NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

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

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of brentuximab vedotin within its marketing authorisation for untreated CD30-positive peripheral T-cell lymphoma.

Background

Non-Hodgkin's lymphomas (NHL) are malignant disorders of the lymphatic system, a part of the immune system. They are a diverse group of conditions which are categorised according to the cell type affected (B-cell or T-cell), as well as the clinical features and rate of progression of the disease. T-cell lymphomas are less common than B-cell lymphomas. T-cell lymphomas can develop from immature or mature T cells. Peripheral T-cell lymphoma (PTCL) is a heterogeneous group with over 20 distinct lymphomas that all develop in a similar way from mature T cells. The commonest PTCLs are PTCL not otherwise specified and anaplastic large cell lymphoma (ALCL). The latter can further be subdivided depending on the expression of anaplastic lymphoma kinase (ALK) into ALK-positive and ALK-negative ALCL. PTCLs are fast growing lymphomas that often present as painless lumps (enlarged lymph nodes) in the neck, armpit or groin but sometimes may start in other parts of the body such as the stomach or bowel (extranodal disease). People may also have loss of appetite, tiredness or night sweats.

CD30 is a cell surface protein expressed on some cancer cells. These tumours are called CD30-positive. CD30 expression varies among PTCL subtypes with high expression in the ACLC subtypes.

There were around 12,065 new cases of NHL in England in 2017.[1] 796 people had a primary diagnosis of peripheral or cutaneous T-cell lymphoma.[1] Estimates suggest that yearly there are about 170 PTCL not otherwise specified diagnoses, 100 ALK-negative ALCL diagnoses and 70 ALK-positive ALCL diagnoses.[2] Most people diagnosed with NHL are 65 or over.[3] Survival rates for NHL are around 68% at 5 years and 63% at 10 years.[3] 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.[2]

The commonest treatment for untreated PTCL in the UK is CHOP (cyclophosphamide, doxorubicin, and prednisolone). Some people may receive CHOEP (CHOP with the drug etoposide). Some people receive first-

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line consolidation with high-dose chemotherapy (most commonly BEAM) and allo-HSCT.

The technology

Brentuximab vedotin (Adcetris, Takeda UK Ltd) is an antibody-drug conjugate that selectively targets tumour cells expressing the CD30 protein, a marker of ALCL. Brentuximab vedotin is administered by intravenous infusion.

Brentuximab vedotin does not currently have a marketing authorisation in the UK for untreated CD-30 positive PTCL. It has been studied in a phase 3 trial in combination with cyclophosphamide, doxorubicin, and prednisolone (CHP) in adults with untreated CD30-positive mature T-cell lymphomas.

Intervention(s)	Brentuximab vedotin with cyclophosphamide, doxorubicin, and prednisolone
Population(s)	Adults with untreated CD30+ peripheral T-cell lymphoma (PTCL)
Comparators	Established clinical management without brentuximab vedotin including but not limited to: • cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone (CHOP) • cyclophosphamide, hydroxydaunorubicin, vincristine, etoposide, and prednisone (CHOEP)
Outcomes	The outcome measures to be considered include: • overall survival • disease free survival • progression free survival • response rate • adverse effects of treatment • health-related quality of life.

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Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.
Other considerations	If the evidence allows the following subgroups will be considered. These include people with PTCL not otherwise specified, people with ACLC, people with ALK-positive ACLC, and ALK-negative ACLC. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** None **Related Guidelines:** Non-Hodgkin's lymphoma: diagnosis and management (2016) NICE guideline 52 Haematological cancers: improving outcomes (2016) NICE guideline 47 **Related Quality Standards:** Haematological cancers (2017) NICE quality standard 150 **Related NICE Pathways:** Blood and bone marrow cancers (2013, updated Feb 2019) NICE pathway Non-Hodgkin's lymphoma (2016, updated March 2019) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)

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	Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 3, 4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England (2013/14) NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.

Questions for consultation

Have all relevant comparators for brentuximab vedotin with cyclophosphamide, doxorubicin, and prednisolone been included in the scope?

Would stem cell transplant be an appropriate comparator?

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 ACLC, and ALK-negative ACLC?

Are the outcomes listed appropriate?

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?

Is CD30 testing carried out routinely in the NHS during diagnosis of peripheral T-cell lymphomas?

Where do you consider brentuximab vedotin with cyclophosphamide, doxorubicin, and prednisolone will fit into the existing NICE pathway, 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.

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)?

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?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

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.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1 Cancer registration statistics, England: 2017, accessed May 2019
2 Haematological Malignancy Research Network (HMRN), HMRN 2010-2016, accessed May 2019
3 Cancer research UK, accessed May 2019

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