NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Epcoritamab for treating relapsed or refractory diffuse large B-cell lymphoma when a stem cell transplant has failed or is unsuitable

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of epcoritamab within its marketing authorisation for treating relapsed or refractory diffuse large B-cell lymphoma when a stem cell transplant has failed or is unsuitable.

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 12,065 people diagnosed with NHL in England in 2017.[1] It is estimated that about 40% of people with NHL have DLBCL,[2] which would equate to 4,826 registrations of DLBCL per year.

Most people diagnosed with DLBCL are 65 or over.[3] Although most people are cured with first-line chemotherapy, about 10-15% have primary refractory disease and a further 20-30% relapse.[4] Survival rates at 5 years for DLBCL are around 65-70% for stage I and II and around 50% at stages III and IV (people diagnosed between 2004 and 2011).[5]

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

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appraisal (TA306) recommends pixantrone monotherapy for people who have relapsed or refractory aggressive non-Hodgkin B-cell lymphoma, when they have 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 tisgenlecleucel therapy for use within the Cancer Drugs Fund as an option for treating relapsed of 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 phase III clinical trial, compared to chemotherapy, in people with relapsed or refractory DLBCL and whose disease did not respond to or who or are not eligible for autologous stem cell transplant.

Intervention	Epcoritamab
Population	Adults with relapsed or refractory diffuse large B-cell lymphoma after 1 systemic therapy

Comparators	Established clinical management without epcoritamab including but not limited to:
	• Salvage chemotherapy with or without rituximab:
	  ○ DHAP (dexamethasone, cytarabine, cisplatin)
	  ○ ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin)
	  ○ GDP (gemcitabine, dexamethasone, cisplatin)
	  ○ GEMOX (gemcitabine and oxaliplatin)
	  ○ ICE (ifosfamide, carboplatin, etoposide)
	  ○ IVE (ifosfamide, etoposide, epirubicin)
	• Pixantrone
	• Polatuzumab vedotin with rituximab and bendamustine (only when stem cell transplantation is not suitable)
	• Axicabtagene ciloleucel for treating refractory or relapsed DLBCL after 2 or more systemic therapies (subject to NICE appraisal process)
	• Tafasitamab with lenalidomide (only when stem cell transplantation is unsuitable and subject to NICE appraisal process)

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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.
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:** 'Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma' (2020) NICE Technology appraisal guidance TA649 'Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma after 2 or more systemic therapies' (2019) NICE Technology appraisal guidance TA559 'Tisagenlecleucel for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies' (2019) NICE Technology appraisal guidance TA567 'Pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma' (2014). NICE Technology appraisal guidance TA306. Review date November 2016. **Related appraisals in development:**

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	'Tafasitamab with lenalidomide for treating relapsed or refractory diffuse large B-cell lymphoma' NICE Technology appraisals [ID3795]. Publication expected October 2022. '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) [ID3980]. Publication expected November 2022. 'Axicabtagene ciloleucel for treating relapsed or refractory diffuse large B-cell lymphoma after 1 systemic therapy' NICE Technology appraisals [ID1684]. Publication expected January 2023. 'Glofitamab for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies' NICE Technology appraisals [ID3970]. Publication date to be confirmed 'Loncastuximab tesirine for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies' NICE Technology appraisals [ID3943]. Publication expected November 2023. 'Lisocabtagene maraleucel for treating relapsed or refractory aggressive B-cell non-Hodgkin lymphoma after 1 systemic treatment' NICE Technology appraisals [ID3869]. Publication date to be confirmed. **Related Guidelines:** 'Non-Hodgkin's lymphoma: diagnosis and management' (2016). NICE Guideline NG52. Review date to be confirmed. 'Haematological cancers: improving outcomes' (2016). NICE Guideline 47. Review date to be confirmed. Non-Hodgkin's lymphoma: rituximab subcutaneous injection (2014) NICE evidence summary of new medicines 46. **Related Quality Standards:** Haematological cancers (2017) NICE quality standard 150.
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) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 to 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

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Questions for consultation

Where do you consider epcoritamab will fit into the existing care pathway for DLBCL?

Would epcoritamab be a candidate for managed access?

Do you consider that the use of epcoritamab can result in any potential 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 committee to take account of these benefits.

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 epcoritamab 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Office for National Statistics. Cancer registration statistics, England. 2019. Accessed October 2022.

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.

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