National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Brentuximab vedotin for untreated CD30-positive peripheral T-cell lymphoma (ID1586)

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
Wording	Takeda UK Limited	We would suggest that the wording of the remit be modified to match the expected marketing authorisation, in specific that brentuximab vedotin is used in combination with CHP and that this appraisal is focused on adult populations. We would suggest the following remit or appraisal objective: To appraise the clinical and cost effectiveness of brentuximab vedotin in combination with cyclophosphamide, doxorubicin, and prednisone (CHP) within its marketing authorisation for adult patients with previously untreated CD30+ positive peripheral T-cell lymphoma (PTCL).	Comment noted. The remit is kept broad, partly so that confidential wording is not shared and partly in case the wording of the marketing authorisation isn't what was expected.
Timing Issues	Takeda UK Limited	No comment	No action required.
Additional comments on the draft remit	Takeda UK Limited	No comment	No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Lymphoma Action	Survival rates are incorrect according to the cited reference. The sentence should read: 'Survival for T-cell lymphoma is 50% at 5 years with 25%, 45% and 80% for PTCL not otherwise specified, ALK-negative ALCL and ALK-positive ALCL respectively.' For most peripheral T-cell lymphomas, consolidation with autologous stem cell transplant is more common than allogeneic stem cell transplant.	Comment noted. The background information has been updated.
	Takeda UK Limited	Suggested revision regarding the following sentence: The commonest PTCLs are PTCL not otherwise specified and systemic anaplastic large cell lymphoma (sALCL). The most common types of PTCL are the nodal subtypes which include Peripheral T-Cell Lymphoma Not Otherwise Specified (PTCL-NOS), followed by Angioimmunoblastic T-Cell Lymphoma (AITL) and then systemic Anaplastic Large Cell Lymphoma (sALCL). AITL is more common than sALCL therefore we would recommend revising this in the scope.	Comment noted. The background information has been updated.

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		Suggested revisions regarding the description of sALCL: CD30 expression varies among PTCL subtypes with high expression in the ALCL subtypes. There are two types of ALCL: primary cutaneous ALCL (pcALCL) and systemic ALCL (sALCL). The relevant type of ALCL for the appraisal in question is systemic ALCL (sALCL). Therefore, for the avoidance of doubt we would recommend that all mentions of ALCL be revised to sALCL. Furthermore, sALCL is characterised by uniform expression of the CD30 protein, with all sALCL patients being fully CD30-positive.[1,2] We would recommend the sentence be changed to the following: CD30 expression varies among PTCL subtypes but is uniformly expressed in systemic ALCL (sALCL). [1]Bossard C et al. Immunohistochemistry as a valuable tool to assess CD30 expression in peripheral T-cell lymphomas: high correlation with mRNA levels. Blood. 2014 Nov 6;124(19):2983-6. [2]Sabattini et al. CD30 expression in peripheral T-cell lymphomas. Haematologica. 2013 Aug;98(8):e81-2.	Comment noted. The background information has been updated.
		Suggested revision regarding the outcome statistics of PTCL: Survival rate for T-cell lymphoma is 50% at 5 years with 26.7%, 80% and 44.2% for PTCL not otherwise specified, ALK-negative ALCL and ALK-positive ALCL respectively. There is a typo in the sentence above as well as a slight variation between the reference figures and those presented in the draft scope ; the five-year survival rate of PTCL-NOS should be 25.4%, ALK-negative sALCL should be 44.7% and for ALK-positive sALCL should be 80.2%.	Comment noted. The background information has been updated.

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		Suggested revisions regarding the treatment pathway: The commonest treatment for untreated PTCL in the UK is CHOP (cyclophosphamide, doxorubicin, and prednisolone). There is a typo in the sentence above, vincristine or Oncovin (O of CHOP) has been omitted from the sentence.	Comment noted. The background information has been updated.
		The draft scope currently states: Some people may receive CHOEP (CHOP with the drug etoposide). Etoposide is not considered as standard of care for frontline PTCL in the NHS: • The current British Society of Haematology (BSH) guidelines recommend treatment with CHOP for frontline PTCL and do not mention the addition of etoposide.[3] • The NICE Pathways for Non-Hodgkin's lymphomas only recommend CHOP for patients with untreated PTCL.[4] In 2019 audit by the Haematological Malignancy Research Network (HMRN) in Yorkshire of 267 PTCL patients diagnosed with PTCL between 2004 and 2016, [redacted].[5] The HMRN region comprises a total population of 3.8 million and covers the area formerly served by the Yorkshire and the Humber & Yorkshire Coast Cancer Network.[5] The limited use of etoposide and the lack of evidence supporting the efficacy of adding etoposide to CHOP in PTCL reflects these guidelines. There are no randomised controlled trials which report on the efficacy of CHOEP. While some studies have shown a directional progression-free survival (PFS) increase for only select subtypes of patients, no overall survival (OS) benefit has been observed with the addition of etoposide. Furthermore, the addition	Comment noted. The background information section gives an overview of existing treatment options both commonly and rarely used once. No action required.

