National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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

Section	Consultee/ Commentator	Comments	Action
Wording	MSD UK	MSD agrees that it is appropriate for this topic to be referred to NICE for appraisal.	Thank you for your comment.
	National Cancer Research Institute and Royal College of Physicians	Yes. In particular there are 2 populations: 1. relapse post Agitated saline contrast test (ASCT) 2. refractory patients in whom ASCT is not an option because they are unfit for it, or because they cannot get into a suitable remission	Thank you for your comment. People with relapsed or refractory classical Hodgkin lymphoma who have received autologous stem cell transplant and those who are not suitable for autologous stem cell transplant are included in the scope
Timing Issues	MSD UK	For patients with relapsed or refractory classic Hodgkin lymphoma there is currently a lack of consensus around the clinical pathway. In addition, NICE are currently appraising two technologies for	Thank you for your comment.

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		patients with classic Hodgkin lymphoma; which, dependent on outcome could influence the clinical pathway. We anticipate that the proposed appraisal should be scheduled to enable NICE to issue final guidance soon after regulatory approval.	
	National Cancer Research Institute and Royal College of Physicians	Sadly most people with classical Hodgkin Lymphoma are young and people are still dying of the disease. So it is urgent.	Thank you for your comment.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	MSD UK	No comments	Thank you.
	National Cancer Research Institute and Royal College of Physicians	Yes. The other active agent in multiply relapsed disease is bendamustine although sadly this is not reimbursed in the UK	Thank you for your comment. Bendamustine has not been added because it does not reflect general current practice
The technology/ intervention	MSD UK	MSD has amended the wording to reflect the anticipated MA. This updated wording has been communicated via email to NICE. Pembrolizumab has a positive opinion for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL) who have	Thank you for your comment. The scope has been amended in line with the positive opinion for pembrolizumab.

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		failed autologous stem cell transplant (ASCT) and Brentuximab Vedotin (BV), or who are transplant-ineligible and have failed BV	
	National Cancer Research Institute and Royal College of Physicians	Yes	Thank you for your comment.
Population	MSD UK	MSD would suggest the following population wording; this is based on the anticipated MA for pembrolizumab. Pembrolizumab has a positive opinion for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL) who have failed autologous stem cell transplant (ASCT) and Brentuximab Vedotin (BV), or who are transplant-ineligible and have failed BV	Thank you for your comment. The scope has been amended in line with the positive opinion for pembrolizumab.
	National Cancer Research Institute and Royal College of Physicians	Yes – these 2 populations are the ones to focus on	Thank you for your comment.
Comparators	MSD UK	MSD request that Brentuximab Vedotin (BV) is removed from the list of comparators. This is to reflect the anticipated MA of pembrolizumab. MSD would also like highlight the potential for a limited evidence base. This relates to: best supportive care and single or combination chemotherapy in the treatment setting described. At this time MSD has not conducted any data synthesis/ appraisal of the literature. However, based on the available evidence considered within the BV NICE submission; it is anticipated that comparative analysis will be extremely challenging and potentially limited due to poor quality evidence.	Thank you for your comment. The scope has been amended in line with the positive opinion for pembrolizumab.

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	National Cancer Research Institute and Royal College of Physicians	Bendamustine is active also but not reimbursed in the UK. However some centres still use it and the trust absorbs the cost.	Thank you for your comment. Bendamustine has not been added as a comparator because it is unlikely to reflect general current practice if it is not routinely reimbursed.
Outcomes	MSD UK	MSD agrees with the proposed outcome measures. However, it is known that the response to immunotherapies (immuno-oncology drugs) may be delayed, but once triggered, is likely to be durable, bringing unquantifiable long term survival benefit for a subset of patients. This benefit is not captured by the proposed outcome measures, thus MSD suggests the inclusion of “Duration of Response” as an additional outcome measure.	Thank you for your comment. Duration of response should be captured as part of the ‘response rates’ outcome and has not been included separately.
	National Cancer Research Institute and Royal College of Physicians	Yes.	Thank you.
Economic analysis	MSD UK	No comments	Thank you.
	National Cancer Research Institute and Royal College of Physicians	It is important the allogeneic transplant is mentioned. This is potential curative and for pembrolizumab to act as an effective bridge to allow allogenic stem cell transplant (SCT) is an important outcome.	Thank you for your comment. Allogeneic stem cell transplant has been included under ‘other considerations’ as a potential scenario analysis, but this will

Section	Consultee/ Commentator	Comments [sic]	Action
			depend on the evidence that is available.
Equality and Diversity	MSD UK	No comments	Thank you.
	National Cancer Research Institute and Royal College of Physicians	We don't foresee any equality issues.	Thank you for your comment.
Other considerations	MSD UK	No comments	Thank you.
Innovation	MSD UK	MSD considers pembrolizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits. Pembrolizumab has the potential to improve outcomes for patients with classical Hodgkin lymphoma representing being a step-change in the management of these patients.	Thank you for your comment.
	National Cancer Research Institute and Royal College of Physicians	Yes – PD1 inhibition is a completely novel approach in Hodgkin lymphoma. PD1 inhibitors are now used in a variety of malignancies. However their activity is by far the highest in Hodgkin lymphoma. They are also well tolerated and can induce durable remissions, even partial remissions. So we do consider that the technology can result in significant helath-related benefits. The big issue is that relapsed Hodgkin is rare so the trials are small. Accurate OS and HRQoL data will therefore be impossible. These rare diseases challenge the usual processes used by NICE.	Thank you for your comment.

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Questions for consultation	MSD UK	No questions	Thank you.
Additional comments on the draft scope	MSD UK	None	Thank you for your comment.
	National Cancer Research Institute and Royal College of Physicians	1. Standard of care across the world is brentuximab vedotin for both groups. This is being subjected to a NICE appraisal. If this is not approved then then there will be no standard of care. The drugs listed are reasonable (but not very good) alternatives. 2. Best supportive care would be regular clinic visits, occasional blood transfusions, pain relief and medication for intractable itch (which can be very hard to define). Palliative care consultant and nurse input. 3. Duration of remission would also be appropriate. Data for OS, HRQoL will be very difficult to ascertain accurately due to the phase II nature of the studies. 4. I cannot think of a subgroup that would benefit more from this. 5. No equality issues. 6. Yes, the PD1 inhibitors (nivo and pembro) are step changes in the treatment of Hodgkin lymphoma. They are very active, well tolerated and produce durable remissions (even partial remission and stable disease can be durable) 7. Bridge to transplant is an important consideration which may improve significantly health related benefits without necessarily being captured within HRQoL. Need to collect alloSCT rates. NB – these will be higher in the UK than other countries so published data may not be reflective of the benefit seen to a UK population.	Thank you for your comment. The outcomes listed are examples and are not intended to be an exhaustive list. Allogeneic stem cell transplant has been included under 'other considerations' as a potential scenario analysis, but this will depend on the evidence that is available.

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		8. NICE STAs are very robust and well respected processes. However they really only work for more common indications where there are phase III trials. Relapsed Hodgkin is not this sort of condition. I do worry that NICE STAs are not well suitable to assessing technologies within a rare disease group like this where there is only phase II data available. Personally I think NICE should come up with a different approach to assess these areas.	

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

Department of Health