National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma after autologous stem cell transplant, or at least one prior therapy

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 [sic]	Action
Appropriateness	MSD	Yes, this topic is appropriate for a NICE appraisal.	Thank you for your comment. No action needed.
Wording	MSD	The wording in the remit "treating relapsed or refractory classical Hodgkin lymphoma", should be amended to reflect the proposed wording for marketing authorisation to "[redacted]."	Thank you for your comment. The expected marketing authorisation population is marked confidential. The population is based on the key clinical trials. No action required.
Timing Issues	MSD	There is a significant need for effective, therapies for relapsed or refractory Classical Hodgkin Lymphoma (cHL), for patients who have failed autologous	Thank you for your comment. NICE aims to

Section	Consultee/ Commentator	Comments [sic]	Action
		stem cell transplant (ASCT) and for patients who have received at least one prior therapy when ASCT or multi-agent-chemotherapy is not a treatment option. The proposed appraisal timelines should be scheduled to ensure patients have the opportunity to access pembrolizumab treatment as soon as possible after marketing authorisation. Based on published literature only 53% of patients achieved ORR when Brentuximab Vedotin (BV) was used to treat in the third line setting, further highlighting the need for a more effective treatment option at this stage in the pathway. (Eyre et al. 2017 Results of a multicentre UK-wide retrospective study evaluating the efficacy of brentuximab vedotin in relapsed, refractory classical Hodgkin lymphoma in the transplant naïve setting).	provide draft guidance to the NHS within 6 months from the date when marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme. No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	MSD	MSD proposes a more relevant and specific information to the population of interest by replacing the following sentence: "Between 15% and 30% of people with Hodgkin lymphoma do not achieve long-term remission with these therapies" to "up to 5-10% patients are refractory with these therapies and 10-30% will relapse after achieving initial remission." (*https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2978071/#:~:text=9.3.-,Advanced%20HL,initial%20therapy%20followed%20by%20restaging*) MSD want to highlight the figures for the number of deaths "304 registered deaths from Hodgkin lymphoma in 2017" does not reflect the figures of 275 deaths from the Cancer Registration Statistics, England, 2017.	Thank you for your comments. The background section has been updated.

Section	Consultee/ Commentator	Comments [sic]	Action
The technology/ intervention	MSD	The sentence, “Pembrolizumab does not have a marketing authorisation in the UK for treating people with relapsed or refractory Hodgkin lymphoma who have received an autologous stem cell transplant or after at least two prior therapies when autologous stem cell transplant or multi-agent chemotherapy is not a treatment option”, should be amended to, “Pembrolizumab does not have a marketing authorisation in the UK for treating people who have [redacted]” [redacted]	Thank you for your comments. The section has been updated in line with the population of the key clinical trials.
Population	MSD	The 3 populations outlined in the scope do not accurately reflect the population included in the proposed EU marketing authorisation and should be removed. Please replace with the populations which this indication covers; Adult subpopulations 1. [redacted]	Comment noted. The expected marketing authorisation population is marked confidential. The population is based on the key clinical trials and was updated to: • autologous stem cell transplant or • at least one prior therapy when autologous stem cell transplant is not a treatment option

Section	Consultee/ Commentator	Comments [sic]	Action
Comparators	MSD	Subpopulations 1 and 2 –BV Subpopulation 3 – Chemotherapy regimens Please note that a variety of regimens can be administered as salvage chemotherapy to relapsed/refractory patients but there is no clear pathway or clear recommendation for one over another. Recent guidelines (https://rmpartners.nhs.uk/wp-content/uploads/2020/01/Pan-London-Hodgkin-Guidelines-Jan-2020.pdf) state that *"Choice of conditioning regimen should be based on familiarity of the treatment centre with the regimen."* As such, a UK publication from Eyre et al. 2017 (Results of a multicentre UK-wide retrospective study evaluating the efficacy of brentuximab vedotin in relapsed, refractory classical Hodgkin lymphoma in the transplant naïve setting) along with clinical expert opinion was used to select a list which is representative of the salvage chemotherapy regimens administered in the clinical practice in the UK. • Dexamethasone, cisplatin, high-dose cytarabine (DHAP) • Ifosfamide, carboplatin, etoposide (ICE) • Ifosfamide, gemcitabine, vinorelbine (IGEV) • Ifosfamide, epirubicin, etoposide (IVE) • Etoposide, methylprednisone, high-dose cytarabine, cisplatin (ESHAP) • Gemcitabine, dexamethasone, cisplatin (GDP) • Bendamustine, gemcitabine, vinorelbine (BEGEV) • BEACOPP/eBEACOPP • ChlVPP-based (chlorambucil, vinblastine, prednisolone, procarbazine MSD is currently conducting a MAIC feasibility assessment to investigate whether there is enough evidence to compare against the chemotherapy regimens for the subpopulation 3	Comment noted. Chemotherapy regimens were added as a comparator for people who did not have at least two prior therapies when autologous stem cell transplant is not a treatment option.

Section	Consultee/ Commentator	Comments [sic]	Action
Outcomes	MSD	MSD agrees with the proposed outcome measures. [redacted] In addition, 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. Additionally, Complete Remission Rate (CRR) will be reported as a secondary endpoint due to its indication of patients', with haematological malignancies, response to treatment. Therefore, MSD suggests inclusion of this endpoint as an additional outcome measure.	Comment noted. No change to scope required.
Economic analysis	MSD	List prices or publicly available prices will be taken into account for comparators in the economic analysis.	Comment noted. No change to scope required
Equality and Diversity	MSD	No comments	-
Other considerations	MSD	Regarding subgroups described in the scope which states, "If the evidence allows the following subgroups may be considered - people who could have a subsequent stem cell transplant (autologous or allogeneic) if they respond to treatment - people for whom stem cell transplant is contraindicated because of comorbidities" MSD would like to seek clarification at the decision problem meeting as to	Thank you for your comments. Subgroups will be considered in detail by the committee during the appraisal. Please provide all evidence available for

Section	Consultee/ Commentator	Comments [sic]	Action
		what evidence is required for the subgroups listed above. MSD would like to note that as stated above [redacted] are included in the proposed marketing authorisation. Hence, MSD will present clinical data relating to this population.	the relevant subgroups. No action needed.
Innovation	MSD	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 comments. Innovation will be considered in detail by the committee during the appraisal. No action needed.
Questions for consultation	MSD	**Which treatments are considered to be established clinical practice in the NHS for people with relapsed or refractory classical Hodgkin lymphoma who have had a autologous stem cell transplant (ASCT) or are not suitable for ASCT and/or multi-agent chemotherapy?** This question should read "Which treatments are considered to be established clinical practice in the NHS for people with relapsed or refractory classical Hodgkin lymphoma who [redacted]?" The comparators listed earlier in the table are established clinical practice for the respective subpopulations. **Do you consider that the use of pembrolizumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?** [redacted] will provide supportive evidence for the proposed license indication. However, since this clinical trial is conducted in the [redacted] population this will not be taken into consideration the cost effectiveness modelling. Therefore, the health-related benefits of the intervention to the	Comments noted. Chemotherapy regimens were added as a comparator for people who did not have at least two prior therapies when autologous stem cell transplant is not a treatment option.

Section	Consultee/ Commentator	Comments [sic]	Action
		[redacted] population will not be included in the QALY calculation. **Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.** [redacted] will provide clinical evidence for this population.	
Additional comments on the draft scope		N/A	-

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

Lymphoma Action.