

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Loncastuximab tesirine for treating relapsed or refractory diffuse large B-cell lymphoma and high-grade B-cell lymphoma after 2 or more systemic therapies

Final scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of loncastuximab tesirine within its marketing authorisation for treating relapsed or refractory diffuse large B-cell lymphoma and high-grade B-cell lymphoma after 2 or more systemic therapies

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. High-grade NHL is an aggressive, fast-growing form of the disease.

The most common B-cell lymphomas are follicular lymphoma which is a slow growing, low grade form of NHL and diffuse large B-cell lymphomas (DLBCL), a fast growing, high grade NHL. Some FLs transform into high grade DLBCL (transformed high grade FL). There are also other forms of high grade B-cell lymphomas.¹

There were 11,788 people diagnosed with NHL in England in 2019.² It is estimated that around 40% of NHL cases are DLBCL, which would equate to 4,715 cases of DLBCL in 2019.³ DLBCL is more common in men than women and most cases are diagnosed in people aged 65 years or older^{3,4}. Around 60% of people will survive 5 years or more following a diagnosis of DLBCL.⁵ Although most patients are cured with first-line chemotherapy, about 10-15% have primary refractory disease and a further 20-30% relapse.

NICE guideline [NG52](#) recommends multi-agent chemotherapy in combination with rituximab for relapsed or refractory disease, potentially followed by stem cell transplantation for people 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 or immunotherapy may be used alone.

For people with relapsed or refractory DLBCL, NICE recommends:

- [NICE technology appraisal 306](#) recommends pixantrone monotherapy for people who have multiply relapsed or refractory aggressive non-Hodgkin B-cell lymphoma, when they have been treated previously with rituximab and are receiving third- or fourth-line treatment.

Final scope for the evaluation of loncastuximab tesirine for treating relapsed or refractory diffuse large B-cell lymphoma and high-grade B-cell lymphoma after 2 or more systemic therapies

- [NICE technology appraisal 649](#) recommends polatuzumab vedotin with rituximab and bendamustine for relapsed or refractory DLBCL in adults who cannot have a haematopoietic stem cell transplant.
- NICE technology appraisals [559](#) and [567](#) recommend axicabtagene ciloleucel and tisagenlecleucel therapy for use within the Cancer Drugs Fund respectively for relapsed or refractory DCBCL after two or more systemic therapies

The technology

Loncastuximab tesirine (Zynlonta, Swedish Orphan Biovitrum) does not currently have a marketing authorisation in the UK for the treatment of diffuse large B-cell lymphoma and high-grade lymphoma. Loncastuximab tesirine has been studied in clinical trials alone, in people with relapsed or refractory large B-cell lymphoma.

Intervention(s)	Loncastuximab tesirine
Population(s)	Adults with relapsed or refractory diffuse large B-cell lymphoma and high-grade B-cell lymphoma who have had two or more systemic therapies
Comparators	<p>Established clinical management which may include:</p> <ul style="list-style-type: none"> • Chemotherapy, with or without rituximab, such as: <ul style="list-style-type: none"> ○ DHAP (cisplatin, cytarabine, dexamethasone) ○ GDP (cisplatin, gemcitabine, dexamethasone) ○ ICE (ifosfamide, carboplatin, etoposide) ○ IVE (ifosfamide, epirubicin and etoposide) ○ R-GemOx (rituximab, gemcitabine oxaliplatin) ○ BR (bendamustine, rituximab) • polatuzumab vedotin with rituximab and bendamustine (for DLBCL if haematopoietic stem cell transplantation is not possible) • pixantrone • axicabtagene ciloleucel (subject to NICE evaluation) • tafasitamab with lenalidomide (if haematopoietic stem cell transplantation is not possible, subject to NICE evaluation)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rates • 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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and costs of biosimilar and generic products 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	<p>Related Technology Appraisals:</p> <p>Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma (2020) NICE Technology Appraisal 649. Review date: 2023</p> <p>Tisagenlecleucel for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies (2019) NICE Technology Appraisal 567. Under review</p> <p>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 559. Under review</p> <p>Pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma (2014, Reviewed March 2021) NICE Technology Appraisal 306. Review date TBC</p> <p>Tafasitamab with lenalidomide for treating relapsed or refractory diffuse large B-cell lymphoma (2022) NICE Technology Appraisal ID3795. Review date TBC</p> <p>Appraisals in development:</p> <p>Glofitamab for treating relapsed or refractory B-cell lymphoma NICE technology appraisals guidance [ID3970] Publication date TBC</p> <p>Related Guidelines:</p> <p>Non-Hodgkin's lymphoma: diagnosis and management</p>

	<p>(2016) NG52, section 1.6.</p> <p>Haematological cancers: improving outcomes (2016) NICE guideline 47.</p> <p>Related Interventional Procedures:</p> <p>None</p> <p>Related Public Health Guidance/Guidelines:</p> <p>None</p> <p>Related Quality Standards:</p> <p>Haematological cancers (2017) NICE quality standard 150</p>
Related National Policy	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 105: Specialist cancer services (adults).</p>

References

1. Cancer Research UK, [High grade NHL](#) (accessed November 2022)
2. NHS Digital. [Cancer Registration Statistics, England 2019](#). (2021) Accessed February 2022. (accessed October 2022)
3. 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.
4. Cancer Research UK, [Diffuse large B-cell lymphoma](#) (accessed October 2022)
5. Cancer Research UK, [Survival: non-Hodgkin lymphoma](#) (accessed October 2022)