NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Axicabtagene ciloleucel for treating relapsed or refractory diffuse large B-cell lymphoma after 1 systemic therapy

Draft scope

Draft 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.

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 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 patients 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 (patients 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 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 or immunotherapy may be used alone. NICE TA649 recommends polatuzumab vedotin with rituximab and bendamustine for relapsed or refractory DLBCL in adults who cannot have stem cell transplantation.

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 has a marketing authorisation for treating relapsed or refractory diffuse large B-cell non-Hodgkin lymphoma and primary mediastinal large B-cell lymphoma, after 2 or more lines of systemic therapy. It does not currently have a marketing authorisation in the UK for treating relapsed or refractory diffuse large B-cell non-Hodgkin lymphoma after 1 systemic therapy. It has been studied in a clinical trial in adults with relapsed or refractory DLBCL compared with standard care (defined as the investigators choice of second-line salvage chemotherapy).

Intervention(s)	Axicabtagene ciloleucel
Population(s)	Adults with relapsed or refractory diffuse large B-cell lymphoma after 1 systemic therapy

Comparators	Established clinical management without axicabtagene ciloleucel including but not limited to:
	• salvage chemotherapy with or without rituximab, such as:
	  ○ 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)
	• polatuzumab vedotin with rituximab and bendamustine (only for people not suitable for transplant)
	• tafasitamab with lenalidomide (subject to NICE appraisal)

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 of any managed access arrangement for the intervention 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 and NICE Pathways	**Related Technology Appraisals:**'Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma' NICE Technology Appraisal 649. Review date 2023. **Terminated appraisals** 'Rituximab for aggressive non-Hodgkin's lymphoma' (withdrawn appraisal – routinely used outside its licensed indication in clinical practice) (2003). NICE Technology Appraisal 65. **Appraisals in development (including suspended appraisals)** 'Axicabtagene ciloleucel for treating relapsed or refractory low-grade non-Hodgkin lymphoma' NICE technology appraisals guidance [ID1685]. Expected publication date to be confirmed. 'Tafasitamab with lenalidomide for treating relapsed or refractory diffuse large B-cell lymphoma' NICE technology appraisals guidance [ID3795]. Expected publication date August 2022. 'Nivolumab for treating relapsed or refractory diffuse large B-cell lymphoma' NICE technology appraisals guidance [ID986]. Suspended – company advised that they would not be seeking regulatory approval from the European Medicines Authority for this indication. **Related Guidelines:** 'Non-Hodgkin's lymphoma: diagnosis and management'

	(2016) NICE Guideline 52. 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 NICE Pathways:** Blood and bone marrow cancers (2016) NICE pathway
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. 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

Questions for consultation

Have all relevant comparators for axicabtagene ciloleucel (as a second-line treatment option for DLBCL) been included in the scope?

- What salvage chemotherapy regimens are used in clinical practice as a second-line treatment?
- Is polatuzumab vedotin with rituximab and bendamustine an appropriate comparator for axicabtagene ciloleucel?
- Is ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin) used as a second-line treatment in clinical practice in the NHS in England?
- Are any other treatments used currently as a second-line treatment option?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom axicabtagene ciloleucel is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider axicabtagene ciloleucel will fit into the existing NICE pathway, Blood and bone marrow cancers?

- Do you expect axicabtagene ciloleucel to be positioned for both patients suitable and unsuitable for high-dose chemotherapy and stem cell transplantation?

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 axicabtagene ciloleucel 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.

Do you consider axicabtagene ciloleucel to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of axicabtagene ciloleucel can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Office for National Statistics. Cancer registration statistics, England. 2019. Accessed October 2021.

2. Cancer Research UK. Diffuse large B cell lymphoma. Accessed October 2021.

3. Lymphoma association. Diffuse B-cell lymphoma. Accessed October 2021.

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 March 2021.