NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma after autologous stem cell transplant, or at least one prior therapy

Final scope

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. Reed-Sternberg cells typically express integral membrane antigen CD30. The initial symptom of Hodgkin lymphoma is often swelling of the 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. Nearly 2,000 people are diagnosed with Hodgkin lymphoma each year in the UK [1]. In England, there were 1,802 people diagnosed with Hodgkin lymphoma and 275 registered deaths from Hodgkin lymphoma in 2017.[2] 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.[3]

Current first-line treatment for Hodgkin lymphoma is chemotherapy alone or chemotherapy combined with radiotherapy. Up to 5-10% of patients are refractory with these therapies and 10-30% will relapse after achieving initial remission.[4] 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.

NICE technology appraisal guidance 524 recommends brentuximab vedotin 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 technology appraisal guidance 462 also recommends nivolumab as an option for treating relapsed or refractory classical Hodgkin lymphoma in adults after autologous stem cell transplant and treatment with brentuximab vedotin. However, pembrolizumab is not recommended for treating relapsed or refractory classical Hodgkin lymphoma in adults who have had autologous stem cell transplant and brentuximab vedotin (NICE technology appraisal guidance 540) but the same guidance recommends pembrolizumab for use within the Cancer Drugs Fund as an option for treating relapsed or refractory classical Hodgkin lymphoma in adults who have had brentuximab vedotin and cannot have autologous stem cell transplant.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised, anti-programmed 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 people with relapsed or refractory Hodgkin lymphoma who have received an autologous stem cell transplant or after at least one prior therapy when autologous stem cell transplant is not a treatment option. It does have a marketing authorisation for adults with relapsed or refractory classical Hodgkin lymphoma who have failed autologous stem cell transplant and brentuximab vedotin, or who are transplant ineligible and have failed brentuximab vedotin. It has been studied in an open label, randomised phase 3 study, in adults with relapsed or refractory Classical Hodgkin Lymphoma comparing pembrolizumab with brentuxumab vedotin. It has also been studied in a single arm study in adults with relapsed or refractory Hodgkin Lymphoma and a single arm study in children with solid cancers and with PD-L1-positive relapsed or refractory Hodgkin lymphoma.

Intervention	Pembrolizumab
Population(s)	People with relapsed or refractory classical Hodgkin lymphoma who have received: • autologous stem cell transplant or • at least one prior therapy when autologous stem cell transplant is not a treatment option
Comparators	• Brentuximab vedotin For people who did not have *at least two* prior therapies when autologous stem cell transplant is not a treatment option • Chemotherapy regimens

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • proportion receiving subsequent stem cell transplant • 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 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. If the evidence allows the following subgroups may be considered • people who could have a subsequent stem cell transplant (autologous or allogeneic) if they respond to treatment • people for whom stem cell transplant is contraindicated because of comorbidities
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma (2018) NICE technology appraisal guidance 540. Review date July 2022. Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma (2018) NICE technology appraisal 524.

	Review date June 2021. Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma (2017) NICE technology appraisal 462. Review date July 2020. Appraisals in development (including suspended appraisals) Brentuximab vedotin for untreated advanced Hodgkin lymphoma [1258] NICE technology appraisal guidance Publication date to be confirmed. Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma after autologous stem cell transplant [ID1103] NICE technology appraisal guidance suspended. Related Guidelines: Haematological cancers: improving outcomes' (2016) NICE guideline NG47. Review date May 2019.
Related National Policy	NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 105, Specialist Cancer services (adults) Department of Health (2016) NHS Outcomes Framework 2016-2017. Domains 1 and 2.

References

1. Lymphoma Action (2019) Hodgkin lymphoma

2.Office for national statistics (2019) Cancer registration statistics, England: 2017

3. Cancer Research UK (2019) Hodgkin lymphoma statistics .

4. Quddus, F and Armitage, J O (2009) Salvage Therapy for Hodgkin's Lymphoma. Cancer Journal Vol 15 (2) :161-3