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		of etoposide is associated with a considerable increase in the toxicity and side effects experienced by patients. Deng et al. (2019) consider the literature that are available and present the results of a meta-analysis for CHOP vs. CHOEP; results indicate no differences in therapeutic effect but that the CHOEP group had significantly increased adverse events.6 Clinician feedback provided to Takeda supports the BSH and NICE guidelines and echoes the lack of evidence in this area. Therefore, due to the limited evidence supporting the efficacy of adding etoposide and the increase in toxicity, CHOEP is not frequently used in the UK. [3]Dearden et al. Br J Haematol. 2011 May;153(4):451-85. [4]NICE pathways; https://pathways.nice.org.uk/pathways/non-hodgkins-lymphoma#path=view%3A/pathways/non-hodgkins-lymphoma/managing-non-hodgkins-lymphoma.xml&content=view-node%3Anodes-anaplastic-large-cell-lymphoma [5] Takeda data on file. Haematological Malignancy Research Network: Clinical Management and Outcome of Peripheral T-cell Lymphoma. March 2019.	
		Although the use of consolidative stem cell transplantation (SCT) is noted by the NICE Pathways, it's use in clinical practice in the UK is variable with many centres opting not to consolidate with an SCT. This is due to the lack of robust evidence supporting the efficacy of an SCT, in particular a lack of evidence of an increase in OS. It should be noted that for the most common types of PTCL (i.e. PTCL-NOS, AITL and sALCL), if consolidation was considered, it would be done with an autologous stem cell transplant (ASCT) and not an allogeneic stem cell transplant (alloSCT). We would recommend that the following wording be considered to remove alloSCT: Some people receive first-line consolidation with high-dose chemotherapy (most commonly BEAM) and allo-HSCT.	Comment noted. The background information has been updated.

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		The standard of care in the NHS for patients who have sALCL and are either relapsed or refractory (RR) to frontline treatment is brentuximab vedotin monotherapy. Brentuximab vedotin has been available for RR sALCL for patients in the NHS since 2012. The original funding was via the Cancer Drugs Fund however NICE appraised brentuximab vedotin for RR sALCL and issued a positive recommendation in 2017 (TA478). For completeness of scope, we recommend that the treatment of RR sALCL with brentuximab vedotin be included within the disease background and current standard of care.	Comment noted. Relapsed or refractory sALCL is out of the remit of this scope. No action required.
The technology/ intervention	Lymphoma Action	CD30 is expressed in peripheral T-cell lymphomas other than ALCL.	Comment noted. The technology section has been updated.
	Takeda UK Limited	Regarding the following statement: Brentuximab vedotin (Adcetris, Takeda UK Ltd) is an antibody-drug conjugate that selectively targets tumour cells expressing the CD30 protein, a marker of ALCL. Although brentuximab vedotin does target CD30 and sALCL uniformly expresses CD30, other lymphomas such as PTCL-NOS may also express CD30 albeit in varying levels.[1,2] Brentuximab vedotin is approved and funded in various types of CD30 expressing lymphomas. Therefore, a more accurate description would be: Brentuximab vedotin (Adcetris, Takeda UK Ltd) is an antibody-drug conjugate that selectively targets tumour cells expressing the CD30 protein. CD30 is expressed in all cases of sALCL and is variably expressed in other PTCL subtypes.	Comment noted. The technology section has been updated.

