NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Brentuximab vedotin for treating CD30-positive cutaneous T-cell lymphoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of brentuximab vedotin within its marketing authorisation for treating 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 or plaques on the skin, which progress to skin tumours, and may be itchy and sometimes painful. Some people with cutaneous T-cell lymphoma experience swelling of the lymph nodes.

Within the group of cutaneous T-cell lymphoma, distinct subtypes can be distinguished. Not all subtypes of cutaneous T-cell lymphoma express CD30. CD30 expression is present in primary cutaneous anaplastic large cell lymphoma and lymphomatoid papulosis and together they form the group of primary cutaneous CD30 positive lymphoproliferative disorders. Mycosis fungoides and Sézary syndrome can also express CD30. Sézary syndrome is closely related to mycosis fungoides but cancerous T-cells (called Sézary cells) are also found in the blood. Mycosis fungoides is the most common type of cutaneous T-cell lymphoma and primary cutaneous anaplastic large cell lymphoma is one of the less common subtypes.

Between 2009 and 2013, 1,659 people were newly diagnosed with cutaneous T-cell lymphomas 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]. The majority of people diagnosed with cutaneous T-cell lymphoma are over the age of 50 but it can also affect young people[1,2]

Treatment options depend on a number of factors, including how much of the skin is involved, nature of the disease (aggressive or slow growing), the type of lesion and whether the cutaneous T-cell lymphoma has spread to lymph nodes or other organs. Current management of cutaneous T-cell lymphoma

consists of skin directed therapies and systemic therapies. Skin directed therapies are aimed primarily at the skin and include photo therapy (such as psoralen and ultraviolet A treatment - PUVA, narrow band ultraviolet B treatment); radiotherapy; total skin electron beam therapy (TSEBT); and topical chemotherapy agents, topical corticosteroids and topical retinoids. Systemic therapies are aimed at treating the skin and/or internal organs affected or at risk, and include chemotherapy (such as methotrexate, gemcitabine, liposomal doxorubicin or multi-agent chemotherapy–cyclophosphamide, doxorubicin, vincristine, and prednisone), and immunotherapy (such as bexarotene, interferon alpha, or extracorporeal photopheresis - ECP). Stem cell or bone marrow transplant (such as allogeneic-SCT) may also be a treatment option for some people (for example those with advanced disease, a poor response to systemic therapy, multiple relapses or a short remission). Treatment options for cutaneous T-cell lymphoma can be used either alone or in combination. People 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 for treating CD30-positive cutaneous T-cell lymphoma. It is being studied in a phase III clinical trial compared with 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 CD30-positive primary cutaneous anaplastic large cell lymphoma who had received radiotherapy and/or at least one previous systemic therapy. It has also been studied in 2 phase II clinical trials. One trial includes people with mycosis fungoides, primary cutaneous anaplastic large cell lymphoma or lymphomatoid papulosis and whose disease has progressed after local radiation therapy, phototherapy, topical chemotherapy, or systemic therapy (with one or more single agent or one multi-agent chemotherapy). The other trial includes people with fungoides or Sézary syndrome and whose disease has progressed after 1 systemic therapy.

Brentuximab vedotin has a marketing authorisation in the UK for treating relapsed or refractory CD30-positive Hodgkin lymphoma and relapsed or refractory systemic anaplastic large cell lymphoma.

Intervention	Brentuximab vedotin

Population	People with relapsed or refractory CD30-positive cutaneous T-cell lymphoma following directed skin therapies and/or at least one systemic therapy.
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. If the evidence allows, the economic analysis should model stem cell transplantation further down the treatment pathway 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

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