NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma after 2 or more systemic therapies (CDF review of TA559)

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of axicabtagene ciloleucel within its marketing authorisation for treating relapsed or refractory diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma after 2 or more lines of systemic therapy.

Background (not updated from TA559)

Lymphomas are cancers of the lymphatic system, which is a part of the immune system. Lymphomas are divided into Hodgkin lymphoma and non-Hodgkin lymphoma. Non-Hodgkin lymphomas (NHL) are a diverse group of conditions which are categorised according to the cell type affected (B-cell or T-cell), as well as the clinical features and rate of progression of the disease.

The most common B-cell lymphomas are follicular lymphoma (FL) which is a slow growing, low grade form of NHL and diffuse large B-cell lymphomas (DLBCL), a fast growing ('aggressive'), high grade form of NHL. Some FL will transform into high grade DLBCL (transformed high grade FL). Primary mediastinal large B-cell lymphoma (PMBCL) is a rare type of NHL which develops in the mediastinum. The symptoms differ depending on what organ or tissues the lymphoma is affecting. NHL often presents as painless lumps (enlarged lymph nodes) in the neck, armpit or groin but sometimes may start in other parts of the body such as the stomach or bowel (extranodal disease). People may also have loss of appetite, tiredness or night sweats.

There were around 11,690 new cases of non-Hodgkin lymphoma (NHL) in England in 2015 with 6,322 of these DLBCL[1]. Approximately 3% of lymphomas in the UK are PMBC[2]L and 10-70% of low grade lymphomas transform into a high grade form[2,3] Most people diagnosed with DLBCL are 65 or over[4]. 5-year survival rates for DLBCL are around 65-70% for stage 1 and 2 and around 50% at stages 3 and 4[5].

The most widely used first-line treatment for DLBCL (including transformed follicular lymphoma and primary mediastinal (thymic) large B-cell lymphoma), is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone). Sometimes etoposide is added to this regimen. NICE guideline NG52 recommends salvage therapy with rituximab in combination with chemotherapy for relapsed or refractory disease followed by stem cell transplantation. If stem cell transplantation is not suitable chemotherapy or immunotherapy may be used alone.

NICE technology appraisal 306 recommends pixantrone monotherapy for people who have multiply relapsed, been treated previously with rituximab and are on the third or fourth line of treatment.

The technology

Axicabtagene ciloleucel (Yescarta, Kite, a Gilead company) is a type of immunotherapy that uses autologous T cells directed against the tumour antigen CD19. It is administered intravenously.

Axicabtagene ciloleucel has a marketing authorisation for the treatment of adults with relapsed or refractory DLBCL and PMBCL, after two or more lines of systemic therapy

Table not updated from TA559

Intervention(s)	Axicabtagene ciloleucel
Population(s)	Adults with relapsed or refractory diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma.
Comparators	• DHAP, cisplatin, cytarabine, dexamethasone (with or without rituximab) • GDP, cisplatin, gemcitabine, dexamethasone (with or without rituximab) • ICE, ifosfamide, carboplatin, etoposide (with or without rituximab) • IVE, ifosfamide, epirubicin and etoposide (with or without rituximab) • pixantrone monotherapy (in people who have had 2 of more prior therapies, including rituximab) • best supportive care (including radiotherapy).
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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention 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: 'Pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma' (2014). NICE Technology Appraisal 306. Review date to be confirmed. Related Guidelines: Haematological cancers: improving outcomes (2016) NICE guideline 47. Non-Hodgkin's lymphoma: diagnosis and management (2016) NICE guideline 52. Review date to be confirmed. Non-Hodgkin's lymphoma: rituximab subcutaneous injection (2014) NICE evidence summary 46.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 105 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1-5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1. Office for National Statistics. Cancer Registration Statistics, England, 2017. Office of National Statistics. Accessed January 2022.

2. Low grade NHL. Cancer research UK. Accessed November 2017.

3. Diffuse B-cell lymphoma. Lymphoma association. Accessed November 2017.

4. Survival for high grade lymphomas. Cancer Research UK. Accessed November 2017.