NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Brentuximab vedotin for treating CD30-positive Hodgkin's lymphoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of brentuximab vedotin within its marketing authorisation for treating people with CD30-positive Hodgkin's lymphoma.

Background

Hodgkin's lymphoma is a cancer of the lymphatic system which arises from cancerous B lymphocyte cells (also known as Reed-Sternberg cells). Some tumours express the integral membrane antigen CD30. The initial symptom of Hodgkin's lymphoma is 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's lymphoma accounts for around 20% of all diagnosed lymphomas. In England, there were 1517 people diagnosed with Hodgkin's lymphoma in 2011 and 256 registered deaths from Hodgkin's lymphoma in 2012. The age-specific incidence of Hodgkin's lymphoma shows two peaks, one in people aged 20–25 years and the second in people aged over 70 years.

Current first-line treatment for Hodgkin's lymphoma is chemotherapy alone or chemotherapy combined with radiotherapy. Between 15 and 30% of people with Hodgkin's lymphoma do not achieve long-term remission with these therapies. For these people, high-dose chemotherapy followed by autologous stem cell transplant is a potentially curative treatment that is effective in approximately 50% of people. However, autologous stem cell transplant may not be an option in some circumstances; for example, if the disease is refractory to chemotherapy, or if the person's age or co-morbidities prohibit this intervention. Following autologous stem cell transplant, people are considered to be at 'high risk' of residual disease if they have any of the following:

- primary refractory disease
- disease relapse within 1 year of completing first-line treatment
- a positive PET scan prior to autologous stem cell transplant
- extra-nodal involvement at the time of relapse prior to autologous stem cell transplant.

There is no standard therapy administered after autologous stem cell transplant to delay disease progression. People whose disease relapses after autologous stem cell transplant may be treated with single or combination

treatment regimens that may include chemotherapy such as gemcitabine, vinblastine, or vinorelbine (alone or in combination) or ChlVPP (chlorambucil, vinblastine, procarbazine and prednisolone). Some chemotherapy regimens are used outside their marketing authorisation.

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 has a marketing authorisation in the UK for the treatment of adults with relapsed or refractory CD30-positive Hodgkin's 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 company is seeking an extension to the marketing authorisation, based on a clinical trial that compared brentuximab vedotin with placebo in adults with CD30-positive Hodgkin's lymphoma following autologous stem cell transplant who are at high risk of residual disease.

Intervention(s)	Brentuximab vedotin
Population(s)	• People with CD30-positive Hodgkin's lymphoma following autologous stem cell transplant: – who are at high risk of residual disease (as defined in the background section) or – who have relapsed or refractory disease. • People with CD30-positive Hodgkin's lymphoma following at least 2 previous therapies when autologous stem cell transplant or multi-agent chemotherapy is not a treatment option.

Comparators	Following autologous stem cell transplant for people who are at high risk of residual disease: • Best supportive care Following autologous stem cell transplant for people who have relapsed or refractory disease: • Established clinical management without brentuximab vedotin including: – Single or combination treatment regimens which may include chemotherapy such as gemcitabine, vinblastine or vinorelbine – ChlVPP (chlorambucil, vinblastine, procarbazine and prednisolone) Following at least 2 previous therapies when autologous stem cell transplant or multi-agent chemotherapy is not a treatment option: • Best supportive care
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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations and NICE	Related Guideline: Cancer Service Guidance, Improving outcomes in

Pathways	haemato-oncology cancers, October 2003: http://www.nice.org.uk/nicemedia/live/10891/28786/28786.pdf
Related National Policy	NHS England Clinical Commissioning Policy, Haematopoietic Stem Cell Transplantation, April 2013: http://www.england.nhs.uk/wp-content/uploads/2013/04/b04-p-a.pdf