National Institute for Health and Care Excellence

Health Technology Evaluation

Elranatamab for treating relapsed and refractory multiple myeloma after 3 or more treatments (managed access review of TA1023) [ID6653]

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	The topic and proposed evaluation route are appropriate.	Thank you for your comment. No action required.
	Myeloma UK	No comments	Thank you. No action required.
	The UK Myeloma Society	It is appropriate to evaluate this topic, many patients in the UK have derived benefit from access to Elranatamab via the Cancer Drugs Fund and it is reasonable for NICE to now consider whether this should be continued via baseline commissioning.	Thank you for your comment. No action required.
Wording	GlaxoSmithKline	The wording of the remit reflects the issue(s) of clinical and cost effectiveness about this technology that NICE should consider.	Thank you for your comment. No action required.

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	Myeloma UK	Myeloma UK considers the remit to reflect the issues of clinical and cost effectiveness	Thank you for your comment. No action required.
	The UK Myeloma Society	Yes, the comparators listed are an accurate reflection of the current NICE pathway. One of the main questions will be whether patients require access to two different bi-specific antibodies targeting BCMA since Teclistamab was approved after Elrantamab. There are some differences between the two drugs in terms of dosing and efficacy from the early phase trials which will need to be considered carefully in the appraisal.	Thank you for your comment. The committee will discuss relevant comparators as part of its deliberations. No action required.
Timing Issues	GlaxoSmithKline	Teclistamab is available through routine commissioning and is broadly comparable in mechanism of action (BCMAxCD3 bispecific antibody), efficacy (ORR 63% bs 61% in trials for this population), safety profile (CRS,ICANs and infections) and administration schedule (both sub-cutaneous with step up dosing requirements). Acknowledging there are nuances to the safety profile that may provide clinicians and patients with more options. Talquetamab is also available in this cohort through routine commissioning providing another bispecific antobody treatment option with a different therapeutic target and safety profile but similar high rates of efficacy in a refractory population. Given the above we consider the relative urgency low. <u>References</u> MajesTEC-1 (teclistamab)	Thank you for your comment. The appraisal has been scheduled into the NICE work programme.

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		Moreau et al., NEJM 2022, Moreau et al., J Clin Oncol 2023 (ASCO abstract 8011) Garfall et al., IMS 2024 MagnetisMM-3 (elranatamab) Lesokhin et al., Nat Med 2023 Tomasson et al., HemaSphere 2024 Prince et al., Blood 2024 (ASH abstract 4738) MonumenTAL-1 (talquetamab) Chari et al., NEJM 2022 Schinke et al., J Clin Oncol 2023 (ASCO abstract 8036) Rasche et al., Blood 2024 (ASH abstract)	
	Myeloma UK	No comments	Thank you. No action required.
	The UK Myeloma Society	It is important that it is considered prior to the expiry of CDF funding.	Thank you for your comment. The appraisal has been scheduled into the NICE work programme.
Additional comments on the draft remit	GlaxoSmithKline	N/A	Thank you. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	GlaxoSmithKline	The background information is considered to be accurate and complete.	Thank you for your comment. No action required.
	Myeloma UK	We consider this information to be sufficient and accurate	Thank you for your comment. No action required.
	The UK Myeloma Society	This is an accurate description of the condition.	Thank you for your comment. No action required.
Population	GlaxoSmithKline	The population is appropriately defined.	Thank you for your comment. No action required.
	Myeloma UK	We consider the population to be appropriately defined. We welcome that it has not been restricted and is in line with the approved marketing authorisation. Despite approvals for treating myeloma in recent years given the heterogeneity of the disease, an unmet need remains and there is a need for flexibility at each stage of the pathway. If the company seeks to pursue NICE approval for a narrower patient population than the final marketing authorisation, it is vital that this reflects unmet need, current and likely future gaps in the pathway, and is not just driven by commercial considerations.	Thank you for your comment. No action required.

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	The UK Myeloma Society	The indication is in line with the licence for Elrantamab (3 or more lines of treatment, triple class exposed.)	Thank you for your comment. No action required.
Subgroups	GlaxoSmithKline	No subgroups suggested.	Thank you for your comment. No action required.
	Myeloma UK	No comments	Thank you. No action required.
	The UK Myeloma Society	No	Thank you for your comment. No action required.
Comparators	GlaxoSmithKline	'Belantamab mafodotin plus bortezomib and dexamethasone (subject to NICE evaluation)' has received technology appraisal guidance • This treatment should not be considered a comparator 'for people who have had 3 prior therapies' or 'for people who have had 4 prior therapies' given it has received recommendations within the 2L RRMM setting. • This treatment should also be removed from 'related NICE recommendations' section	Thank you for your comment. Belantamab mafodotin plus bortezomib and dexamethasone has been removed from the list of comparators and list of related technology appraisals in development.
	Myeloma UK	We agree that most of the comparators listed are treatments available to this patient population.	Thank you for your comment. The comparators have been kept broad to include all

