NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of brentuximab vedotin within its marketing authorisation for treating relapsed or refractory CD30-positive cutaneous T-cell lymphoma.

Background

Lymphomas are cancers of the lymphatic system. They are broadly divided into Hodgkin's and non-Hodgkin's lymphomas. Cutaneous T-cell lymphoma 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. Many types of cutaneous T-cell lymphoma start as flat red patches (tumours) on the skin, which may be itchy and sometimes painful. Some people with cutaneous T-cell lymphoma experience swelling of the lymph nodes. Mycosis fungoides is the most common type of cutaneous T-cell lymphoma. Primary cutaneous anaplastic large cell lymphoma is one of the less common subtypes, and together with lymphomatoid papulosis forms the group of primary cutaneous CD30-positive lymphoproliferative disorders. Mycosis fungoides and sézary syndrome, which is another type of cutaneous T-cell lymphoma, can also express CD30.

In England, 1,659 new cutaneous T-cell lymphomas were diagnosed from 2009 to 2013, of which around 55% were mycosis fungoides and around 10% were primary cutaneous CD30-positive lymphoproliferative disorders[1]. The overall incidence of cutaneous T-cell lymphomas in 2013 was around 0.75 per 100,000 (England), and it was more common in men than women (ratio around 1.6:1)[1]. In Wales, 120 new cutaneous T-cell lymphomas were diagnosed from 2003 to 2011, which relates to an overall incidence of around 0.4 per 100,000[2]. The majority of cutaneous T-cell lymphoma cases are in those over the age of 50 but can also affect young people too[1,2].

Current management of relapsed or refractory cutaneous T-cell lymphoma consists of the following treatment options: skin-directed therapy (such as psoralen and ultraviolet A treatment - PUVA, narrow band ultraviolet B treatment, and extracorporeal photopheresis - ECP); radiotherapy; total skin electron beam therapy (TSEBT); chemotherapy (such as methotrexate, gemcitabine or liposomal doxorubicin); retinoids (such as bexarotene); interferon alpha; stem cell or bone marrow transplant (such as allogeneic-

SCT). These treatments are used either alone or in combination, depending on how much of the skin is involved and whether the cutaneous T-cell lymphoma has spread to other organs. Patients may have multiple sequential treatments and remain on maintenance therapy with palliative intent although there is no established standard of care.

The technology

Brentuximab vedotin (Adcetris, Takeda UK) is an antibody–drug conjugate comprising an anti-CD30 monoclonal antibody attached by an enzyme-cleavable linker to a potent chemotherapeutic agent, monomethyl auristatin E. The antibody–drug conjugate allows for the selective targeting of CD30-expressing cancer cells. It is administered intravenously.

Brentuximab vedotin does not currently have a marketing authorisation in the UK. It is being studied in a phase III clinical trial versus physician's choice (methotrexate or bexarotene) in adults with CD30-positive cutaneous T-cell lymphoma. This trial includes people with CD30-positive mycosis fungoides who had received at least one previous systemic therapy and people with primary cutaneous anaplastic large cell lymphoma who had received at least one previous systemic therapy or radiotherapy.

Intervention(s)	Brentuximab vedotin
Population(s)	People with relapsed or refractory CD30-positive cutaneous T-cell lymphoma.
Comparators	Established clinical management without brentuximab vedotin
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life.

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, consideration will be given to subgroups based on cancer histology (mycosis fungoides and primary cutaneous anaplastic large cell lymphoma). 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: 'Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma' (2017) NICE technology appraisal 446. Review date June 2020. 'Brentuximab vedotin for treating relapsed or refractory systemic anaplastic large cell lymphoma' NICE technology appraisal guidance [ID512]. Publication expected October 2017.
Related National Policy	NHS England (May 2016) Manual for prescribed specialised services. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf Department of Health (April 2016) NHS Outcomes Framework 2016-2017. Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

	Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 http://www.cancerresearchuk.org/about-us/cancer-strategy-in-england Department of Health (2014) The national cancer strategy: 4th annual report https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report NHS England (2013) B15. Cancer: Chemotherapy (Adult). NHS Standard Contract. https://www.england.nhs.uk/wp-content/uploads/2013/06/b15-cancr-chemoth.pdf

Questions for consultation

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?

Are the outcomes listed appropriate?

If the evidence allows, it appropriate to consider allogeneic stem cell transplantation further down the treatment pathway?

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?

Where do you consider brentuximab vedotin will fit into the existing NICE non-Hodgkin's lymphoma pathway?

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;

- 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. Public Health England (2016) Registration of Cutaneous T-Cell Lymphoma (CTCL) in England. National Cancer Registration and Analysis Services Short Report 2016397

2. Abbott, R.A., Aldridge, C., Dojcinov, S. and Piguet, V. (2013), Incidence of primary cutaneous T-cell lymphoma in Wales. Br J Dermatol 169: 1366–1367

