study of carfilzomib vs low-dose corticosteroids with optional cyclophosphamide in relapsed and refractory multiple myeloma (FOCUS) Leukemia; 31: 107–114	

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		2. Auner HW., Brown SR., Walker K., et al. (2022) Ixazomib with cyclophosphamide and dexamethasone in relapsed or refractory myeloma: MUKeight phase II randomised controlled trial results. Blood Cancer J.; 12(4):52 3. NHS England (2020) Clinical Commissioning Policy: Bendamustine for relapsed multiple myeloma (all ages). Available online: 1608-Policy-bendamustine-relapsed-multiple-myeloma.pdf (england.nhs.uk) [Accessed: 6 June 2022]	
		Would belantamab mafodotin be a candidate for managed access? The Company is [redacted]	Thank you for your response. No action needed.
		Do you consider belantamab mafodotin to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? Yes, the Company considers belantamab mafodotin to be innovative in its potential to make a significant and substantial impact on health-related benefits. Belantamab mafodotin is an innovative medicine with a new mechanism of action that has demonstrated high efficacy in relapsed and refractory multiple myeloma. Belantamab mafodotin is a first-in-class innovative therapy that targets B-cell maturation antigen (BCMA), which is highly expressed on plasma and multiple myeloma cells and associated with progression of multiple myeloma.[1,2,3] BCMA-targeted therapies interfere with the ability of multiple myeloma cells to divide and grow, as well as stimulate the immune system to attack multiple myeloma cells.[4] Thus, antibody-drug conjugates targeting BCMA provide a much-needed novel mechanism of action to address the unmet need arising from multidrug-refractory multiple myeloma.	Thank you for your comment. The appraisal committee will consider the innovative nature of the technology. No action needed.

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		The role of belantamab mafodotin as a treatment option for relapsed and refractory multiple myeloma has been recognised both by key regulatory agencies and in international treatment guidelines. Belantamab mafodotin is currently approved by the FDA[5], EMA and MHRA[6] in the fifth line plus triple class refractory multiple myeloma population in which the improvement of survival outcomes and the durability of response have been demonstrated in the phase 2 evidence from the DREAMM-2 study.[7] Furthermore, international guidelines such as the EHA-ESMO Joint Guidelines for Multiple Myeloma and the NCCN Clinical Practice Guidelines in Oncology for Multiple Myeloma, recommend belantamab mafodotin as a treatment option for triple-class refractory patients.[8] In this context, belantamab mafodotin was recognised as a major therapeutic advantage.[9] On 31st May 2022, the MHRA awarded an Innovation Passport for belantamab mafodotin and its innovative offerings to the treatment of myeloma. The Company will now be pursuing the Innovative Licensing and Access Pathway[10]. References 1. Cho SF., Anderson KC., Tai YT. (2018) Targeting B Cell Maturation Antigen (BCMA) in Multiple Myeloma: Potential Uses of BCMA-Based Immunotherapy. Front Immunol.;9:1821. 2. Shaffer A. (2020) BCMA-Targeting Drugs Take Center Stage in Myeloma. Available from: https://www.onclive.com/view/bcma-targeting-drugs-take-center-stage-in-myeloma [Accessed: 6 June 2022] 3. Shah N., Chari A., Scott E., et al., (2020) B-cell maturation antigen (BCMA) in multiple myeloma: rationale for targeting and current therapeutic approaches. Leukemia;34(4):985-1005. 4. European Medicines Agency (2020) European Public Assessment Report: Blenrep (belantamab mafodotin).	

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		5. EMA. (2020) Belantamab mafodotin summary of product characteristics.Available online: https://www.ema.europa.eu/en/documents/product-information/blenrep-epar-product-information_en.pdf [Accessed: 29 June 2022] 6. FDA. (2020) Prescribing information: belantamab mafodotin. Available online: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761158s000lbl.pdf [Accessed: 29 June 2022] 7. Kumar SK., Callander NS., Adekola K., et al (2021) Multiple Myeloma, Version 3.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw.;18(12):1685-717. 8. Dimopoulos MA., Moreau P., Terpos E., et al (2021) Multiple Myeloma: EHA-ESMO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-up. Hemasphere.;5(2):e528 9. Tzogani K., Penttila K., Lahteenvuo J., et al. (2021) EMA Review of Belantamab Mafodotin (Blenrep) for the Treatment of Adult Patients with Relapsed/Refractory Multiple Myeloma. Oncologist; 26(1):70-6. 10. GSK press release, for media and investors only, 15 June 2022, London UK	
		Do you consider that the use of belantamab mafodotin can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? The Company believes it is difficult to quantify the value of having belantamab mafodotin as a new treatment option for a population with limited effective treatment options and limited life expectancy. It is also difficult to quantify this value for carers of patients with multiple myeloma whom themselves have been on an emotional journey.	Thank you for your comment. No action needed.
		Would it be appropriate to use the cost-comparison methodology for this topic? The Company does not consider a cost-comparison methodology appropriate for the appraisal of belantamab mafodotin in a heavily pre-treated triple-class refractory multiple myeloma population.	Thank you for your comment. No action needed.

