NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

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

Draft scope

Draft 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 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 (MOR208, MorphoSys AG partnered with 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.

Tafasitamab does not currently have marketing authorisation in the UK for any indication. It has been studied in combination with lenalidomide in an ongoing single-arm, open-label clinical trial in adult patients with relapsed or refractory DLBCL who have had at least one, but no more than three prior systemic treatment regimens and who are not eligible for high dose chemotherapy with autologous stem-cell transplantation.

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, or are unwilling to have, high dose chemotherapy with autologous stem-cell transplantation.

Comparators	Established clinical management without tafasitamab including but not limited to: • Chemotherapy with or without rituximab: - 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) • Pixantrone • Polatuzumab (subject to ongoing NICE appraisal) • Best supportive care
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	The availability and cost of biosimilar products should be taken into account. 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:** '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. '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. 'Tisagenlecleucel-T for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies' (2019). NICE Technology Appraisal guidance 567. **Appraisals in development (including suspended appraisals)** 'Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma' NICE technology appraisal ID1576. Expected publication date 23 September 2020 'Nivolumab for treating relapsed or refractory diffuse large B-cell lymphoma' NICE technology appraisals guidance ID986. Suspended. **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 (Published 2016): Domains 1-5

Questions for consultation

How do you define people for whom autologous stem-cell transplantation (ASCT) is not suitable?

Have all relevant comparators for tafasitamab in people with relapsed or refractory diffuse large B-cell lymphoma who are not eligible for, or are unwilling to have ASCT been included in the scope? Which treatments are considered to be established clinical practice in the NHS for treating relapsed/refractory DLBCL for people who are not eligible for ASCT?

What is the current treatment for patients who are unwilling to have ASCT (as per the pivotal clinical trial)? Does this differ to those who are not eligible for ASCT?

Would DHAP (dexamethasone, cytarabine, cisplatin), GDP (gemcitabine, dexamethasone, cisplatin), ICE (ifosfamide, carboplatin, etoposide) and IVE (ifosfamide, etoposide, epirubicin) be a relevant comparator for any patients in this population?

How should best supportive care be defined?

Are the outcomes listed appropriate?

Would you expect ASCT to be feasible after treatment with tafasitamab in this population?

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

Where do you consider tafasitamab in combination with lenalidomide will fit into the existing NICE pathway, Blood and bone marrow cancers?

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 tafasitamab in combination with lenalidomide 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 tafasitamab in combination with lenalidomide 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 tafasitamab in combination with lenalidomide 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Office for National Statistics. Cancer registration statistics, England. 2019. Accessed July 2020

2. Lymphoma association. Diffuse Large B-cell lymphoma. Accessed July 2020.

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 July 2020.