National Institute for Health and Care Excellence

SingleTechnology Appraisal (STA)

Brentuximab vedotin for treating relapsed or refractory CD30-positive cutaneous T-cell lymphoma

Response to consultee and commentator 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

Section	Consultee/ Commentator	Comments [sic]	Action
Wording	Takeda	The remit does not accurately reflect the proposed marketing authorisation. Please modify to: To appraise the clinical and cost effectiveness of brentuximab vedotin within its proposed marketing authorisation for the treatment of adult patients with CD30+ cutaneous T-cell lymphoma (CTCL) who require systemic therapy.	Comment noted. The remit has been kept broad to ensure that it captures possible wording of the marketing authorisation from the European Medicines Agency.
	Royal College of Pathologists/British Society of Haematologists	To appraise the clinical and cost effectiveness of brentuximab vedotin within its marketing authorisation for treating relapsed or refractory to skin directed therapy CD30-positive cutaneous T-cell lymphoma.	Comment noted. The remit has been kept broad to ensure that it captures possible wording of the marketing authorisation

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			from the European Medicines Agency.
Timing Issues	Takeda	Urgent as CTCL is an incurable and disfiguring disease in need of new therapeutic options that achieve durable responses. The compelling evidence from the phase 3 ALCANZA trial shows that brentuximab vedotin has the potential for practice changing implications for patients.	Comment noted. The appraisal has been scheduled into the Technology Appraisal programme.
Additional comments on the draft remit	Takeda	The proposed indication submitted to EMA is slightly broader than the population included within the ALCANZA trial however, the patient population for the NICE submission will be based on the strongest available data which is in line with the ALCANZA trial. The proposed population for consideration of NICE will be adult patients with CD30-expressing mycosis fungoides (MF) who received ≥1 prior system therapy or primary cutaneous anaplastic large cell lymphoma (pcALCL) who received ≥1 prior systemic therapy or radiotherapy.	Comment noted. The company can outline how it intends to approach the decision problem when invited to prepare the STA evidence submission. See section 3.2.2 of NICE's 'Guide to the processes of technology appraisal' available at https://www.nice.org.uk/process/pmg19/chapter/the-appraisal-process

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Takeda	There are no comments to the incidence or prevalence sections; however, Takeda would like to make a number of additions and clarification to the disease description, classification and treatment sections. Please add the following to the description of the disease (added text to the proposed description is underlined): **Disease Description** • Cutaneous T-cell lymphoma (CTCL) is a rare type of non-Hodgkin's lymphoma that affects the skin with no evidence of extracutaneous disease at diagnosis. • CTCL is a heterogeneous group of neoplasms of skin-homing T cells that show considerable variation in clinical presentation, histologic appearance and prognosis. • Many types of cutaneous T-cell lymphoma start as flat red patches which progress to plaques and finally tumours on the skin, which may be itchy and sometimes painful. **Classification** • The European Society for Medical Oncology description of CTCL staging and classification can be found on the following link: http://www.esmo.org/Guidelines/Haematological-Malignancies/Primary-Cutaneous-Lymphoma **Treatment** • Due to the heterogeneity and rarity of CTCL controlled trials are rare, there is no standard initial therapy and treatment options are diverse.	Comments noted. The background section of the scope is only intended to briefly describe the disease, prognosis associated with the condition, epidemiology and treatments currently used in the NHS. The scope has been amended in line with some of the comments.

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		• Treatment options are dependent on the stage of disease and disease progression of the each individual patient (indolent or aggressive). Please see the ESMO guidelines for staging and classification above. • The most common types of CTCL are mycoses fungoides (MF) and Sezary Syndrome (SS). The treatment for MF is described below. • The early stages of disease (IA-IIA, III) and indolent disease can be managed with skin direct therapies such as topical steroids, PUVA, UVB, topical cytostatic agents, local electron beam therapy (EBT). • For resistant early-stage disease, advanced stage disease (IIB-IV) and aggressive disease the recommended treatment options include: total skin EBT, PUVA or systemic treatment. The first line systemic treatment options are oral methotrexate and retinoids including bexarotene. Interferon is used as a systemic therapy but is not indicated for use in CTCL in Europe. • In advanced refractory patients, once first systemic treatment options have been exhausted, depending on the treatment goals and prognosis, patients can receive traditional chemotherapy therapies. In this stage, patients are generally treated with gemcitabine. • Multi-agent chemotherapy (CHOP) is only indicated in patients with extensive disease (stage IV), once all treatment options have been exhausted. • Sezary syndrome (3% of CTCL) is a leukaemia closely related to MF and should be treated with systemic treatment, such as IFN, retinoids, TSEBT and ECP. • pcALCL patients are treated similarly to MF except that the first recommended first systemic treatment for pcACLC is methotrexate.	

