NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for treating relapsed or refractory classical 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 1,790 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 to 24 years and the second in people aged over 75 years.[2]

Current first-line treatment for Hodgkin lymphoma is chemotherapy alone or chemotherapy combined with radiotherapy. Between 15 and 30% of people with Hodgkin 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 about 50% of people. However, autologous stem cell transplant may not be an option in some circumstances; for example, when the disease is refractory to chemotherapy, or when the person's age or co-morbidities prohibit this intervention.

Brentuximab vedotin is indicated for relapsed or refractory CD30+ Hodgkin lymphoma (CD30 is an integral membrane antigen expressed by some tumours) after autologous stem cell transplant, or after at least 2 prior therapies when autologous stem cell transplant or multi-agent chemotherapy is not a treatment option (NICE guidance is in development, funded by the Cancer Drugs Fund in the interim).

There is no standard therapy administered after autologous stem cell transplant and brentuximab vedotin. People 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 aim of treatment is generally to attain a sufficient response for allogeneic stem cell transplant.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised, antiprogrammed cell death 1 (PD-1) antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Pembrolizumab does not have a marketing authorisation in the UK for treating relapsed or refractory classical Hodgkin lymphoma. Pembrolizumab has a positive opinion for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma who have failed autologous stem cell transplant and brentuximab vedotin or who are not eligible for a transplant and have failed brentuximab vedotin.

Intervention(s)	Pembrolizumab
Population(s)	People with relapsed or refractory classical Hodgkin lymphoma who have received: • autologous stem cell transplant and brentuximab vedotin • brentuximab vedotin when autologous stem cell transplant is not a treatment option.
Comparators	• Single or combination chemotherapy including drugs such as gemcitabine, vinblastine and cisplatin • Best supportive care.
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, a scenario analysis including allogeneic stem cell transplant as a subsequent treatment after pembrolizumab or its comparators will be considered. This should reflect the proportion of people who proceed to allogeneic stem cell transplant after each treatment, as well as the costs and quality-adjusted life year benefits of the procedure. 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	**Appraisals in development (including suspended appraisals)** 'Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma' NICE technology appraisals guidance [ID722]. Publication expected May 2017. 'Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma' NICE technology appraisals guidance [ID972]. Publication expected July 2017. 'Nivolumab for treating relapsed or refractory classical Hodgkin's lymphoma after autologous stem cell transplant' NICE technology appraisals guidance [ID1103]. Publication expected April 2018. **Related Guidelines** 'Haematological cancers: improving outcomes' (2016) NICE guideline NG47. Review date May 2019.
Related National	Department of Health, NHS Outcomes Framework

Policy	2016-2017 (published 2016): Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1. Office for national statistics (2016) Cancer registration statistics, England: 2014. Accessed November 2016.

2. Cancer Research UK (2013) Hodgkin lymphoma incidence statistics. Accessed November 2016.