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		However, Myeloma UK believes that bispecifics teclistamab and talquetamab are the main comparators at fourth and fifth line, for patients who have received at least three prior treatments including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. In current clinical practice, it is our understanding that patients in this group fit enough to receive bispecifics would receive: - Teclistamab - Talquetamab - Clinical Trial - Compassionate use/Early access scheme We believe that the following treatments are unlikely to be comparators in practice: - The combination of panobinostat plus bortezomib and dexamethasone is not widely used in clinical practice and should not be used as a comparator in this NICE appraisal. - Daratumumab, lenalidomide and isatuximab containing combinations would not typically be used in this patient population, due to drug resistance from previous exposure - Belantamab mafodotin with bortezomib and dexamethasone is approved for patients who have had one prior treatment only, therefore it is not a comparator for this appraisal - NICE appraisal for linvoseltamab have only recently closed scoping consultation, and therefore should not be considered comparator as it is not available, or approved for, routine clinical use. - NICE appraisals for Ciltacabtagene autoleucel has not started scoping and therefore should not be included as comparators in this appraisal. There are also several appraisals in development that may start within the next year, which are not listed (e.g, ID6549, ID12333, ID6625, ID6629)	potentially relevant comparators. A potential comparator is one which has final guidance before the first committee meeting for the appraisal of the intervention in question. Comparators are included in the scope subject to NICE evaluation to account for any changes in appraisal timelines. The committee will discuss relevant comparators as part of its deliberations. Belantamab mafodotin plus bortezomib and dexamethasone has been removed from the list of comparators and list of related technology appraisals in development.

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		- While selinexor plus dexamethasone (Sd) or pomalidomide plus dexamethasone (Pom-Dex) could be considered comparators at fifth line or beyond, our understanding is that both Sd and Pom-Dex are considered salvage/end of life treatments if a bispecific or clinical trial is suitable, it would be considered unethical to give Sd or Pom-Dex, considering their far shorter PFS and ORR. We therefore would not consider Pom-Dex a comparator at fourth line, or Sd/Pom-Dex at fifth line if bispecifics (teclistamab/talquetamab) are suitable	
	Pfizer Ltd	**Comment 1** Please review recommendation wording for all treatments to align with NICE website recommendations. For example, • NICE technology appraisal guidance 1015 recommends teclistamab as a treatment option for adults who have had at least 3 previous treatments. Should read, • Recommends teclistimab as an option for treating relapsed and refractory multiple myeloma in adults, only after 3 or more lines of treatment (including an immunomodulatory drug, a proteasome inhibitor and an anti-CD38 antibody) when the myeloma has progressed on the last treatment. **Comment 2**	Thankyou for your comment. The wording has been amended for some of the recommendations. Thank you for your comment. Belantamab mafodotin plus bortezomib and

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		Please remove the following from the comparator scope. This evaluation has concluded and has been approved in a different indication to the one under consideration. • Belantamab mafodotin with bortezomib and dexamethasone (subject to NICE evaluation) **Comment 3** Please would it be possible to include a new section to align with the stated recommendation(s) and update PICOS table accordingly. For people who have had at least **2 prior therapies**: • NICE technology appraisal guidance 171 recommends lenalidomide plus dexamethasone as a treatment option for people who have had at least 2 prior treatments. • NICE technology appraisal guidance 380 recommends panobinostat plus bortezomib and dexamethasone as a treatment option for adults who have had at least 2 prior treatments including bortezomib and an immunomodulatory agent. **Comment 4** As section 6.2.3 in the manual states "The committee will normally be guided by established practice in the NHS when identifying the appropriate comparators." Many of those comparators identified in the	dexamethasone has been removed from the list of comparators and list of related technology appraisals in development. Thank you for your comment. The population described in the scope is adults who have received at least three prior therapies. So, no new section has been added. No action required.