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	Royal College of Pathologists/British Society of Haematologists	Tumours are different from patches which are flat whilst tumours are raised >1cm and indicative of advanced stage disease. Consider changing first paragraph to: Lymphomas are cancers of the lymphatic system. They are broadly divided into Hodgkin's and non-Hodgkin's lymphomas. Cutaneous T-cell lymphoma (CTCL) is a rare type of non-Hodgkin's lymphoma that affects the skin. It is caused by the uncontrolled growth of T-lymphocytes within the skin. The most common type of cutaneous T-cell lymphoma is mycosis fungoides which typically starts as flat red scaly patches or plaques on the skin, which may be itchy and sometimes painful. Some patients with mycosis fungoides develop advanced disease with tumours of the skin, extensive involvement of the lymph nodes, blood involvement or spread to other organs such as liver, lungs or brain. Primary cutaneous anaplastic large cell lymphoma is one of the less common subtypes of CTCL, and together with lymphomatoid papulosis forms the group of primary cutaneous CD30-positive lymphoproliferative disorders. Mycosis fungoides (usually in tumour stage) and Sézary syndrome, which is another type of cutaneous T-cell lymphoma with widespread skin involvement (erythroderma) and leukaemic blood involvement, can also express CD30. Current management consists of the following: immunotherapy such as interferon-2 alpha, bexarotene or extracorporeal photopheresis (the latter in erythrodermic disease), total skin electron beam therapy (TSEBT); chemotherapy (such as methotrexate, gemcitabine or liposomal doxorubicin or CHOP) leading to allogeneic stem cell transplant in select patients achieving a complete response. Response rates are around 40–60% with	Comments noted. The background section of the scope is only intended to briefly describe the disease, prognosis associated with the condition, epidemiology and treatments currently used in the NHS. The scope has been amended in places.

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		response duration typically less than one year. Patients may have multiple sequential treatments and remain on treatment until loss of response.	
The technology/ intervention	Takeda	For clarification purposes, please amend the first sentence in the second paragraph to accurately reflect the brentuximab vedotin's regulatory status. Although the technology currently does not have a marketing authorisation for the indication in question, CTCL, brentuximab vedotin does have a marketing authorisation for the conditions listed below. Brentuximab vedotin is indicated for the treatment for the treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma (HL): 1. following autologous stem cell transplant (ASCT) or 2. following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option. Brentuximab vedotin is also indicated for the treatment of adult patients with CD30+ HL at increased risk of relapse or progression following ASCT (see section 5.1). Brentuximab vedotin is indicated for the treatment of adult patients with relapsed or refractory systemic anaplastic large cell lymphoma (sALCL).	Comments noted. The scope has been amended.
	Royal College of Pathologists/British Society of Haematologists	The drug is administered intravenously over 30 minutes. It does not currently have marketing authorisation in the UK for CTCL. The results of the Phase III Clinical Trial recently published in the Lancet – [1] The primary endpoint was an objective response lasting 4 months (ORR4). The results showed significant improvement in objective response lasting at	Comments noted. No change to the scope required.

