NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Brentuximab vedotin for untreated advanced Hodgkin lymphoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of brentuximab vedotin within its marketing authorisation for untreated advanced Hodgkin lymphoma.

Background

Hodgkin lymphoma is a cancer of the lymphatic system. It can be classified into 2 main groups; the classical types, and the nodular lymphocyte predominant type. Classical Hodgkin lymphomas contain the Reed-Sternberg cells (which are cancerous B lymphocyte cells), whereas the nodular lymphocyte predominant type contains other abnormal cells, but not Reed-Sternberg cells. The initial symptom of Hodgkin lymphoma is often swelling of lymph nodes in the neck, armpit or groin. Other symptoms include recurring fever, night sweats, weight loss, cough, breathlessness, abdominal pain, and itching.

Hodgkin lymphoma accounts for around 20% of all diagnosed lymphomas. In England, there were 1790 people diagnosed with Hodgkin lymphoma and 293 registered deaths from Hodgkin lymphoma in 2014.[1] The age-specific incidence of Hodgkin lymphoma shows two peaks, one in people aged 20–24 years and the second in people aged over 75 years.[2] The incidence rates for Hodgkin Lymphoma have been predicted to rise by 5% in the UK between 2014 and 2035.[2]

Current first- line treatment for advanced Hodgkin lymphoma is chemotherapy alone or chemotherapy combined with radiotherapy. Doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) is recommended as first-line therapy with or without radiation therapy, depending on the stage of the Hodgkin lymphoma as well as the person's overall health status. Between 15 and 30% of people with Hodgkin lymphoma do not achieve long-term remission with these therapies.[3] For these people, high-dose chemotherapy followed by autologous stem cell transplant is a potentially curative treatment that is effective in about 50% of people circumstances; for example, when the disease is refractory to chemotherapy, or when the person's age or co-morbidities prohibit this intervention.

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

(MMAE). The antibody–drug conjugate allows for the selective targeting of CD30-expressing cancer cells. It is administered by intravenous infusion.

Brentuximab vedotin does not have a UK marketing authorisation for the first-line treatment of advanced Hodgkin lymphoma. It has been studied in an open-label, randomised phase 3 study, in adults with untreated advanced Hodgkin lymphoma. The study compared brentuximab vedotin in combination with doxorubicin, vinblastine and dacarbazine (AVD), with a multi-agent chemotherapy combination of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD).

Brentuximab vedotin has a marketing authorisation in the UK for:

- the treatment of adults with relapsed or refractory CD30-positive Hodgkin lymphoma:
    - following autologous stem cell transplant, or
    - following at least 2 previous therapies when autologous stem cell transplant or multi-agent chemotherapy is not a treatment option,
- the treatment of adult patients with CD30-positive Hodgkin Lymphoma at increased risk of relapse or progression following autologous stem cell transplant.

NICE technology appraisal guidance 446 recommends brentuximab vedotin as an option for treating CD30-positive Hodgkin lymphoma in adults with relapsed or refractory disease after autologous stem cell transplant for routine use in the NHS. It also recommends brentuximab vedotin in the Cancer Drugs Fund as an option for treating CD30-positive Hodgkin lymphoma in adults that have relapsed or refractory disease after at least 2 previous therapies and they cannot have autologous stem cell transplant or multi-agent chemotherapy.

Intervention(s)	Brentuximab vedotin in combination with a multi-agent chemotherapy
Population(s)	Adults with untreated advanced Hodgkin lymphoma
Comparators	Established clinical management without brentuximab vedotin for example, multi-agent chemotherapy with or without radiotherapy

Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • objective response rate • complete response rate • 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	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 guidance 446. Review date June 2020 'Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma' (2017) NICE technology appraisal guidance 462. Review date July 2020 Appraisals in development (including suspended appraisals) 'Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma'. NICE technology appraisals guidance [ID1062]. Publication expected May 2018. 'Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma after autologous stem cell

	transplant' NICE technology appraisal [ID1103] (suspended). Publication date to be confirmed. Brentuximab vedotin for treating CD30-positive Hodgkin's lymphoma (CDF Review of TA446) [ID1366] Related Guidelines: 'Haematological cancers: improving outcomes' (2016) NICE guideline NG47 Review date May 2019. Related NICE Pathways: 'Blood and bone marrow cancers' (Published 2013, updated 2017) NICE Pathway
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1 & 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Will brentuximab vedotin be used with or without multi-agent chemotherapy? If it is to be used in combination with multi-agent chemotherapy, which chemotherapy regimens will be used?

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 untreated advanced Hodgkin lymphoma?

Are the outcomes listed appropriate? Is the rate of autologous stem cell transplantation a relevant outcome?

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?

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. Office for national statistics (2016) Cancer registration statistics, England: 2014. Accessed January 2018.

2. Cancer Research UK (2014). Hodgkin Lymphoma Incidence Statistics. Access January 2018

3. National Institute for Health and Clinical Excellence (2015) Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma [ID722]. Final scope