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		Brentuximab vedotin does not currently have a marketing authorisation in the UK for untreated CD-30 positive PTCL. Brentuximab vedotin does not currently have a marketing authorisation in the UK for untreated CD-30 positive PTCL. However, brentuximab vedotin does currently have a marketing authorisation for R/R sALCL. Brentuximab vedotin is recommended by NICE for R/R sALCL (TA478) and has become the standard of care in the UK for R/R sALCL, a subtype of PTCL. [1]Bossard C et al. Immunohistochemistry as a valuable tool to assess CD30 expression in peripheral T-cell lymphomas: high correlation with mRNA levels. Blood. 2014 Nov 6;124(19):2983-6. [2]Sabattini et al. CD30 expression in peripheral T-cell lymphomas. Haematologica. 2013 Aug;98(8):e81-2.	Comment noted. Relapsed or refractory sALCL is out of the remit of this scope. No action required.
		The ECHELON-2 trial studied brentuximab vedotin in combination with cyclophosphamide, doxorubicin and prednisone (CHP) in adult patients with previously untreated CD30-positive peripheral T-cell lymphoma. Please note that although the disease may sometimes be referred to as mature T-cell lymphoma, the more correct and commonly used term is peripheral T-cell lymphoma (PTCL). For the avoidance of doubt, it is recommended the scope be changed to reflect the more commonly used term, PTCL.	Comment noted. The technology section has been updated.
Population	Lymphoma Action	The pivotal ECHELON 2 study was powered for intent-to-treat analysis of the entire study population (CD30-positive peripheral T-cell lymphomas). It was not powered to show differences in efficacy based on specific peripheral T-cell lymphoma subtype. As mandated by the EMA, 75% of patients in the study had ALCL. The number of patients with non-ALCL T-cell lymphomas was small. Further data may be required to perform adequate subgroup analysis.	Comment noted. The population has been updated.

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		Angioimmunoblastic T-cell lymphoma (AITL) is another sub-group of PTCL that would benefit from separate analysis if there was sufficient data to do so.	
	Takeda UK Limited	The ECHELON-2 trial population and the anticipated marketing authorisation is for correctly defined in the draft scope as: Adults with previously untreated CD30-positive peripheral T-cell lymphoma (PTCL).	Comment noted. The population has been updated.
Comparators	Lymphoma Action	Established comparators are CHOP or CHEOP followed by consolidation with autologous stem cell transplant, except ALK-positive ALCL where CHOP alone can produce very high cure rates. Autologous stem cell transplant would be an appropriate comparator from a cost point of view if the use of brentuximab vedotin would reduce the use of autologous transplantation consolidation treatment. At present, approximately half of all patients with peripheral T-cell lymphomas undergo autologous stem cell transplantation in first remission.	Comment noted. Having received clinical expert feedback, he comparator section has been updated to include CHOP with or without consolidation.
	Takeda UK Limited	Recommendations regarding the following statement: Established clinical management without brentuximab vedotin including but not limited to: • cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone (CHOP) • cyclophosphamide, hydroxydaunorubicin, vincristine, etoposide, and prednisone (CHOEP) As described in the Background Information section above, the standard of care for the management of untreated PTCL in the UK is cyclophosphamide,	Comment noted. Having received clinical expert feedback, he comparator section has been updated to include CHOP with or without consolidation.

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		hydroxydaunorubicin (doxorubicin), vincristine, and prednisone (i.e. CHOP). CHOP is the recommended treatment in the BSH guidelines and the only treatment option in the NICE Pathways for Non-Hodgkin lymphomas.[3,4] The addition of etoposide to CHOP (i.e. the CHOEP regimen) is not frequently or consistently used across the NHS for the treatment of PTCL and would not be considered as standard of care. CHOEP is not currently recommended by the BSH Guidelines nor is it included in the NICE Pathways. There is limited evidence supporting the efficacy of adding etoposide to CHOP in PTCL, with no randomised controlled trials being conducted in this setting and mixed results across different trials and different subtypes of PTCL. While some trials have shown a directional improvement in PFS for select subtypes of patients, no OS benefit has been observed with CHOEP when compared to CHOP. The addition of etoposide is however associated with a considerable increase in the toxicity and side effects experienced by patients and is therefore not considered for patients older than 60 years. Due to the limited evidence supporting the efficacy of adding etoposide to CHOP and the increase in toxicity, CHOEP is not frequently or consistently used in the UK. The limited adoption of etoposide across the UK is demonstrated by the [redacted].[5] [3]Dearden et al. Br J Haematol. 2011 May;153(4):451-85. [4]NICE pathways; https://pathways.nice.org.uk/pathways/non-hodgkins-lymphoma#path=view%3A/pathways/non-hodgkins-lymphoma/managing-non-hodgkins-lymphoma.xml&content=view-node%3Anodes-anaplastic-large-cell-lymphoma [5](Takeda data on file. Haematological Malignancy Research Network: Clinical Management and Outcome of Peripheral T-cell Lymphoma. March 2019.)	