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		least 4 months with BV versus physician's choice of methotrexate or bexarotene [1]. 131 patients were enrolled and randomly assigned to a group (66 to brentuximab vedotin and 65 to physician's choice), with 128 analysed in the intention-to-treat population (64 in each group). At a median follow-up of 22·9 months (95% CI 18·4–26·1), the proportion of patients achieving ORR4 was 56·3% (36 of 64 patients) with BV versus 12·5% (eight of 64) with physician's choice, resulting in a between-group difference of 43·8% (95% CI 29·1–58·4; p<0·0001). Grade 3–4 adverse events were reported in 27 (41%) of 66 patients in the brentuximab vedotin group and 29 (47%) of 62 patients in the physician's choice group. Patient-reported burden of symptoms to reflect quality of life, measured by the Skindex-29, showed significantly greater symptom reduction in the BV group, compared with the physician's choice group, p<0·0001). [1] Prince HM, Kim YH, Whittaker S, Horwitz S, Dummer R, Scarisbrick J, Quaglino P, Zinzani P-L, Wolter P, Y Wang, MC Palanca-Wessels, E Zagadailov, WL Trepicchio, H-M Lin, M Little, Duvic M. Brentuximab Vedotin in Patients With CD30-expressing Cutaneous T-Cell Lymphoma Versus Methotrexate or Bexarotene: the Phase 3 ALCANZA study. Lancet. 2017;6736(17):31266-7.	
Population	Takeda	CTCL is a heterogeneous disease with considerable variation in patient presentation and disease progression. Unlike other lymphomas where patients are seen as frontline or relapsed / refractory, CTCL patients are treated according to their staging, underlying tumour type and the nature of their disease (aggressive or indolent). As this is an incurable disease, all patients will relapse throughout the course of their disease and could be considered relapsed, therefore a more appropriate characterisation of	Comments noted. The population in the scope has been amended to ensure that the wording captures the populations in the trials.

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		patients is based on the requirement of systemic treatment (determined from the aforementioned criteria). Some patients with early stage CTCL will achieve disease control with topical and skin directed treatments only and not require further systemic treatment; meanwhile others will require systemic treatment. The appropriate group of patients who would be considered for treatment with brentuximab vedotin are CTCL patients who require systemic therapy. Furthermore, there are two types of patients who receive systemic treatment: i.) those with slow progressing tumours which are no longer responsive to skin directed therapy (i.e. resistant early stage disease) and ii.) those with highly aggressive tumours in advanced stage disease. Brentuximab vedotin would be considered for both groups of patients however, the treatment objectives with the two groups of patients are different (see *Outcomes* below). As the most robust data for brentuximab vedotin for the treatment of CTCL is from the ALCANZA trial which included patients with either MF or pcALCL who have had one prior systemic therapy or radiotherapy for pcALCL, the economic assessment should focus on these patient populations.	
	Royal College of Pathologists/ British Society of Haematologists	CD30 expressing CTCL are a subgroup of CTCL. CD30 is not normally expressed on T-lymphocytes and this aberrant expression is typically associated with large cell transformation which is a poor prognostic indicator in CTCL. CD30 expressing CTCL represent a small group of patients with CTCL (an orphan disease), A recent large study of 1275 patients with advanced CTCL (stages IIB-IVB) found 23% to be CD30 expressing [2]. In	Comments noted. No change to the scope required.

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		early stage patients (IA-IIA) CD30 expression may also occur and was found to be a marker of disease progression [3]. Brentuximab vedotin has been shown to be more effective in those with CD30 expression >5%. A phase II investigator-initiated study led by Kim et al [4] reported on 32 patients with MF or Sezary syndrome (SS) who had received a prior systemic therapy and were treated with BV (1.8 mg/kg every 21 days). A clinical response was recorded in 21 of 30 evaluable patients (70%). The median time to response was 6.6 weeks (range: 3–27 weeks). The median number of brentuximab vedotin doses was 6 (range: 1–16). This study correlated CD30 expression with response and found a global response was more likely in those with CD30 expression 5% or greater ($p < 0.005$). [2]Scarisbrick JJ, Prince M, Vermeer MH et al Cutaneous Lymphoma International Consortium (CLIC) Study of Outcome in Advanced Stages of Mycosis Fungoides & Sézary Syndrome: Effect of specific prognostic markers on survival and development of a prognostic model. J Clin Oncology. 2015;33 (32):3766-73 [3]Wernham AG, Shah F, Amel-Kashipaz R, Cobbold M, Scarisbrick J. Stage I mycosis fungoides: frequent association with a favourable prognosis but disease progression and disease specific mortality may occur. Br J Dermatol. 2015;173 (5):1295-7. [4] Kim YH, Tavallaee M, Sundram U et al. Phase II investigator-initiated study of brentuximab vedotin in mycosis fungoides and sézary syndrome with variable CD30expression level: a multi-institution collaborative project. J. Clin. Oncol. 33(32),3750–3758 (2015).	

