

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Evaluation

### Epcoritamab for treating relapsed or refractory large B-cell lymphoma after 2 or more systemic treatments

#### Final scope

#### Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of epcoritamab within its marketing authorisation for treating relapsed or refractory large B-cell 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 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, a slow growing, low grade form of NHL, and diffuse large B-cell lymphoma (DLBCL), a fast growing, high grade form of NHL. Some follicular lymphomas transform into high grade DLBCL (transformed high grade follicular lymphoma). The symptoms differ depending on which organ or tissues are affected by the lymphoma. NHL often presents as painless lumps (enlarged lymph nodes) in the neck, armpit or groin but it can start in other parts of the body such as the stomach or bowel (extranodal disease). People may have loss of appetite, tiredness or night sweats.

There were around 10,710 people diagnosed with NHL in England in 2020.<sup>1</sup> It is estimated that about 40% of people with NHL have DLBCL<sup>2</sup>. In 2020, 4209 people had DLBCL<sup>1</sup>. Most people diagnosed with DLBCL are 65 or over.<sup>3</sup> Although most people are cured with first-line chemotherapy, about 10-15% have primary refractory disease and a further 20-30% relapse.<sup>4</sup> Survival rates at 5 years for DLBCL are around 60%<sup>5</sup>

The most widely used first-line treatment for DLBCL is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone). Sometimes etoposide is added to this regimen. For relapsed or refractory disease after 1 systemic therapy, [NICE guideline NG52](#) recommends a multi-agent chemotherapy, potentially in combination with rituximab, followed by stem cell transplantation for people who are fit enough to have it. Chemotherapy regimens commonly used in clinical practice include DHAP (dexamethasone, cytarabine, cisplatin), GDP (gemcitabine, dexamethasone, cisplatin), ICE (ifosfamide, carboplatin, etoposide) and IVE (ifosfamide, etoposide, epirubicin).

If stem cell transplantation is not suitable, further chemotherapy, with or without immunotherapy, may be used. [NICE technology appraisal \(TA649\)](#) recommends polatuzumab vedotin with rituximab and bendamustine for relapsed or refractory DLBCL in adults who cannot have stem cell transplantation. [NICE technology appraisal \(TA306\)](#) recommends pixantrone monotherapy for people who have relapsed or refractory aggressive non-Hodgkin B-cell lymphoma, when they have

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received previous treatment with rituximab and are in the third or fourth line of treatment. [NICE technology appraisal \(TA559\)](#) recommends axicabtagene ciloleucel therapy for use within the Cancer Drugs Fund as an option for treating relapsed or refractory DLBCL in adults after 2 or more systemic therapies. [NICE technology appraisal \(TA567\)](#) recommends tisagenlecleucel therapy for use within the Cancer Drugs Fund as an option for treating relapsed or refractory DLBCL after 2 or more systemic therapies.

### The technology

Epcoritamab (DuoBody-CD3Xcd20, AbbVie) does not currently have a marketing authorisation in the UK for treating relapsed or refractory DLBCL. Epcoritamab is being studied in a single arm phase Ib/II clinical trial in people with relapsed or refractory LBCL who have received two or more lines of systemic therapy. Epcoritamab is also being studied in a phase III clinical trial, compared to chemotherapy, in people with relapsed or refractory LBCL and whose disease did not respond to or who are not eligible for autologous stem cell transplant.

<b>Intervention</b>	Epcoritamab
<b>Population</b>	Adults with relapsed or refractory large B-cell lymphoma who have had 2 or more systemic treatments
<b>Comparators</b>	<p>Established clinical management without epcoritamab including but not limited to:</p> <ul style="list-style-type: none"> <li>• Salvage chemoimmunotherapy with rituximab: <ul style="list-style-type: none"> <li>○ DHAP (dexamethasone, cytarabine, cisplatin)</li> <li>○ ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin)</li> <li>○ GDP (gemcitabine, dexamethasone, cisplatin)</li> <li>○ GEMOX (gemcitabine and oxaliplatin)</li> <li>○ ICE (ifosfamide, carboplatin, etoposide)</li> <li>○ IVE (ifosfamide, etoposide, epirubicin)</li> </ul> </li> <li>• Pixantrone</li> <li>• Polatuzumab vedotin with rituximab and bendamustine (only when stem cell transplantation is not suitable)</li> <li>• Axicabtagene ciloleucel for treating refractory or relapsed DLBCL after 2 or more systemic therapies (subject to NICE appraisal process)</li> <li>• Tafasitamab with lenalidomide (only when stem cell transplantation is unsuitable and subject to NICE appraisal process)</li> </ul>