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		Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators? There are additional resource requirements associated with the use of belantamab mafodotin, to support the ophthalmic examinations as stated in the Summary of Product Characteristics. The treating physician should review the patient's ophthalmic examination report before dosing with belantamab mafodotin (at baseline, before the subsequent 3 treatment cycles, and as clinically indicated whilst on treatment). The Company is taking steps to understand how this has been effectively undertaken for those accessing belantamab mafodotin through the [redacted] and will then seek to support NHS Service Pathway needs.	Thank you for your comment. No action needed.
		Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant? The Company considers the captured primary and secondary outcomes to be clinically relevant.	Thank you for your comment. No action needed.
		Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year? DREAMM-3 [NCT04162210],	Thank you for your comment. No action needed.

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		DREAMM-3 is a Phase 3, open-label, randomized study evaluating the efficacy and safety of single agent belantamab mafodotin when compared to pomalidomide and dexamethasone in participants with relapsed and refractory multiple myeloma. DREAMM-3 forms part of the specific EMA regulatory obligation for DREAMM-2 (see below for expected regulatory timelines). In DREAMM-3, patients were eligible for inclusion following ≥2 prior lines of therapy, including ≥2 consecutive cycles of both lenalidomide and a proteasome inhibitor, and refractory to the last line of treatment. There is likely a small DREAMM-2-like population (triple refractory and heavily pre-treated) included within the DREAMM-3 population which may help to validate the estimates of comparative effectiveness of belantamab mafodotin monotherapy versus pomalidomide and dexamethasone. The Company will seek to share this analysis with NICE once available ([redacted]).	
	Janssen-Cilag Limited	Chemotherapy with dexamethasone (Cd), chemotherapy with bortezomib and dexamethasone (VCd), and bortezomib with thalidomide and dexamethasone (VTd) should be explored as potentially relevant options in this setting.	Thank you for your comment. The comparators have been updated to clarify chemotherapy can be had with or without a steroid and with or without thalidomide.
	Myeloma UK	**Where do you consider belantamab mafodotin will fit into the existing care pathway for multiple myeloma?** Within its marketing authorisation for patients who have received 4 prior lines of therapy. (5th Line).	Thank you for your comment. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Are pomalidomide plus dexamethasone, or panobinostat with bortezomib and dexamethasone, considered established clinical practice in the NHS for relapsed or refractory multiple myeloma after at least 4 prior therapies? Pomalidomide and dexamethasone would be the current standard comparator. The combination of panobinostat with bortezomib and dexamethasone is not widely used in clinical practice.	Thank you for your comment. The scope aims to be inclusive, so comparators are included even if only applicable to a small number of people. A rationale should be provided for adding or removing any comparators in the evidence submission, which can be considered by the appraisal committee.
		Are other combinations of chemotherapy and a steroid (with or without thalidomide) used to treat relapsed or refractory multiple myeloma after at least 4 prior therapies? If so, which combinations are used? Melphalan and a corticosteroid.	Thank you for your comment. No action needed.
		Would belantamab mafodotin be a candidate for managed access? Yes, we believe that belantamab mafodotin would be a candidate for managed access.	Thank you for your comment. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Do you consider belantamab mafodotin to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? Yes, due to the heterogenous nature of myeloma it requires treatments with as many different mechanisms of action as possible. Belantamab mafodotin would introduce a treatment with a new mechanism of action into the pathway as it is a B cell maturation antigen (BCMA) treatment. We would therefore consider this to be innovative.	Thank you for your comment. The appraisal committee will consider the innovative nature of the technology. No action needed.

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

Anthony Nolan