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Comparators	Takeda	Please modify to reflect that brentuximab vedotin would be considered for patients who require systemic therapy only, therefore the comparators should be established clinical management of systemic CTCL without brentuximab vedotin. The current systemic treatments used in the NHS which are licensed for use in CTCL are oral methotrexate and oral bexarotene. A potential secondary comparator is interferon as it is used in the UK but is not licensed to be used for cutaneous T-cell lymphoma.	Comments noted. The wording of the population in the scope states '…following directed skin therapies and/or at least one systemic therapy' and therefore provides sufficient clarity on the comparators. No change to the scope required.
	Royal College of Pathologists/British Society of Haematologists	There is no algorithm for treatments, our guidelines [5,6] list treatment options for line of treatment but the choice is made on an individual patient basis following MDT discussion. Immunotherapies are the preferred first line systemic therapy and chemotherapy as second / third line. BV should be considered as a first line option as the recent phase III trial has shown this to be significantly more effective than comparators (bexarotene or methotrexate). FIRST LINE Interferon 2-alpha Bexarotene Extracorporeal photopheresis (in erythroderma) Methotrexate Combinations of interferon 2-alpha, bexarotene +/- extracorporeal photopheresis may be used.	Comments noted. No change to the scope required.

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		SECOND LINE Chemotherapy, gemcitabine, liposomal doxorubicin THIRD LINE CHOP Allogeneic Bone Marrow Transplantation in patients with a durable remission [5] Trautinger F, Eder J, Assaf C, Bagot M, Cozzio A, Dummer R, Gniadecki R, Klemke C-D, Ortiz-Romero P, Papadavid E, Pimpinelli N, Quaglino P, Ranki A, Scarisbrick J, Stadler R, Väkevä L, Vermeer M, Whittaker S, Willemze R, Knobler R. EORTC consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome– update 2017. Eur J Cancer 2017;77:57-74 [6]Whittaker SJ, Marsden JR, Spittle M, Russell-Jones R, Joint British Association of Dermatologists and U.K.. Cutaneous Lymphoma Group guidelines for the management of primary cutaneous T-cell lymphomas. Br J Dermatol 2003;149:1095e107.	
Outcomes	Takeda	Of the proposed outcome measures, Takeda agrees that the following are the most important health related benefits: progression free survival, response rates, adverse effects of treatment and health-related quality of life. Although survival is always an important outcome for oncology, the primary goal of treatment for CTCL patients is disease control and symptom relief. The objective of systemic treatment is tumour burden relief to increase the patients' quality of life. Overall survival is not generally considered when determining treatment success in CTCL and is therefore generally not pre-specified as a primary nor secondary end point in clinical research. Overall survival was therefore not	Comments noted. No change to the scope required.

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		included as a pre-specified primary or secondary endpoint in the ALCANZA trial. The trial reports on event-free survival, a more relative end point for CTCL. In patients with CTCL, short clinical responses often do not equate to meaningful benefit and extending the time of disease control is a main objective of therapy (duration of response and duration of skin response are a key outcomes). The primary endpoint of ALCANZA was the proportion of patients achieving an objective global response lasting (from first to last response) at least 4 months (ORR4). The intent of selecting ORR4 as the primary endpoint was to capture durable response of brentuximab vedotin that is minimally affected by other therapies. This outcome measures two clinically important aspects of treatment success, proportion of patients achieving a response and response duration, in one single measurement. The proportion of patients achieving a complete response is also available and was a key secondary endpoint. In the ALCANZA trial, the impact of symptom burden on the patients' health-related quality of life was measured by the symptom domain of Skindex-29 (a key secondary end point). Health-related quality of life was also captured using the emotional and functional domains of Skindex-29.	
	Royal College of Pathologists/British Society of Haematologists	Yes	Comment noted. No action required.
Economic analysis	Takeda	The economic analysis for brentuximab vedotin for the treatment of systemic CTCL will be expressed as incremental costs per quality-adjusted life years, as per the reference case.	Comments noted. No change to the scope required.

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		The time horizon will be long enough to capture the costs and benefits of the technology. The current patient access scheme available in the NHS for brentuximab vedotin will be reflected in the economic analysis.	
Equality and Diversity	Takeda	No equality issues.	Comment noted. No action required.
	Royal College of Pathologists/British Society of Haematologists	If CTCL with <5% CD30 expression was excluded this may deny a small number of patients a possible efficacious drug as a study found 1 of 6 may respond with CD30<5%.	Comment noted. No change to the scope required. Please see the 'Equalities impact assessment' form.
Innovation	Takeda	**Q: 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)?** A: Clinical experts cite achieving a strong response (response rate) and maintaining that response (duration of response) as the main challenges for CTCL patients requiring systemic therapy. There is limited success with any of the currently available treatments in achieving a response but especially in controlling the disease as even those who respond to current treatments relapse very quickly and exhaust the available treatments quickly. Therefore the prognosis for this debilitating disease has been poor and potential curative treatments, such as stem cell transplants, have not been made	Comments noted. No change to the scope required. Innovative aspects of the technology should be included in the stakeholder submissions and will be explored by the appraisal committee.

