NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma after multi-agent chemotherapy

Draft scope

Draft 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 304 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. 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.

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 two prior therapies when autologous stem cell transplant or multi-agent chemotherapy 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.

Intervention	Pembrolizumab
Population(s)	People with relapsed or refractory classical Hodgkin lymphoma who have received: • autologous stem cell transplant or • two prior therapies when autologous stem cell transplant or multi-agent chemotherapy is not a treatment option • if they previously received brentuximab vedotin, they had a complete or partial response to it
Comparators	• Brentuximab vedotin

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.

Questions for consultation

Is the population for this appraisal clearly defined?

Which treatments are considered to be established clinical practice in the NHS for people with relapsed or refractory classical Hodgkin lymphoma who have had a autologous stem cell transplant (ASCT) or are not suitable for ASCT and/or multi-agent chemotherapy?

Are the outcomes listed appropriate?

Are there any other subgroups of people in whom pembrolizumab 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 pembrolizumab is/are/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 pembrolizumab 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 pembrolizumab 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.

References

1. Lymphoma Action (2019) Hodgkin lymphoma

2.Office for national statistics (2016) Cancer registration statistics, England: 2014.

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