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		current draft scope do not represent current standard of care, some do not fit the current treatment pathway for varying reasons. The company argues there is a need for pragmatism and welcome the precedent set at the recent talquetamab appraisal where the technology was positioned in a comparable 4L+ triple class exposed population, teclistamab was the only active comparator considered relevant as this represented the current standard of care in this setting. We understand the rationale for including additional comparators that are subject to ongoing NICE evaluation; however, we would note that, based on current estimated timelines, such technologies are unlikely to represent standard of care prior to committee evaluation of elranatamab.	Thank you for your comment. The comparators have been kept broad to include all potentially relevant comparators. A potential comparator is one which has final guidance before the first committee meeting for the appraisal of the intervention in question. Comparators are included in the scope subject to NICE evaluation to account for any changes in appraisal timelines. The committee will discuss relevant comparators as part of its deliberations. No action required.
	The UK Myeloma Society	All possible comparators are listed accurately. Some are less relevant than others for example by the point of 4th line therapy almost all patients will be exposed and refractory to daratumumab monotherapy, lenalidomide and bortezomib so these are not as appropriate. In addition Selinexor and	Thank you for your comment. The comparators have been kept broad to include all

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		dexamethasone at 5th line is not an option we would often choose instead of a bi-specific antibody in patients who are otherwise fit due to lower efficacy.	potentially relevant comparators. The committee will discuss relevant comparators as part of its deliberations. No action required.
Outcomes	GlaxoSmithKline	The outcomes listed are appropriate.	Thank you for your comment. No action required.
	Myeloma UK	Yes	Thank you for your comment. No action required.
	The UK Myeloma Society	Yes	Thank you for your comment. No action required.
Equality	GlaxoSmithKline	No equality issues identified.	Thank you for your comment. No action required.
	Myeloma UK	We don't anticipate that a positive recommendation would impact people within the patient population for which the treatment is be licensed, who are 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. For bi-	Thank you for your comment. The committee will consider equalities issues during the appraisal.

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		specific treatments, like elranatamab, this includes the requirement to stay in or near the hospital after each step-up dose (until first full dose, usually on day 8 for elranatamab). Implementation plans must ensure all patients have the opportunity to access this treatment.	
	The UK Myeloma Society	No comment	Thank you. No action required.
Other considerations	GlaxoSmithKline	The high rates of hypogammaglobulinemia with BCMA-directed BsAb and consequent infections, support universal use of immunoglobulin (IG) replacement therapy.[1] The service impact arising from this should be considered, in particular the cost and administration burden. In the UK, the national shortage of intravenous IG should also be considered as an access barrier in this context.[2] References: 1 Garfall, A. L., E. A. Stadtmauer. Understanding Infection Risk with Anti-BCMA Bispecific Antibodies. Blood Cancer Discovery: OF1-OF3. In 2023. 2 Immunodeficiency [Internet]. 2020 [cited 2023 Oct 23]. Available from: http://www.immunodeficiencyuk.org/	Thank you for your comment. The committee will consider the effect of the technology on resource use. No action required.
	Myeloma UK	No additional suggestions	Thank you for your comment. No action required.

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	The UK Myeloma Society	Elranatamab may have advantaged in terms of dosing and manufacture given that the doses are fixed which makes the drug easier for pharmacy units to manufacture and prepare than teclistamab which is weight based. This should be considered as many pharmacy units are now working above capacity and may prefer a more straight forward drug.	Thank you for your comment. The committee will consider the effect of the technology on resource use. No action required.
Questions for consultation	GlaxoSmithKline	N/A	Thank you. No action required.
	Myeloma UK	**Where do you consider elranatamab will fit into the existing care pathway for multiple myeloma?** We consider that elranatamab would be given at fourth line and beyond. This is where it has been used in clinical practice whilst approved via the CDF. The PFS and ORR data for elranatamab suggests positive response, which is important for patients who are aware that as they move further and further through the pathway, achieving long periods of deep remission becomes increasingly difficult. Bispecifics like elranatamab have a vital role to play in providing patients with treatment options which have long, durable periods of remission. **Do you consider that the use of elranatamab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Myeloma remains incurable and even after successful treatment, almost all patients eventually become resistant to existing treatments. New drugs and treatment approaches are urgently needed to overcome treatment resistance.	Thank you for your comment. No action required.

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		While there is a bispecific antibody with the same mechanism of action approved, elranatamab may be given less frequently (every 4 weeks) after a period of initial treatment (48 weeks), compared with teclistamab which is given fortnightly. Less frequent dosing of elranatamab may offer distinct social, financial, practical and psychological QoL advantages to patients through substantially fewer hospital trips for treatment.	
	The UK Myeloma Society	It would be helpful to review any real world data on progression free survival for Elra and Tec from patients who have received these drugs in the UK, perhaps from the SACT dataset.	Thank you for your comments. The committee will consider all available types of evidence in its evaluation. No action required.
Additional comments on the draft scope	GlaxoSmithKline	N/A	Thank you. No action required.

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

British Society of Interventional Radiology, British Society for Haematology, Takeda UK, Sanofi