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		available to these patients are they seldom achieve sufficient responses to be eligible. Brentuximab vedotin has been studied in the largest phase III clinical trial for CTCL to date, ALCANZA, and has demonstrated unprecedented efficacy for these difficult to treat patients. At median follow-up of 22.0 months, 67% of patients achieved an objective global response compared to 20% in the physician's choice group who received either methotrexate or bexarotene, and this response lasted for 4 months of more (ORR4) in 56% of brenxuimab patients versus 13% of patients on the physician's choice arm. Furthermore complete response (CR), which is rarely achieved in clinical practice for CTCL, was reached by 16% of brentuximab vedotin patients and only 2% of patients on bexarotene or methotrexate. These results demonstrate that brentuximab vedotin has the potential to substantially modify the trajectory of the disease by enabling significantly improved disease control for a sustained duration of time. By controlling the disease and controlling the associated morbidity, it makes a significant difference to the quality of life of patients who live with this incurable debilitating disease. **Q: 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?** A: Having CTCL has been described as 'wearing your lymphoma on your skin' and therefore has a large psychological impact on patients with CTCL. While health-related quality of life measurements such as EQ5D and Skindex-29 capture the traditional impacts on quality of life and quantify the extent of the tumour burden on the skin, they do little to capture the significant	

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		psychological burden of the disease. Depression, isolation and anxiety are common amongst CTCL patients due to the visible tumours, plagues and lesions from their lymphoma. The extent of the psychological burden, its impact on the patients' daily life as well as the improvement of both when disease control is achieved is not currently captured by the QALY calculation.	
	Royal College of Pathologists/ British Society of Haematologists	Yes brentuximab vedotin would be a welcome addition to the anti-CTCL therapies for the CD30+ CTCL. The phase III study has shown improved efficacy, progression free survival and quality of life (QOL) with a similar number of side effects to comparators. Patients with CTCL have been shown to have a reduced QOL	Comment noted**.** No change to the scope required. Innovative aspects of the technology should be included in the stakeholder submissions and will be explored by the appraisal committee
Other considerations	Royal College of Pathologists/British Society of Haematologists	Prince HM, Kim YH, Whittaker S, Horwitz S, Dummer R, Scarisbrick J, Quaglino P, Zinzani P-L, Wolter P, Y Wang, MC Palanca-Wessels, E Zagadailov, WL Trepicchio, H-M Lin, M Little, Duvic M. Brentuximab Vedotin in Patients With CD30-expressing Cutaneous T-Cell Lymphoma Versus Methotrexate or Bexarotene: the Phase 3 ALCANZA study. Lancet. 2017;6736(17):31266-7. Duvic M, Tetzlaff MT, Gangar P, Clos AL, Sui D, Talpur R. Results of a Phase II trial of brentuximab vedotin for CD30+ cutaneous T-cell lymphoma and lymphomatoid papulosis. J. Clin. Oncol. 33(32), 3759–3765 (2015).	Comment noted. No action required.

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		Kim YH, Tavallaee M, Sundram U et al. Phase II investigator-initiated study of brentuximab vedotin in mycosis fungoides and sézary syndrome with variable CD30 expression level: a multi-institution collaborative project. J. Clin. Oncol. 33(32), 3750–3758 (2015).	
Questions for consultation	Takeda	**Q: Which treatments are considered to be established clinical practice in the NHS for people with CD30-positive cutaneous T-cell lymphoma who require systemic therapy? How should established clinical management be defined?** A: Methotrexate and bexarotene are considered established clinical practice in the NHS for the treatment of CTCL patients who require systemic therapy. The aforementioned therapies are used frequently and with comparable results therefore the selection of the specific therapy is based on physician choice, the tumour type and patient preference. Once patients have exhausted the first systemic treatments mentioned above, they can be treated with standard chemotherapy (gemcitabine and CHOP) later in the disease progression. However, the treatment decision for these highly advanced patients with poor prognosis is dependent on the treatment goals of each patient. Established clinical management should be defined as therapies which are licensed for the treatment of CTCL and are routinely used and available across all of the NHS, and not limited to large centres only. **Q: Are the outcomes listed appropriate?** **If the evidence allows, it appropriate to consider allogeneic stem cell transplantation further down the treatment pathway?**	Comments noted. Comment noted. The comparator has been kept broad because of the complexity of the treatment pathway. No change to the scope required.