<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rates</li> <li>• adverse effects of treatment</li> <li>• time on treatment</li> <li>• health-related quality of life</li> </ul>
<b>Economic analysis</b>	<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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>
<b>Other considerations</b>	<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>
<b>Related NICE recommendations</b>	<p><b>Related Technology Appraisals:</b></p> <p><a href="#">‘Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma’</a> (2020) NICE Technology appraisal guidance TA649</p> <p><a href="#">‘Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma after 2 or more systemic therapies’</a> (2019) NICE Technology appraisal guidance TA559</p> <p><a href="#">‘Tisagenlecleucel for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies’</a> (2019) NICE Technology appraisal guidance TA567</p> <p><a href="#">‘Pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin’s B-cell lymphoma’</a> (2014). NICE Technology appraisal guidance TA306. Review date November 2016.</p>

	<p><b>Related appraisals in development:</b></p> <p><a href="#">‘Tafasitamab with lenalidomide for treating relapsed or refractory diffuse large B-cell lymphoma’</a> NICE Technology appraisals [ID3795]. Publication expected to be confirmed.</p> <p><a href="#">‘Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma after 2 or more systemic therapies’</a> (CDF review of TA559) [ID3980]. Publication expected February 2023.</p> <p><a href="#">‘Axicabtagene ciloleucel for treating relapsed or refractory diffuse large B-cell lymphoma after 1 systemic therapy’</a> NICE Technology appraisals [ID1684]. Publication expected to be confirmed.</p> <p><a href="#">‘Glofitamab for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies’</a> NICE Technology appraisals [ID3970]. Publication October 2023</p> <p><a href="#">‘Loncastuximab tesirine for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies’</a> NICE Technology appraisals [ID3943]. Publication expected November 2023.</p> <p><a href="#">‘Lisocabtagene maraleucel for treating relapsed or refractory aggressive B-cell non-Hodgkin lymphoma after 1 systemic treatment’</a> NICE Technology appraisals [ID3869]. Publication date to be confirmed.</p> <p><b>Related Guidelines:</b></p> <p><a href="#">‘Non-Hodgkin’s lymphoma: diagnosis and management’</a> (2016). NICE Guideline NG52. Review date to be confirmed.</p> <p><a href="#">‘Haematological cancers: improving outcomes’</a> (2016). NICE Guideline 47. Review date to be confirmed.</p> <p><a href="#">Non-Hodgkin’s lymphoma: rituximab subcutaneous injection (2014)</a> NICE evidence summary of new medicines 46.</p> <p><b>Related Quality Standards:</b></p> <p>Haematological cancers (2017) <a href="#">NICE quality standard 150</a>.</p>
<p><b>Related National Policy</b></p>	<p>The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2018/2019) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a></p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 to 5. <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a></p>

## References

1. Office for National Statistics. [Cancer registration statistics, England](#). 2020. Accessed January 2023.
2. Cancer Research UK. [Diffuse large B cell lymphoma](#). Accessed October 2022.
3. Lymphoma association. [Diffuse B-cell lymphoma](#). Accessed October 2022.
4. Chaganti S, Illidge T, Barrington S, McKay P, Linton K, Cwynarski K, et al. Guidelines for the management of diffuse large B-cell lymphoma. *British journal of haematology*. 2016;174(1):43-56. Available from: <https://doi.org/10.1111/bjh.14136>
5. Cancer Research UK. [Non-Hodgkin lymphoma- Survival](#). Accessed October 2022.