**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Single Technology Appraisal**

# Tafasitamab with lenalidomide for treating relapsed or refractory diffuse large B-cell lymphoma

**Final scope**

## Final remit/appraisal objective

To appraise the clinical and cost effectiveness of tafasitamab with lenalidomide followed by tafasitamab monotherapy within its marketing authorisation for treating adults with 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 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 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 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 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 around 12,065 people diagnosed with NHL in England in 2017.[1] It is estimated that about 53% of people with NHL have DLBCL, which equates to around 6,391 people diagnosed with DLBCL per year.[1]

Most people diagnosed with DLBCL are 65 or over.[2] Although most patients are cured with first-line chemotherapy, about 10-15% have primary refractory disease and a further 20-30% relapse.[3] Survival rates at 5 years for DLBCL are around 65-70% for stage 1 and 2 and around 50% at stages 3 and 4.[4]

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. NICE guideline NG52 recommends salvage therapy, a multi-agent chemotherapy with or without rituximab, for relapsed or refractory disease in patients who are fit and eligible for subsequent stem cell transplant. 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).

There is no established clinical management for people who have co-morbidities or are not fit enough for stem cell transplant. Further chemotherapy, with or without immunotherapy, may be used. This may include R-GemOx (rituximab, gemcitabine oxaliplatin), R-Gem (rituximab gemcitabine), R-P-MitCEBO (rituximab, prednisolone,

mitoxantrone cyclophosphamide, etoposide bleomycin, vincristine), (R-)DECC (rituximab, dexamethasone, etoposide, chlorambucil, lomustine) and BR (bendamustine, rituximab).

NICE technology appraisal 306 (TA306) recommends pixantrone monotherapy for people who have multiply 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 469 (TA649) recommends polatuzumab vedotin with rituximab and bendamustine as an option for treating relapsed or refractory DLBCL in adults who cannot have a haematopoietic stem cell transplant. NICE technology appraisal 559 (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 567 (TA567) recommends tisagenlecleucel 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.

**The technology**

Tafasitamab (Minjuvi, Incyte Corp) is an investigational humanised Fc-engineered monoclonal antibody directed against CD19 antigen, a protein which is found on the surface of B-cells. It is administered by intravenous infusion.

Lenalidomide (Revlimid, Celgene) is an immunomodulator and a structural analogue of thalidomide. It has anti-neoplastic, anti-angiogenic and proerythropoeitic properties. It is administered orally.

Tafasitamab with lenalidomide followed by tafasitamab monotherapy has a European Medicines Agency conditional marketing authorisation for the treatment of adults with relapsed or refractory DLBCL who are not eligible for autologous stem cell transplant.

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| **Intervention(s)** | Tafasitamab with lenalidomide followed by tafasitamab monotherapy |
| **Population(s)** | Adults with relapsed or refractory diffuse large B-cell lymphoma and who are not eligible for have autologous stem-cell transplantation. |

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| **Comparators** | Established clinical management without tafasitamab which may include:<br>• Chemotherapy with or without rituximab:<br>  ○ R-GemOx (rituximab, gemcitabine oxaliplatin), R-Gem (rituximab gemcitabine), R-P-MitCEBO (rituximab, prednisolone, mitoxantrone cyclophosphamide, etoposide bleomycin, vincristine), (R-)DECC (rituximab, dexamethasone, etoposide, chlorambucil, lomustine), BR (bendamustine, rituximab)<br>• Pixantrone<br>• Polatuzumab vedotin in combination with bendamustine and rituximab<br>• Best supportive care |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rates<br>• adverse effects of treatment<br>• 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.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>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** | The availability and cost of biosimilar products should be taken into account.<br>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. |

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| **Related NICE recommendations and NICE Pathways** | **Related Technology Appraisals:**<br>'Pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma' (2014). NICE Technology Appraisal guidance TA306. Review date to be confirmed.<br>'Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal B-cell lymphoma and after 2 or more systemic therapies' (2019). NICE technology appraisal guidance TA559.<br>'Tisagenlecleucel-T for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies' (2019). NICE Technology Appraisal guidance 567.<br>'Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma' (2020). NICE technology appraisal guidance TA649. Review date 2023<br>**Appraisals in development (including suspended appraisals)**<br>'Lisocabtagene maraleucel for treating relapsed or refractory aggressive B-cell non-Hodgkin lymphoma' NICE technology appraisals guidance ID1444. Expected publication date to be confirmed.<br>'Nivolumab for treating relapsed or refractory diffuse large B-cell lymphoma' NICE technology appraisals guidance ID986. Suspended.<br>**Related Guidelines:**<br>'Non-Hodgkin's lymphoma: diagnosis and management' (2016) NICE Guideline 52. Review date to be confirmed.<br>'Haematological cancers: improving outcomes' (2016). NICE Guideline 47. Review date to be confirmed.<br>Non-Hodgkin's lymphoma: rituximab subcutaneous injection (2014) NICE evidence summary of new medicines 46.<br>**Related Quality Standards:**<br>Haematological cancers (2017) NICE quality standard 150.<br>**Related NICE Pathways:**<br>Blood and bone marrow cancers (2016) NICE pathway |
| **Related National Policy** | The NHS Long Term Plan, 2019. NHS Long Term Plan<br>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105<br>Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (Published 2016): Domains 1-5 |

## References


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

2. Lymphoma association. Diffuse Large B-cell lymphoma. Accessed September 2021.

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. Available from: https://doi.org/10.1111/bjh.14136

4. Cancer Research UK. Non-Hodgkin lymphoma- Survival. Accessed September 2021.