NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of loncastuximab tesirine for treating relapsed or refractory diffuse large 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. 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, high grade form of NHL. Some FLs transform into high grade DLBCL (transformed high grade FL). 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 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 11,788 people diagnosed with NHL in England in 2019.[1] It is estimated that around 40% of NHL cases are DLBCL, which would equate to 4,715 cases of DLBCL in 2019.[2] DLBCL is more common in men than women and most cases are diagnosed in people aged 65 years or older[2,3]. Around 60% of people will survive 5 years or more following a diagnosis of DLBCL.[4]

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.

- 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 relapse 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. 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 who have had two or more systemic therapies

Comparators	Established clinical management which may include:
	• Chemotherapy, such as:
	  ○ DHAP (cisplatin, cytarabine, dexamethasone)
	  ○ GDP (cisplatin, gemcitabine, dexamethasone)
	  ○ ICE (ifosfamide, carboplatin, etoposide)
	  ○ IVE (ifosfamide, epirubicin and etoposide)
	• polatuzumab vedotin with rituximab and bendamustine (if haematopoietic stem cell transplantation is not possible)
	• pixantrone
	• axicabtagene ciloleucel (subject to NICE evaluation)

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 and costs of biosimilar and generic products should 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 649. Review date: 2023 Tisagenlecleucel for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies (2019) NICE Technology Appraisal 567. Under review 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 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 Tafasitamab with lenalidomide for treating relapsed or refractory diffuse large B-cell lymphoma (2022) NICE Technology Appraisal ID3795. Review date TBC **Appraisals in development:** Glofitamab for treating relapsed or refractory B-cell lymphoma NICE technology appraisals guidance [ID3970] Publication date TBC **Related Guidelines:** Non-Hodgkin's lymphoma: diagnosis and management

	(2016) NG52, section 1.6. Haematological cancers: improving outcomes (2016) NICE guideline 47. **Related Interventional Procedures:** None **Related Public Health Guidance/Guidelines:** None **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). Chapter 105: Specialist cancer services (adults).

Questions for consultation

Have all the relevant comparators for loncastuximab tesirine been included in the scope? Which treatments are considered to be established clinical practice in the NHS for relapsed or refractory DLBCL after 2 or more systemic therapies?

Are the outcomes listed appropriate?

Would loncastuximab tesirine be a candidate for managed access?

Do you consider that the use of loncastuximab tesirine 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 loncastuximab tesirine 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. NHS Digital. Cancer Registration Statistics, England 2019. (2021) Accessed February 2022. (accessed October 2022)

2. 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.

3. Cancer Research UK, Diffuse large B-cell lymphoma (accessed October 2022)

4. Cancer Research UK, Survival: non-Hodgkin lymphoma (accessed October 2022)