

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma, mediastinal B-cell lymphoma and follicular lymphoma

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, primary mediastinal large B-cell lymphoma or transformed follicular lymphoma.

Background

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 DLBCL¹. Approximately 3% of lymphomas in the UK are PMBCL and 10-70% of low grade lymphomas transform into a high grade form^{2,3}. Most people diagnosed with DLBCL are 65 or over⁴. 5-year survival rates for DLBCL are around 65-70% for stage I and II and around 50% at stages III and IV⁵.

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 CG52 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 TA306 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 does not currently have a marketing authorisation in the UK for treating relapsed or refractory diffuse large B-cell non-Hodgkin lymphoma primary mediastinal large B-cell lymphoma or transformed follicular lymphoma. It has been studied in a single-arm open-label study in adults with relapsed or refractory diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma or transformed follicular lymphoma.

Intervention(s)	Axicabtagene ciloleucel
Population(s)	Adults with relapsed or refractory diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma or transformed follicular lymphoma.
Comparators	<ul style="list-style-type: none"> • 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	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.</p> <p>The availability and cost of biosimilar products of should be taken into account.</p>
Other considerations	<p>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.</p>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>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.</p> <p>Related Guidelines:</p> <p>Haematological cancers: improving outcomes (2016) NICE guideline NG47.</p> <p>Non-Hodgkin's lymphoma: diagnosis and management (2016) NICE guideline NG52. Next review date July 2018.</p>

	<p>Non-Hodgkin's lymphoma: rituximab subcutaneous injection (2014) NICE evidence summary of new medicines 46.</p> <p>Related NICE Pathways:</p> <p>Blood and bone marrow cancers (last updated May 2016) NICE pathway.</p>
<p>Related National Policy</p>	<p>National Service Frameworks</p> <p>Cancer</p> <p>Other policies</p> <p>Department of Health (2016) NHS outcomes framework 2016 to 2017</p> <p>Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020</p> <p>Department of Health (2014) The national cancer strategy: 4th annual report</p> <p>Department of Health (2011) Improving outcomes: a strategy for cancer</p> <p>Department of Health (2009) Cancer commissioning guidance</p> <p>Department of Health (2007) Cancer reform strategy</p>

References

1. [Office for National Statistics. Cancer Registration Statistics, England, 2015](#). Office of National Statistics. Accessed November 2017.
2. [High grade NHL. Cancer research UK](#). Accessed November 2017.
3. [Low grade NHL. Cancer research UK](#). Accessed November 2017.
4. [Diffuse B-cell lymphoma](#). Lymphoma association. Accessed November 2017.
5. [Survival for high grade lymphomas](#). Cancer Research UK. Accessed November 2017.