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		As mentioned above, brentuximab vedotin is currently approved and funded for RR sALCL (NICE TA478). It has been the standard of care for RR sALCL, a subtype of PTCL, since 2012 and is the standard therapy used in this setting (i.e. after the failure of frontline CHOP) across the NHS. Therefore, as brentuximab vedotin is the current standard of care and an established part of PTCL management, it is misleading to state that the comparator should be: Established clinical management without brentuximab vedotin. We recommend that the comparator be revised to reflect the UK clinical pathway and the comparator definition should therefore state: 'Established clinical management including but not limited to: - cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone (CHOP)"	Comment noted. Relapsed or refractory sALCL is out of the remit of this scope. No action required.

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Outcomes	Lymphoma Action	Yes.	No action required.
	Takeda UK Limited	The relevant outcome measures when assessing agents in untreated PTCL are progression-free survival, overall survival, overall response rates (including complete response), health related quality of life and adverse effects of treatment. All the aforementioned end-points are commonly included in clinical trials in PTCL and are either primary or secondary end-points in the ECHELON-2 trial. Disease-free is not a commonly used end-point in PTCL and was therefore not included in the ECHELON-2 trial. Instead the more relevant and more commonly used end-point is progression-free survival and ultimately overall survival. Takeda recommends that disease-free survival be removed from the list of outcome measures for this appraisal.	Comment noted. The list of outcomes has been amended.
Economic analysis	Takeda UK Limited	The economic analysis will follow the NICE reference case.	Comment noted. No action required.
Equality and Diversity	Takeda UK Limited	There are no equality considerations for this appraisal.	Comment noted. No action required.
Other considerations	Takeda UK Limited	Recommendations regarding the following statement: If the evidence allows the following subgroups will be considered. These include people with PTCL not otherwise specified, people with sALCL, people with ALK-positive sALCL, and ALK-negative sALCL. As described in the Disease Background section, there are different subtypes of PTCL, and the most common subtypes are PTCL-NOS, AITL and sALCL, all of which are considered nodal PTCLs. The recommended frontline	Comment noted. The other consideration section has been updated.

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		management for nodal PTCLs is generally the same across subtypes. There is a difference in the management of relapsed or refractory disease as brentuximab vedotin is approved and funded for RR sALCL only. The main target for brentuximab vedotin, CD30, expresses variably across the main subtypes of PTCL but is uniformly expressed in sALCL. Although the ECHELON-2 trial included various subtypes of PTCL, the pre-specified analysis of the main end-points was planned for the Intention To Treat (ITT) and sALCL subgroup only (the latter due to a regulatory requirement). A key subgroup of interest is sALCL, however it is not recommended to separate sALCL according to ALK status. To be eligible for ECHELON-2, ALK+ve sALCL patients were required to be higher risk patients with an IPI score of 2 or above. Clinical literature supports that ALK+ve patients with a high IPI score have similar outcomes as ALK-ve sALCL patients. Histologically both groups express CD30 uniformly and there is no difference in the management of the condition in the relapsed setting. UK clinical experts at an advisory panel held by Takeda strongly recommended that ALK+ve and ALK-ve sALCL groups be considered as one combined sALCL group. As the frontline management of the key subtypes of PTCL is the same and the ECHELON-2 trial was not designed to look at outcomes per subtype (except for sALCL where this was a pre-specified analysis), we recommend that the main group for the appraisal should be in line with the expected marketing authorisation which is all previously untreated CD30-positive PTCL. A subgroup analysis of sALCL could be considered as its pathway differs in the relapsed/refractory setting (due to the availability of brentuximab vedotin) and it was a pre-specified analysis in the ECHELON-2 trial.	
Innovation	Lymphoma Action	Brentuximab vedotin represents a paradigm shift in the management of peripheral T-cell lymphomas, with a 29% improvement in progression-free survival and a 34% lower risk of death in a prospective double-blind randomised phase 3 trial. The ECHELON 2 study showed the first	Comment noted. No action required.

