National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Brentuximab vedotin for treating relapsed or refractory systemic anaplastic large cell 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 [sic]	Action
Appropriateness	Takeda UK	YES	Comment noted. No action required.
	The Royal College of Pathologists	Very appropriate as this an area of unmet need with a new effective treatment now available.	Comment noted. No action required.
Wording	Takeda UK	YES	Comment noted. No action required.
	The Royal College of Pathologists	Yes	Comment noted. No action required.
Timing Issues	Takeda UK	URGENT, although NHS patients in England currently have access via the National Cancer Drugs Fund	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	The Royal College of Pathologists	Relatively urgently as otherwise patients will be denied access to an effective intervention.	Comment noted. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Takeda UK	As noted, systemic anaplastic large cell lymphoma (sALCL) is a rare (ultra-orphan) but aggressive type of non-Hodgkin T-cell lymphoma. It should be noted that there are 2 subtypes of sALCL; Anaplastic lymphoma kinase (ALK) positive (60%) and ALK negative (40%). The outcomes for patients with ALK negative sALCL are significantly worse than those with ALK positive disease and the treatment approach can also differ. For patients with ALK negative disease, the treatment approach is similar to peripheral T-cell lymphoma not otherwise specified (PTCL-NOS) and may include a consolidative stem cell transplant during first remission. Reference: Dearden et al., Guidelines for the Management of Mature T-cell and NK-cell Neoplasms. British Committee for Standards in Haematology. Updated August 2013 For patients who relapse following front line therapy with a CHOP-based regimen, the options are extremely limited. Of those treatments listed in the draft scope only gemcitabine is available for use within the NHS. The other medicines are either not licensed (at all) in Europe (pralatrexate and romidepsin) or not licensed or funded for sALCL (bortezomib, alemtuzumab).	Comment noted. The scope background has been amended to note the 2 subtypes of systemic anaplastic large cell lymphoma. The scope background has been amended to remove the list of treatment options after CHOP-based chemotherapy.

Section	Consultee/ Commentator	Comments [sic]	Action
The technology/ intervention	Takeda UK	YES	Comment noted. No action required.
	The Royal College of Pathologists	Yes	Comment noted. No action required.
Population	Takeda UK	YES	Comment noted. No action required.
	The Royal College of Pathologists	May be useful to consider survival outcomes for both transplant eligible and non-transplant eligible patients	Comment noted. The economic analysis would include both people who are, and those who are not, eligible for transplant, which would capture the outcomes in both groups. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Comparators	Takeda UK	Alternative treatment options are extremely limited and there is a paucity of published data for comparator treatments in this indication. The single arm, phase II study investigating brentuximab vedotin in relapsed or refractory (R/R) sALCL is the largest ever prospective study in sALCL (n=58) It should be noted that brentuximab vedotin is the standard of care within England for patients with R/R sALCL.	Comment noted. The inclusion of established clinical management without brentuximab vedotin as a comparator reflects the absence of standard of care for this condition. No action required.
	The Royal College of Pathologists	Currently there is no accepted standard of care that can be used as a comparator. The comparator drugs listed in the background information has many which are not available to use in the NHS (bortezomib, pralatrexate and romidepsin for instance) and others such as alemtuzumab which are rarely used due to toxicity.	Comment noted. The inclusion of established clinical management without brentuximab vedotin as a comparator reflects the absence of standard of care for this condition. The scope background has been amended to remove the list of treatment options after CHOP-based chemotherapy.

Section	Consultee/ Commentator	Comments [sic]	Action
Outcomes	Takeda UK	In addition to the outcomes listed, rate of autologous stem cell transplantation should also be added.	Comment noted. The scope has been amended to include the rate of both autologous and allogeneic stem cell transplant as an outcome.
	The Royal College of Pathologists	Yes	Comment noted. No action required.
Economic analysis	Takeda UK	It should be noted that there is a paucity of published data on comparators in this clinical setting	Comment noted. No action required.
	The Royal College of Pathologists	2-3 year survival and QOL data would be most useful to compare.	Comment noted. Survival and health-related quality of life are included as outcomes in the scope. No action required.
Equality and Diversity	Takeda UK	No equality issues	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Innovation	Takeda UK	YES. Brentuximab vedotin is viewed by the clinical community as a step change in the management of R/R sALCL and has made a significant and substantial impact on health related benefits including overall survival in this orphan indication.	Comment noted. The company is encouraged to describe the innovative nature of brentuximab vedotin in its submission to NICE. No action required.
	The Royal College of Pathologists	Brentuximab vedotin represents a technology breakthrough and is a step-change in the management of systemic anaplastic large cell lymphomas. Patients with this condition have a poor outlook which can be significantly improved with this technology. Brentuximab is likely to result in not only better response rates and survival for patients but can make several patients eligible for a stem cell transplant potentially leading to cures. It is relatively free from toxicity compared with alternative treatments which can have a significant positive effect on productivity and QOL.	Comment noted. The innovative nature of brentuximab vedotin will be taken into account in the committee's discussion. No action required.
Other considerations	Takeda UK	The economic analysis should include a scenario analysis in which ***autologous or*** allogeneic stem cell transplantation is modelled further down the pathway. Brentuximab vedotin is licensed as a single agent in this setting.	Comment noted. The scope has been amended to state that, if the evidence allows, the economic analysis should model stem cell transplantation (which includes either type of transplantation) further down the treatment pathway.

Section	Consultee/ Commentator	Comments [sic]	Action
	The Royal College of Pathologists	Quality of life issues.	Comment noted. Health-related quality of life is included as an outcome in the scope. No action required.
Questions for consultation	Takeda UK	**Q:** Have all relevant comparators for brentuximab vedotin been included in the scope? Which treatments are considered to be established clinical practice in the NHS for relapsed or refractory systemic anaplastic large cell lymphoma? **A:** There are no other established, licensed or evidence-based treatments for R/R sALCL. Since its launch in 2012, brentuximab vedotin rapidly became the standard of care for these patients. **Q:** Are the outcomes listed appropriate? Is the rate of allogeneic stem cell transplantation a relevant outcome? **A:** Yes, it is relevant but probably more important is the rate of autologous stem cell transplant (ASCT) which is the most common type of transplant used in this setting. The use of allogeneic SCT is still experimental in this setting. ASCT should be added to the list of outcomes. **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:** No, brentuximab vedotin is equally effective across patients with ALK positive and ALK negative sALCL	Comment noted. The scope has been amended to include the rate of both autologous and allogeneic stem cell transplant as an outcome.
	The Royal College of Pathologists	None to add in addition to comments made above	Comment noted. No action required.