NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma after brentuximab vedotin [review of TA540]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for treating relapsed or refractory classical Hodgkin lymphoma after brentuximab vedotin.

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[1]. Classical Hodgkin lymphomas contain the Reed–Sternberg cells (which are cancerous B lymphocyte cells). Nodular lymphocyte-predominant lymphoma contains lymphocyte-predominant cells, a variant of Reed–Sternberg cells[1]. Reed–Sternberg cells typically express integral membrane antigen CD30[2]. The most common symptom of Hodgkin lymphoma is often swelling of the lymph nodes in the neck, armpit or groin[3]. Other symptoms include recurring fever, night sweats, weight loss, cough, breathlessness, abdominal pain, and itching.

Around 2,100 people are diagnosed with Hodgkin lymphoma each year in the UK, and over 300 people die from Hodgkin lymphoma each year[1,4]. In England, there were 1,802 people diagnosed with Hodgkin lymphoma and 275 registered deaths from Hodgkin lymphoma in 2017[5]. 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[4].

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[6]. 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. 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 does recommend 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. NICE technology appraisal guidance 772 recommends pembrolizumab as an option for treating relapsed or refractory classical Hodgkin lymphoma in people aged 3 and older, if they have had an autologous stem cell transplant that has not worked or they have had at least 2 previous therapies and an autologous stem cell transplant is not an option, and only if they have not had brentuximab vedotin.

This review of technology appraisal guidance 540 only covers the population eligible for treatment according to that guidance; that is, adults who have had brentuximab vedotin and cannot have autologous stem cell transplant.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) has a UK marketing authorisation for the treatment of adult and paediatric patients aged 3 years and older with relapsed or refractory classical Hodgkin lymphoma who have failed autologous stem cell transplant (ASCT) or following at least two prior therapies when ASCT is not a treatment option.

Intervention(s)	Pembrolizumab
Population(s)	People with relapsed or refractory classical Hodgkin lymphoma who have had brentuximab vedotin and cannot have autologous stem cell transplant.
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. • time to allogeneic stem cell transplantation

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 commercial arrangements for the intervention, comparator and subsequent treatment 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	**Related technology appraisals:** Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma after stem cell transplant or at least 2 previous therapies (2022) NICE technology appraisal guidance 772 Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma (2018) NICE technology appraisal guidance 540. Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma (2018) NICE technology appraisal 524. Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma (2017) NICE technology appraisal 462. Brentuximab vedotin for untreated advanced Hodgkin lymphoma [terminated appraisal] (2019) NICE technology appraisal guidance 594 Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma after autologous stem cell transplant [ID1103] NICE technology appraisal guidance suspended. **Related NICE guidelines:** Haematological cancers: improving outcomes (2016) NICE guideline NG47.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019) Chapter 105. Specialist cancer services (adults)

	NHS England (2020) Clinical Commissioning Policy Statement: Bendamustine for relapsed/refractory classical Hodgkin lymphoma (all ages) [1828] [Publication reference: 200701P] NHS England (2018) B15/S/a 2013/14 NHS standard contract for cancer: chemotherapy (adult). Section B Part 1 - Service specifications

References

1. Lymphoma Action (2022). Hodgkin lymphoma. Accessed 17 May 2023.

2. Haluska, F, Brufsky, A and Canellos, G (1994). The Cellular Biology of the Reed–Sternberg Cell. Blood Vol 84 (4): 1,005-1,019.

3. Cancer Research UK (2020). Hodgkin lymphoma: Symptoms. Accessed 17 May 2023.

4. Cancer Research UK. Hodgkin lymphoma statistics. Accessed 17 May 2023.

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

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