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		improvement in overall survival ever demonstrated in peripheral T-cell lymphoma against standard of care CHOP +/- transplant. The data supporting the role of brentuximab vedotin in ALCL in particular is convincing and practice-changing. Based on the pooled data, it might be reasonably expected that brentuximab vedotin also has a role in other CD30-positive peripheral T-cell lymphomas but the number of non-ALCL patients in the pivotal study was small. The rarity and heterogeneity of different subtypes of peripheral T-cell lymphomas can make it difficult to assess them in large clinical trials. However, these subtypes currently have the fewest treatment options and the greatest unmet need. Horwitz S, et al. Brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (ECHELON-2): a global, double-blind, randomised, phase 3 trial. Lancet, 2019; 393(10168): 229-240. Fanale MA, et al. Five-year outcomes for frontline brentuximab vedotin with CHP for CD30-expressing peripheral T-cell lymphomas. Blood 2018; 131: 2120–24.	
	Takeda UK Limited	The addition of brentuximab vedotin to CHP is a step-change in the management of PTCL as it is the first molecule to show an improvement in outcomes in patients with PTCL compared to the standard of care, CHOP, for over 30 years. The ECHELON-2 trial was the first randomised controlled trial to show a statistically significant improvement in both progression-free survival (PFS) and overall survival (OS) for CD30+ untreated PTCLs. In the ECHELON-2 trial, brentuximab vedotin in combination with CHP had a statistically significant improvement of median PFS of 48.2 months compared to 20.8 months with CHOP (HR= 0.71, CI [0.54, 0.93], p = 0.011). Furthermore, the addition of brentuximab vedotin to CHP demonstrated a 34% reduction in risk	Comment noted. No action required.

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		of death compared to CHOP (HR=0.66; P=0.0244). Therefore, the addition of brentuximab vedotin to CHP offers a substantial improvement in outcomes in PTCL, a very aggressive form of cancer.	
Questions for consultation	Lymphoma Action	CD30 testing is carried out routinely in the NHS during diagnosis of peripheral T-cell lymphomas. In the existing NICE pathway, Non-Hodgkin's lymphoma, brentuximab vedotin with cyclophosphamide, doxorubicin, and prednisolone will fit in: • first-line treatment of ALK positive and ALK-negative ALCL first-line treatment of CD30-positive peripheral T-cell lymphoma.	Comment noted. No action required.
	Takeda UK Limited	**Have all relevant comparators for brentuximab vedotin with cyclophosphamide, doxorubicin, and prednisolone been included in the scope?** Please refer to the *Comparator* section above. **Would stem cell transplant be an appropriate comparator?** As described in the *Disease Background* and Comparator sections above, according to the BSH Guidelines and NICE Pathways, the established management of previously untreated PTCL in the UK is frontline treatment with CHOP.[3,4] Although consolidation with an autologous stem cell transplant (ASCT) could be considered for patients who are eligible and achieve a complete response with CHOP, this would be considered as subsequent treatment following the completion of the CHOP regimen. It should be noted that there are limited data supporting the efficacy of consolidating front line treatment of PTCL with an ASCT. The data which do exist are relatively poor	Comment noted. No action required.

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		in quality and results vary by study. Furthermore, in line with the NICE Pathways, transplants will be limited to individuals who are fit enough for transplantation. Therefore, the uptake of consolidative ASCTs across the UK is variable and would not be uniformly considered as standard of care across all subtypes of PTCL. As described above, the ECHELON-2 trial compared brentuximab vedotin in combination with CHP with the standard of care regimen CHOP for previously untreated patients with CD30+ PTCL. Patients who achieved a complete response in the ECHELON-2 trial with either induction regimen were allowed to receive an ASCT at the discretion of their treating physician. This was open to both arms of the trial but importantly any consolidation occurred after the completion of the brentuximab vedotin plus CHP or the CHOP regimen. Therefore, consolidative ASCT would not be considered a comparator but instead a subsequent treatment for the select few patients who receive it. **Which treatments are considered to be established clinical practice in the NHS for untreated CD30-positive peripheral T-cell lymphoma; in particular PTCL not otherwise specified, ALK-positive sALC, and ALK-negative sALCL?** As described in the *Comparator* section, established clinical management of all untreated PTCL in the NHS is treatment with CHOP. This is the recommended frontline treatment in the current BSH Guidelines for the management of PTCL and the only treatment included in the NICE Pathways for Non-Hodgkin's lymphoma.[3,4] Feedback from UK clinical experts in T-cell lymphoma unanimously supports six cycles of CHOP as established management across the UK for untreated PTCL. Some patients who achieve a CR with CHOP could be consolidated with an ASCT after the completion of CHOP. However, limited data supports consolidation with ASCT in PTCL therefore its adoption varies throughout the country and may not be considered established management. Please refer to the *Other*	