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		A: Allogeneic stem cell transplant (alloSCT) is not routinely used in the NHS for the treatment of CTCL. There is limited to no published literature on the effectiveness of allogeneic stem cell transplantation in CTCL in any line of therapy. Furthermore very few CTCL patients achieve the require response level with current treatments to be eligible for a stem cell transplant (complete response is highly recommended to proceed with an alloSCT). Therefore the use of allogeneic stem cell transplants for the treatment of CTCL is rare, experimental and not routinely offered across the NHS for all CTCL patients.	Comment noted. As brentuximab vedotin may have the potential to act as a bridge to transplant, the 'other considerations' section of the scope has been amended to include 'if the evidence allows, the economic analysis should model stem cell transplantation further down the treatment pathway'.
		Q: Are there any subgroups of people in whom brentuximab vedotin is expected to be more clinically effective and cost effective or other groups that should be examined separately? A: The population of CTCL patients expected to benefit the most from brentuximab vedotin are MF or pcALCL patients who require systemic therapy, in line with the strongest available data from the ALCANZA trial.	Comment noted. No change to the scope required.
		Q: Where do you consider brentuximab vedotin will fit into the existing NICE non-Hodgkin's lymphoma pathway?	

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		A: The treatment pathway for Cutaneous T-cell lymphoma (CTCL) specifically is not available on the NICE non-Hodgkin's lymphoma pathway, only the Peripheral T-cell lymphoma pathway (PTCL) is described. Although CTLC does fit within the PTCL umbrella, this umbrella covers a wide range of very heterogeneous cancers that don't belong to any of the other categories. The British Association of Dermatologists (BAD) and U.K. Cutaneous Lymphoma Group published guidelines in 2003 for the management of primary cutaneous T-cell lymphomas; these are the latest available guidelines but are outdated and currently under review with plans to publish updated guidelines shortly. Brentuximab vedotin would be used where systemic therapy is required or currently where bexarotene or methotrexate is used. This is after skin directed or topical treatments but before standard chemotherapy (gemcitabine or CHOP). For early stage (IB-IIA) patients this is when the disease becomes resistant to topical or skin directed treatments and either as first or second line treatment for more advanced patients (IIB or higher). The 2003 guidelines include interferon as an option for systemic treatment; however, as previously mentioned interferon is not currently licensed for use in CTCL and has limited evidence in this disease. In line with the ALCANZA trial, brentuximab is expected to be used after one prior systemic treatment. The guidelines can be accessed on the following link: http://www.bad.org.uk/shared/get-file.ashx?id=58&itemtype=document **Q: 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.**	Comment noted. No change to the scope required. Comment noted. No change to the scope required.

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		Brentuximab vedotin has been available to the NHS through the Cancer Drugs Fund since April 2013 and more recently has been approved under baseline commissioning for the treatment for relapsed/refractory Hodgkin's Lymphoma following autologous stem cell transplant. The intervention has become standard of care in the NHS for the approved indication and has been routinely used. Therefore are not likely to be any barriers to adoption.	Comment noted. No change to the scope required.
	Royal College of Pathologists/British Society of Haematologists	Brentuximab vedotin should be considered alongside other immunotherapies for first line systemic therapy in CD30 expressing CTCL (>5%). This would include MF and primary cutaneous ALCL	Comment noted. Comment noted. No change to the scope required.
Additional comments on the draft scope	Takeda	There is no standard initial therapy for CTCL patients, however, systemic options bexarotene and methotrexate are frequently used. With methotrexate treatment, there is a potential for serious toxic reactions, such as bone marrow, liver, lung, and kidney toxicities. Bexarotene is a retinoid that has been associated with birth defects in humans and can cause major lipid-, liver function-, and thyroid test abnormalities, leukopenia, and anaemia.	Comment noted. The comparator has been kept broad because of the complexity of the treatment pathway. No change to the scope required.

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

Department of Health