Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Lisocabtagene maraleucel for treating relapsed or refractory diffuse large B-cell lymphoma, high grade B-cell lymphoma, primary mediastinal large B-cell lymphoma or follicular lymphoma grade 3B after first-line chemotherapy

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of lisocabtagene maraleucel within its marketing authorisation for treating relapsed or refractory diffuse large B-cell lymphoma, high grade B-cell lymphoma, primary mediastinal large B-cell lymphoma or follicular lymphoma grade 3B after 1 prior therapy.

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.

Large B-cell lymphoma (LBCL) affects B-cells. They become abnormal and grow larger than normal, forming tumours in lymph nodes or other parts of the body. The most common subtype of LBCL is diffuse large B-cell lymphoma (DLBCL). There are also other forms of LBCL such as high-grade B-cell lymphoma (HGBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B). 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 10,710 people diagnosed with NHL in England in 2020.[1] It is estimated that about 40% of people with NHL have DLBCL.[2] In 2020, 4,209 people had DLBCL.[1] 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 relapsed DLBCL are around 30%.[5] Relapsed or refractory LBCL tends to have a poorer prognosis compared with newly diagnosed.

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), GEMOX (gemcitabine and oxaliplatin) and ICE (ifosfamide, carboplatin, etoposide)). NICE technology appraisal (TA895) recommends axicabtagene ciloleucel therapy for use within the Cancer Drugs Fund as an option for treating relapsed or refractory DLBCL in adults for whom autologous stem cell transplant is suitable.

The technology

Lisocabtagene maraleucel (Breyanzi, Bristol-Myers Squibb) does not currently have a marketing authorisation in the UK for treating relapsed or refractory DLBCL, HGBCL, PMBCL or FL3B after 1 prior therapy. Lisocabtagene maraleucel is being studied in a phase 3 randomised clinical trial in people with DLBCL, HGBCL, PMBCL or FL3B, who were eligible for stem cell transplant.

It has a marketing authorisation for the treatment of adult patients with relapsed or refractory DLBCL, PMBCL and FL3B after two or more lines of systemic therapy.

Intervention	Lisocabtagene maraleucel
Population	People with relapsed or refractory aggressive B- refractory DLBCL, HGBCL, PMBCL or FL3B after 1 prior therapy
Comparators	Established clinical management without lisocabtagene maraleucel, including but not limited to: • Immunotherapy with high dose chemotherapy with or without autologous stem cell transplantation (ASCT) • Polatuzumab vedotin with rituximab and bendamustine (if haematopoietic stem cell transplant is not suitable)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • event-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:** 'Loncastuximab tesirine for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies' (2024) NICE technology appraisals 947. 'Glofitamab for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies' (2023) NICE technology appraisals guidance 927. 'Axicabtagene ciloleucel for treating relapsed or refractory diffuse large B-cell lymphoma ' (2023). NICE Technology appraisal guidance TA895. 'Tafasitamab with lenalidomide for treating relapsed or refractory diffuse large B-cell lymphoma' (2023). NICE Technology appraisal guidance TA883. 'Polatuzumab vedotin in combination for untreated diffuse large B-cell lymphoma' (2023). NICE technology appraisal guidance 874. 'Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma after 2 or more systemic therapies' (2023). NICE technology appraisal guidance 872. 'Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma' (2020). NICE technology appraisal guidance 649. 'Pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma' (2014) .NICE Technology Appraisal Guidance 306. **Related appraisals in development:** 'Epcoritamab for treating relapsed or refractory large B-cell lymphoma after 2 or more systemic treatments' NICE technology appraisal guidance [ID4045] Publication expected March 2024. **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 (2023) NHS manual for prescribed specialist services (2023) 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

References

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2. Cancer Research UK. Diffuse large B cell lymphoma. Accessed December 2023.

3. Lymphoma action. Diffuse B-cell lymphoma. Accessed December 2023.

4. Blood Cancer UK. Diffuse large B-cell lymphoma (DLBCL) prognosis. Accessed February 2024.

5. McMillan, A., Martín, A., Haioun, C., Chiappella, A., Di Rocco, A., Rueda, A., Palaska, C. and Davies, A.J. (2016). Post Relapse Survival Rates in Diffuse Large B-Cell Lymphoma. Blood, 128(22), pp.4204–4204. doi:https://doi.org/10.1182/blood.v128.22.4204.4204