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		Considerations section regarding the key subtypes of interest. It should be noted that the established clinical management among the key subtypes only differs in the relapsed/refractory setting where brentuximab vedotin would be considered as established management for RR sALCL only. Brentuximab vedotin for RR sALCL has been available on the NHS since 2012. Initially a CDF medicine, it was recommended by NICE in 2017 for baseline commissioning for RR sALCL and features in the Non-Hodgkin's Lymphoma NICE Pathway in this setting. Please note that there is a typo throughout the document in reference to systemic Anaplastic Large Cell Lymphoma (sALCL); in many instances it is incorrectly written as ACLC. **Are the outcomes listed appropriate?** Please see the comments in the *Outcomes* section above. **Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom brentuximab vedotin with cyclophosphamide, doxorubicin, and prednisolone is expected to be more clinically effective and cost effective or other groups that should be examined separately?** Please refer to the comments in the *Other Considerations* section above. **Is CD30 testing carried out routinely in the NHS during diagnosis of peripheral T-cell lymphomas?** CD30 testing is currently carried out routinely across the NHS during the diagnosis of PTCL as it is a part of the diagnostic panel for an accurate diagnosis of sALCL. As mentioned above, sALCL uniformly expresses CD30	

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		therefore at the diagnosis of a suspected PTCL, a CD30 test will be included in the standard laboratory tests in the NHS. **Where do you consider brentuximab vedotin with cyclophosphamide, doxorubicin, and prednisolone will fit into the existing NICE pathway, Non-Hodgkin's lymphoma?** Based on available evidence from the ECHELON-2 clinical trial and feedback from an advisory panel with clinical experts in T-cell lymphoma from across the UK, brentuximab vedotin in combination with CHP is expected to be used for previously untreated patients with CD30-positive PTCL. It would be an alternative to CHOP as frontline therapy in the current NICE pathway for Non-Hodgkin's lymphoma. **NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:** • **could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which brentuximab vedotin will be licensed;** • **could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;**	

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		• **could have any adverse impact on people with a particular disability or disabilities.** **Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.** Please see the comments in the *Equity* section above. **Do you consider brentuximab vedotin 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)?** As described in the *Innovation* section above, brentuximab vedotin is considered a step-change in the management of CD30-positive PTCL as it is the first novel agent to show benefit over standard chemotherapy with CHOP in over 30 years. The ECHELON-2 trial is the first randomised controlled trial to show a statistically significant improvement in both PFS and OS for CD30+ untreated PTCLs. **Do you consider that the use of brentuximab vedotin can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?** The economic evaluation will follow the NICE reference case, based on a cost per QALY measurement. The efficacy related benefits, observed by PFS and OS will be captured by the QALY.	

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		To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly. No additional barriers are expected as brentuximab vedotin has been available and widely used in the NHS for various lymphomas since 2012. [3]Dearden et al. Br J Haematol. 2011 May;153(4):451-85. [4]NICE pathways; https://pathways.nice.org.uk/pathways/non-hodgkins-lymphoma#path=view%3A/pathways/non-hodgkins-lymphoma/managing-non-hodgkins-lymphoma.xml&content=view-node%3Anodes-anaplastic-large-cell-lymphoma	
Additional comments on the draft scope	Takeda UK Limited	**Related Technology Appraisals** We note that no related technology appraisal has been listed in the draft scope and suggest that this be modified to include the following appraisal: *Brentuximab vedotin for treating relapsed or refractory systemic anaplastic large cell lymphoma [TA478].* This appraisal assessed the cost-effectiveness of brentuximab vedotin later in the disease pathway (i.e. relapsed or refractory disease) of sALCL, a prominent subtype of PTCL and is highly relevant to this appraisal.	Comment noted. Relapsed or refractory sALCL is out of the remit of this scope. No action required.
		Related Guidelines: We recommend the following guidelines be included in the scope: British Society of Haematology (BSH) guidelines for the management of Mature or Peripheral T-Cell Lymphoma accessible on: https://b-s-h.org.uk/media/2895/t-nhl-guideline-3-8-13-updated-with-changes-accepted-v1-rg.pdf	Comment noted. The section on related guidelines refers to NICE guidelines only. No action required.

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

- Leukaemia Care